

ABSCESSTION



BASICS

DEFINITION

An abscess is a focal collection of purulent exudate within a confined tissue space or cavity.

PATHOPHYSIOLOGY

- Bacterial organisms may enter tissue by penetrating trauma, spread from another source of infection (hematogenous or adjacent infected tissues), or migration of a contaminated object (e.g., plant awn).
- Most often, bacteria are inoculated under the skin via puncture or bite wounds.
- When bacteria or foreign objects persist in tissue, purulent exudate accumulates.
- If exudate not quickly resorbed or drained, fibrous capsule forms to “wall off” infection; abscess may eventually rupture.
- With fibrous capsule—to heal, the cavity must fill with granulation tissue from which causative agent may not be totally eliminated; may lead to chronic or intermittent discharge of exudate from a draining tract.
- Sterile abscesses can occur when irritants (injectable medications, venom) or inflammatory processes (pancreatitis, immune mediated, decreased blood supply) lead to local collection of purulent exudate.

SYSTEMS AFFECTED

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

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat and dog.

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

Mammary glands (female); prostate gland (male).

SIGNS

General Comments

- Determined by organ system and/or tissue affected.
- Associated with combination of inflammation (pain, swelling, redness, heat, and loss

of function), tissue destruction, and/or organ system dysfunction caused by accumulation of exudates.

Historical Findings

- Often nonspecific signs (e.g., lethargy, anorexia).
- History of trauma or prior infection.
- Rapidly appearing painful swelling with or without discharge, if affected area is visible.

Physical Examination Findings

- Determined by organ system or tissue affected.
- Classic signs of inflammation (heat, pain, swelling, and loss of function) associated with specific anatomic location of abscess.
- Inflammation and discharge from fistulous tract may be visible if abscess has ruptured to an external surface.
- Variably sized, painful mass of fluctuant to firm consistency attached to surrounding tissues.
- Fever common, but may be absent if abscess has ruptured.
- Sepsis or infection of body cavity (e.g., pyothorax) may be seen if abscess ruptures internally.

CAUSES

- Foreign objects.
- Pyogenic bacteria—*Staphylococcus* spp., *Escherichia coli*, β-hemolytic *Streptococcus* spp., *Pseudomonas*, *Mycoplasma* and *Mycoplasma*-like organisms (l-forms), *Pasteurella multocida*, *Corynebacterium*, *Actinomyces* spp., *Nocardia*, *Bartonella*.
- Obligate anaerobes—*Bacteroides* spp., *Clostridium* spp., *Peptostreptococcus*, *Fusobacterium*.
- Noninfectious—pancreatitis, suture reaction, vaccination, other injectable drug administration, stinging insects, snake envenomation, immune-mediated panniculitis, dermatitis, neoplasia (especially when blood supply outgrown).

RISK FACTORS

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



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Mass Lesions

- Cyst—transiently painful, slower growing, no overt signs of inflammation.
- Fibrous scar tissue—firm, nonpainful.
- Granuloma—less painful, slower growing, firmer without fluctuant center.
- Hematoma/seroma—variable pain, nonencapsulated, rapid initial growth but slows once full size attained, fluctuant initially, may become more firm over time.
- Neoplasia—variable growth, variable pain.

Draining Tracts

- Fungal infection—blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, sporotrichosis.
- Mycobacterial disease.
- Mycetoma—botryomycosis, actinomycotic mycetoma, eumycotic mycetoma.
- Neoplasia.
- Phaeohyphomycosis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—normal, neutrophilia with or without left shift, neutropenia and degenerative left shift (severe infection).
- Serum chemistry profile—depends on severity, system affected. Signs of cholestasis if pancreatic abscess causes obstruction, hyperglycemia if diabetes mellitus, etc.
- Urinalysis—pyuria (prostatic abscess).

OTHER LABORATORY TESTS

- FeLV, FIV testing—recurrent or slow-healing abscesses (cats).
- Cerebrospinal fluid evaluation—increased cellularity and protein with brain abscess.
- Adrenal function—hyperadrenocorticism.

IMAGING

- Radiography—soft-tissue density mass in affected area, may reveal foreign material.
- Ultrasonography—determine if mass is fluid filled; may reveal foreign object; echogenic fluid suggests purulent exudate.
- Echocardiography—pericardial abscess, endocarditis.
- CT or MRI—pulmonary or brain abscess.

DIAGNOSTIC PROCEDURES

Fine-Needle Aspiration

- Red, white, yellow, or greenish liquid.
- Protein content >2.5–3.0 g/dL.
- Nucleated cell count—3,000–100,000 (or more) cells/µL; primarily degenerate neutrophils, fewer macrophages, lymphocytes.
- Bacteria—intra- and extracellular:
 - Gram stain to classify organism for empiric therapy.
 - If causative agent not readily identified with a Romanowsky-type stain, acid-fast

(CONTINUED)

stain to detect mycobacteria or *Nocardia* and periodic acid-Schiff stain to detect fungus.

Biopsy

- Sample should contain both normal and abnormal tissue.
- Impression smears.
- Tissue—for histopathologic examination and culture.
- Necessary to confirm nodular panniculitis.

Culture and Susceptibility Testing

- Affected tissue and/or exudate—aerobic and anaerobic bacterial and fungal.
- Blood and/or urine if systemic disease.

PATHOLOGIC FINDINGS

- Exudate-containing mass lesion accompanied by inflammation.
- Causative agent may be detectable.



TREATMENT

APPROPRIATE HEALTH CARE

- Establish and maintain adequate drainage.
- Surgical removal of nidus of infection or foreign object(s) if necessary.
- Initiate appropriate antimicrobial therapy.
- Outpatient—minor abscesses, localized infection, nodular panniculitis.
- Inpatient—sepsis or systemic inflammation, extensive surgical procedures, treatment requiring hospitalization.

NURSING CARE

- Depends on location of abscess.
- Apply hot packs to inflamed area as needed.
- Use protective bandaging, Elizabethan collar as needed.
- Accumulated exudate—surgical drainage, debridement of necrotic tissue.
- Sepsis, peritonitis, pyothorax—fluid therapy, antimicrobial therapy, intensive care.

ACTIVITY

Restrict until abscess has resolved and adequate healing occurs.

DIET

N/A

CLIENT EDUCATION

- Correct or prevent risk factors.
- Maintain adequate drainage and continue antimicrobial therapy for adequate period of time.

SURGICAL CONSIDERATIONS

- Appropriate debridement and drainage—may need to leave wound open to external surface; may need drain placement.
 - Penrose drains must exit ventrally to encourage drainage; may be bandaged, if bandage is changed regularly.
 - If no ventral drainage, use active drains (e.g., Jackson-Pratt drain).

- Early drainage—to prevent further tissue damage and abscess wall formation.
- Remove foreign objects(s), necrotic tissue, nidus of infection.
- Complications to discuss include progressive tissue damage, necrosis, dehiscence of wound, prolonged healing times in high-motion areas (axillary, inguinal).



MEDICATIONS

DRUG(S) OF CHOICE

- Antimicrobial drugs that are effective against infectious agent and penetrate site of infection.
- Broad-spectrum agent—bactericidal with both aerobic and anaerobic activity until results of culture and sensitivity are known; Gram stain of exudate may guide therapy.
 - Dogs and cats—amoxicillin (22 mg/kg PO q12h); amoxicillin-clavulanic acid (22 mg/kg PO q12h); clindamycin (5–10 mg/kg PO q12h); trimethoprim-sulfadiazine (15 mg/kg PO q12h).
 - Cats only—pradofloxacin (7.5 mg/kg PO q24 for 7 days).
 - Cats with *Mycoplasma* and L-forms—doxycycline (5 mg/kg PO q12h).
- Aggressive IV antimicrobial therapy—sepsis, peritonitis, pyothorax.
- Antimicrobials not required for confirmed sterile abscesses.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Sterile nodular panniculitis—corticosteroids.



FOLLOW-UP

PATIENT MONITORING

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

PREVENTION/AVOIDANCE

- Percutaneous abscesses—prevent fighting; consider castration to reduce roaming or aggressive behavior.
- Anal sac abscesses—prevent impaction; consider anal saculectomy for recurrent cases.
- Prostatic abscesses—consider castration.
- Mastitis—prevent lactation (spay).
- Periorbital abscesses—do not allow chewing on foreign objects.

POSSIBLE COMPLICATIONS

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

EXPECTED COURSE AND PROGNOSIS

Depends on cause, organ system involved, and amount of tissue destruction.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- FeLV or FIV infection.
- Immunosuppression.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Mycobacteria and systemic fungal infections carry some potential.
- If prostatitis secondary to *Brucella canis*.

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Actinomycosis and *Nocardia*.
- Anaerobic Infections.
- Colibacillosis.
- Mycoplasmosis.
- Nocardiosis/Actinomycosis—Cutaneous.
- Sepsis and Bacteremia.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Adam J. Birkenheuer.



Client Education Handout available online

ACIDOSIS, METABOLIC



BASICS

DEFINITION

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

PATHOPHYSIOLOGY

- Metabolic acidosis may develop either from a loss of HCO_3^- (hyperchloremic acidosis) or a gain in acid (high anion gap [AG] acidosis). It is usually secondary to an accumulation of metabolically produced strong anions (strong ion gap or high anion gap acidosis), accumulation of weak acids (hyperphosphatemia), corrected hyperchloremia (hyperchloremic acidosis), or as a compensatory mechanism for respiratory alkalosis.
- High anion gap* acidosis—increase in the concentration of other strong anions through addition (e.g., ethylene glycol toxicity), excessive production (e.g., lactate produced by prolonged anaerobic metabolism), or renal retention (e.g., renal failure) of strong anions other than Cl^- causes metabolic acidosis without increasing Cl^- concentration (so-called normochloremic or high AG metabolic acidosis).

- Hyperphosphatemic* acidosis—increase in plasma weak acids (e.g., inorganic phosphate) is associated with metabolic acidosis and increased AG. At a pH of 7.4, a 1 mg/dL increase in phosphate concentration is associated with a 0.58 mEq/L decrease in HCO_3^- and a 0.58 mEq/L increase in AG. Hyperphosphatemia commonly develops with decreased renal phosphorus excretion (e.g., renal failure, hypoparathyroidism), cellular lysis (e.g., tumor lysis syndrome, trauma, rhabdomyolysis), bone neoplasms (increased bone resorption), and hypervitaminosis D.

- Hyperchloremic* acidosis—may be caused by Cl^- retention (e.g., renal failure, renal tubular acidosis) that typically occurs in response to HCO_3^- loss. Cl^- and HCO_3^- are reciprocally related; loss of HCO_3^- generally results in retention of Cl^- . Other mechanisms for hyperchloremic acidosis include excessive loss of Na^+ relative to Cl^- (e.g., diarrhea, Addison's) and administration of substances containing more Cl^- than Na^+ compared with normal extracellular fluid composition (e.g., administration of KCl, 0.9% NaCl). Acidemia is usually not severe in patients with hyperchloremic acidosis.

SYSTEMS AFFECTED

- Cardiovascular—fall in pH results in increase in sympathetic discharge, but simultaneously causes decrease in responsiveness of cardiac myocytes and vascular smooth muscle to

effects of catecholamines. In mildly acidemic conditions (pH >7.2), effects of increased sympathetic stimulation predominate and result in mild increase in heart rate and cardiac output. More severe acidemia (pH <7.1), especially if acute, may decrease cardiac contractility and predispose heart to ventricular arrhythmias and ventricular fibrillation.

- Respiratory—increased hydrogen ion [H^+] stimulates peripheral and central chemoreceptors to increase alveolar ventilation; hyperventilation decreases PCO_2 , which counters effects of low plasma HCO_3^- on pH. In dogs, a decrease of approximately 1 mmHg in PCO_2 is expected for each 1 mEq/L decrease in plasma HCO_3^- . Little known about compensation in cats, but appears to be almost nonexistent.
- Renal/urologic—kidneys increase net acid excretion, primarily by increasing excretion of NH_4^+ and Cl^- . This compensatory mechanism not very effective in cats.

SIGNALMENT

Any breed, age, or sex of dog and cat.

SIGNS

Historical Findings

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

PHYSICAL EXAMINATION FINDINGS

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

CAUSES

Associated with Hyperchloremia

(*Hyperchloremic Metabolic Acidosis*)

- Renal—renal tubular acidosis; carbonic anhydrase inhibitors.
- Gastrointestinal—diarrhea.
- Other: Cl^- -rich fluids (e.g., 0.9% NaCl, KCl supplementation); total parenteral nutrition with cationic amino acids: lysine, arginine, and histidine; rapid correction of hypcapnia (chronic respiratory alkalosis); NH_4Cl or HCl.

Associated with Normochloremia (High Anion Gap Metabolic Acidosis)

- Renal—uremic acidosis, acute renal failure.
- Ketoacidosis—diabetic ketoacidosis, starvation, liver disease.
- Lactic acidosis—impaired perfusion, impaired carbohydrate metabolism.

- Toxins—ethylene glycol, salicylate, paraldehyde, methanol intoxication.
- Hyperphosphatemia (see Hyperphosphatemia)—raises AG. At a pH of 7.4, each 1 mg/dL increase in phosphate concentration is associated with a 0.58 mEq/L increase in AG.

RISK FACTORS

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



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

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

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Potassium bromide measured as Cl^- in most analyzers; administration artificially decreases AG.

Disorders That May Alter Laboratory Results

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

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Low total CO_2 —total CO_2 in serum samples handled aerobically closely approximates serum HCO_3^- concentration; unfortunately, patients with chronic respiratory alkalosis also have low total CO_2 , and distinction cannot be made without blood gas analysis.
- Metabolic acidoses traditionally divided into hyperchloremic and high AG by means of AG. Anion gap, the difference between the measured cations and the measured anions, is calculated as $AG = [Na^+] - (HCO_3^- + Cl^-)$ or $AG = ([Na^+] + [K^+]) - (HCO_3^- + Cl^-)$, depending on preference of clinician or laboratory. Normal values with potassium included in calculation usually 12–24 mEq/L

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in dogs and 13–27 mEq/L in cats. Negative charges of albumin are major contributors to normal AG; this should be taken into account when evaluating AG in patients with hypoalbuminemia. At pH 7.4 in dogs, decrease of 1 g/dL in albumin associated with decrease of 4.1 mEq/L in AG.

- Normal AG (i.e., hyperchloremic metabolic acidosis).
- High AG (i.e., normochloremic metabolic acidosis).
- Hyperglycemia.
- Azotemia.
- Hyperphosphatemia.
- High lactate concentration.
- Hyperkalemia (*formulas to adjust potassium concentration based on pH changes should not be used*).

OTHER LABORATORY TESTS

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

DIAGNOSTIC PROCEDURES

None

TREATMENT

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



MEDICATIONS

DRUG(S) OF CHOICE

- $NaHCO_3$ may help patients with hyperchloremic, hyperphosphatemic, or uremic acidosis, but not patients with lactic acidosis or diabetic ketoacidosis.
- $NaHCO_3$ may be considered for alkaline diuresis in salicylate toxicity. ° Estimation of HCO_3^- dose—dogs, $0.3 \times$ body weight (kg) $\times (21 - \text{patient } HCO_3^-)$; cats, $0.3 \times$ body weight (kg) $\times (19 - \text{patient } HCO_3^-)$. Give half of this dose slowly IV and reevaluate blood gases before deciding on need for additional administration. Empirical dose of 1–2 mEq/kg followed by reevaluation of blood gas status is safe in most patients.
- ° Potential complications of $NaHCO_3$ administration—volume overload resulting from administered Na^+ , tetany from low ionized calcium concentration, increased

affinity of hemoglobin for oxygen, paradoxical CNS acidosis, overshoot metabolic alkalosis, hypokalemia.

- Hyperchloremic acidosis— $NaHCO_3$ may be effective and considered whenever pH < 7.1 .
- Uremic acidosis—efficacy of $NaHCO_3$ in acute therapy of uremic acidosis is related to shift of phosphate inside cells and consequent amelioration of hyperphosphatemic acidosis.
- Lactic acidosis— $NaHCO_3$ increases lactate production and is of little to no value in lactic acidosis. Therapy should be directed at augmenting oxygen delivery to tissues and reestablishing cardiac output. Small titrated doses of $NaHCO_3$ can be used as temporizing measure to maintain HCO_3^- above 5 mEq/L, if needed.
- Diabetic ketoacidosis— $NaHCO_3$ adversely affects outcome in humans with diabetic ketoacidosis even when pH is < 7.0 . Administration of $NaHCO_3$ to ketoacidotic patients cannot be recommended at any pH. Therapy should be direct at insulin and fluid administration. Reestablishing plasma volume and renal perfusion will allow kidneys to excrete ketoanions, replacing them with Cl^- .

CONTRAINDICATIONS

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

PRECAUTIONS

Use $NaHCO_3$ cautiously in patients with congestive heart failure because Na^+ load may cause decompensation of heart failure.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

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

POSSIBLE COMPLICATIONS

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

ACIDOSIS, METABOLIC

A



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hyperkalemia.
- Hyperchloremia.

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYMS

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

SEE ALSO

- Azotemia and Uremia.
- Diabetes Mellitus With Ketoacidosis.
- Hyperchloremia.
- Hyperkalemia.
- Hyperphosphatemia.
- Lactic Acidosis (Hyperlactatemia).

ABBREVIATIONS

- AG = anion gap.
- BE = base excess.
- H^+ = hydrogen ion.
- HCO_3^- = bicarbonate.
- $NaHCO_3$ = sodium bicarbonate.
- PCO_2 = carbon dioxide tension.

Suggested Reading

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Acknowledgment The author and book editor acknowledge the prior contribution of Lee E. Palmer.

ACNE—CATS



BASICS

OVERVIEW

- Inflammatory dermatitis affecting the chin and lips.
- Symptoms may be recurrent or persistent.

SIGNALMENT

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

SIGNS

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

CAUSES & RISK FACTORS

Precise etiology unknown; often is associated with allergic skin diseases; may be a disorder of keratinization, poor grooming, abnormal sebum production, immunosuppression, viral infection, or stress.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypersensitivity (atopy, flea bite, food, contact).
- Bacterial folliculitis.
- Demodicosis.
- Malassezia* infection.
- Dermatophytosis.
- Neoplasia of sebaceous or apocrine glands.
- Eosinophilic granuloma.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Skin scrapings—demodicosis.
- Bacterial culture—resistant infection.
- Fungal culture—dermatophytosis.
- Cytology—bacteria, *Malassezia*.
- Biopsy—rarely needed; necessary in selected cases to characterize changes such as cystic follicles, to differentiate acne from other diseases such as demodicosis, infections

(bacterial, yeast, or dermatophytes), or to diagnose neoplasia.

PATHOLOGIC FINDINGS

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



TREATMENT

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



MEDICATIONS

DRUG(S) OF CHOICE

Topical

- Shampoo—once or twice weekly with antiseborrheic (sulfur-salicylic acid, benzoyl peroxide, or ethyl lactate).
- Cleansing agents—benzoyl peroxide, salicylic acid, chlorhexidinephosphosporine.
- Medicated wipes.
- Antibiotic ointment—mupirocin 2%.
- Other topicals—clindamycin or erythromycin solution or ointment.
- Combination topicals—benzoyl peroxide-antibiotic gels (e.g., Benzamycin).
- Topical retinoids—tretinoin (e.g., Retin-A® 0.01%): gel more effective because of better penetration.
- In severe inflammatory periods 10–14 days of oral prednisolone (1–2 mg/kg q24h) may help to reduce scar tissue formation.

Systemic

- Antibiotics—amoxicillin with clavulanate, cephalosporin, or fluoroquinolone.

- Severe cases may warrant treatment with isotretinoin (Accutane) or cyclosporine, modified (Atopica®).

- Demodicosis—isoxazoline parasiticides.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

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



FOLLOW-UP

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



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Systemic isotretinoin should not be used on breeding animals.

Suggested Reading

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BASICS

OVERVIEW

- Also (more correctly) muzzle folliculitis and furunculosis.
- Chronic inflammatory disorder of the chin and lips of mostly young animals.
- Characterized by folliculitis and furunculosis; almost never comedogenic as seen in “true acneiform” lesions of human beings.
- Recognized almost exclusively in short-coated breeds.
- Genetic predisposition, local trauma, and allergic disease often play a role.

SIGNALMENT

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

SIGNS

- Ventral chin and lip margins may have few to numerous erythematous papules and sometimes bullae. These may coalesce to form plaques.
- Initial lesions are inflammatory and sterile; bacteria may not be isolated and lesions may not respond to antibiotics.
- Advanced lesions may contain pus or blood, indicating secondary deep bacterial folliculitis and furunculosis.
- Lesions may be pruritic, some are painful on palpation, but most are nonpainful and nonpruritic.
- Chronic and pruritic lesions may become hyperpigmented, lichenified, scarred, and alopecic.

CAUSES & RISK FACTORS

Several short-coated breeds appear to be genetically predisposed to acne. Lesions may be worse in allergic individuals.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dermatophytosis.
- Demodicosis.
- Juvenile cellulitis.
- Contact dermatitis.
- With other symptoms, consider allergic/atopic disease as playing a role.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Impression cytology will help determine if bacteria or yeast are present.
- Skin scrape—demodicosis.
- Dermatophyte culture—dermatophytosis.
- Bacterial culture and sensitivity testing—in patients with suppurative folliculitis and furunculosis that are nonresponsive to initial antibiotic selection.
- Biopsy—histologic confirmation for cases in which diagnosis is in question.

PATHOLOGIC FINDINGS

- Clinical signs and histopathologic findings are diagnostic.
- Characterized histopathologically by folliculitis and furunculosis.
- Bacteria—not always isolated from lesions in early stages.
- As disease progresses, papules enlarge and rupture, promoting a suppurative folliculitis and furunculosis.



TREATMENT

- Reduce behavioral trauma to the chin (e.g., rubbing on the carpet, chewing bones that increase salivation).
- Frequent cleaning with chlorhexidine-containing pads, shampoos, or solutions can be helpful, but instruct owners not to scrub at the area.
- Gentamicin/steroid-containing ointments for the ears work well on the chin when applied twice daily.
- If topicals are not helpful by themselves, add oral antibiotics based on positive cytology and culture and sensitivity testing.
- Severe cases may necessitate short courses of oral steroids.
- Evaluate for underlying allergic/atopic disease and institute proper therapy for diagnosis and control of these diseases; control of allergic disease may permit resolution of muzzle folliculitis and furunculosis.
- Instruct owners to avoid squeezing the lesions; trauma may make inflammation worse.



MEDICATIONS

DRUG(S)

Topical

- Daily cleaning with chlorhexidine-containing pads, shampoos, or solutions can be helpful; instruct owners not to scrub at the areas.

- Gentamicin/steroid-containing ointments for the ears can be applied to localized lesions twice daily; most useful for lesions on the chin, as the pet cannot lick this area. Constant long-term use over months may cause alopecia and cutaneous atrophy: limit frequency and duration of application.

Systemic

- Antibiotics based on culture and sensitivity—when indicated (e.g., cephalaxin, 22–30 mg/kg PO q12h for 2–4 weeks).
- Oral corticosteroids: tapering dosages of prednisolone (initial 0.5 mg/kg/day) to reduce significant inflammation; not for continued use.
- Evaluate for and manage concurrent allergic/atopic skin disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Topical steroids—may cause adrenal suppression and thinning of skin with frequent or constant use.



FOLLOW-UP

PATIENT MONITORING

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

EXPECTED COURSE AND PROGNOSIS

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



MISCELLANEOUS

ASSOCIATED CONDITIONS

Allergic/atopic disease may cause and exacerbate this condition.

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Karen Helton Rhodes.

ACRAL LICK DERMATITIS



BASICS

OVERVIEW

- Compulsion to lick limb/s resulting in plaque formation.
- Skin/exocrine affected.

SIGNALMENT

- Dogs.
- Most common in large breeds—Labrador retrievers, Doberman pinschers, Great Danes, Irish setters, golden retrievers, German shepherd dogs, boxers, and Weimaraners.
- Median age 4 yrs, range 1–12 yrs; no sex predilection.

SIGNS

- Excessive licking of affected area.
- Alopecic, eroded/ulcerated, thickened, and raised firm plaques with scabs and exudation, usually located on dorsal aspect of carpus, metacarpus, tarsus, or metatarsus.
- Single or multiple lesions.

CAUSES & RISK FACTORS

- Anything causing local irritation or lesion may initiate lick–itch cycle.
- Associated diseases: staphylococcal furunculosis, hypersensitivity, endocrinopathy, demodicosis, dermatophytosis, foreign body reaction, neoplasia, underlying joint disease or arthritis, trauma, neuropathy, psychogenic, or sensory nerve dysfunction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplasia.
- Bacterial furunculosis.
- Focal demodicosis.
- Focal dermatophytosis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

Endocrinopathy—total T₄/free T₄/thyroid-stimulating hormone (TSH); adrenocorticotropin hormone (ACTH) stimulation test or low-dose dexamethasone suppression test (LDDST).

IMAGING

Radiology (entire limb +/- neck/lumbar region)—neoplasia; local trauma; radiopaque foreign bodies; bony proliferation may be seen secondary to chronic irritation; evidence of underlying arthritis if over a joint.

DIAGNOSTIC PROCEDURES

- Skin scrapings—demodicosis.
- Dermatophyte PCR and/or culture—fungal infection.
- Epidermal cytology—bacterial infection.

- Bacterial culture and sensitivity—tissue cultures may differ from surface culture.
- Food elimination diet—determine food allergy.
- Intradermal allergy testing—atopy.
- Biopsy—to rule out neoplasia, other infections.
- Behavioral history (additional behavioral signs typical).
- Neurologic and orthopedic evaluation.

PATHOLOGIC FINDINGS

Histopathology—epidermal hyperplasia, plasmacytic dermal inflammation, folliculitis, furunculosis, perihidradenitis, hidradenitis, epitrichial gland dilation/rupture, vertical streaking fibrosis.



TREATMENT

- Rule in/out bacterial, fungal, ectoparasitic, endocrine causes and treat accordingly along with pruritus control.
- If infection resolves and pruritus and/or lesions persist, consider biopsy, allergy workup, neurologic/orthopedic exam, radiographs, behavioral modification.
- Physical restraints—to permit healing.
- Limited research to support effectiveness: radiation, acupuncture, CO₂ laser, cryosurgery, standard surgery.
- Difficult to treat, especially if no underlying cause found; warn owner that patience and time are necessary.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

Based on bacterial culture/susceptibility. Administer until resolution of infection plus 2 weeks.

Systemic

- Pruritis—antihistamines (2 weeks for response typically), e.g., hydroxyzine (2.2 mg/kg PO q8h); chlorpheniramine (4–8 mg/dog PO q8–12h; maximum of 0.5 mg/kg q12h); amitriptyline (1–2 mg/kg PO q12h), also tricyclic antidepressant (TCA); corticosteroids, e.g., prednisolone 1 mg/kg PO q24h and taper based on response (or other steroid equivalent).
- Behavioral—selective serotonin reuptake inhibitors (SSRIs), e.g., fluoxetine (1 mg/kg PO q24h); TCAs, e.g., amitriptyline (1–2 mg/kg PO q12h, also antihistamine); doxepin (3–5 mg/kg PO q12h; maximum 150 mg q12h); clomipramine (2–4 mg/kg PO q24h); dopamine antagonists, e.g., naltrexone (2.2 mg/kg PO q24h).

- Combine/withdraw administration of these medications carefully.

Topical

Pruritus—flunixin meglumine and flucinolone in dimethyl sulfoxide (combined), topical capsaicin products; intralesional corticosteroids rarely helpful; wear gloves when applying; prevent licking of area for 10–15 minutes.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

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



FOLLOW-UP

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



MISCELLANEOUS

AGE-RELATED FACTORS

Dogs <5 years old—strongly consider allergy.

ZOONOTIC POTENTIAL

Dermatophytosis (rare) and methicillin-resistant *Staphylococcus aureus* may have zoonotic implications.

ABBREVIATIONS

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

Suggested Reading

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Consulting Editor Alexander H. Werner Resnick

Acknowledgment The author acknowledges the prior contribution of Alexander H. Werner Resnick.



BASICS

DEFINITION

Nonepisodic diarrhea of fewer than 7 days' duration.

PATHOPHYSIOLOGY

Excess water and/or solid content of feces is caused by five main mechanisms:

- Osmotic—from maldigestion, ingestion of poorly absorbable compounds, toxins.
- Decreased absorption—mucosal damage causing loss of absorptive cells from infection, inflammation, or toxins.
- Increased secretion (secretory)—mediated by toxins, inflammation, parasympathetic stimulation.
- Increased permeability/exudative—severe mucosal, lacteal, and vessel damage, due to inflammation, ulceration, or direct damage.
- Dysmotility—increased or decreased motility alters digestion, absorption, secretion, and therefore water regulation.

SYSTEMS AFFECTED

- Cardiovascular—fluid losses can be significant, with progressive dehydration to hypovolemia.
- Gastrointestinal (GI)—colitis can develop secondary to oral causes of diarrhea.
- Immune—with enterocyte loss, the mucosal barrier can be compromised, leading to translocation of GI bacteria and sepsis.
- Metabolic—electrolyte losses, especially bicarbonate and potassium. Hypokalemia is common with concurrent hypoxemia.
- Vascular—albumin and globulin losses via increased permeability can be significant and lead to hypoalbuminemia, decreased vascular oncotic pressure, and edema or cavitary effusion.

GENETICS

N/A

INCIDENCE/PREVALENCE

Increased incidence due to dietary indiscretion or infectious etiologies in young patients.

GEOGRAPHIC DISTRIBUTION

Some infectious etiologies have specific geographic distributions.

SIGNALMENT

- Species—dog and cat.
- Breed predilections—none.
- Mean age and range—common in puppies and kittens due to dietary indiscretion and infectious etiologies.
- Predominant sex—N/A.

SIGNS

General Comments

- Acute diarrhea common, and usually self-limiting. Most animals stable, and require minimal diagnostics/treatment.
- In patients that are unstable, with cardiovascular or metabolic compromise, more aggressive diagnostic and treatment approach is warranted.

Historical Findings

- Dietary history, dietary indiscretion, medication/toxin history, and general husbandry should be investigated.
- Special care should be taken to identify potentially contagious causes of diarrhea, and isolate these patients early.
- Patients that should be isolated for further diagnostics include unvaccinated, raw diet consumption, housing with many other cats/dogs, or multiple cats/dogs from same household affected.

- Varying activity levels can be seen, from normal to lethargic.
- Character of diarrhea can help localize etiology:

 - Small intestinal diarrhea characteristics: large volume, normal frequency, concurrent weight loss and/or vomiting.
 - Melena, if present, points to gastric or upper small intestinal bleed.
 - Steatorrhea, if present, points to maldigestive disorder like exocrine pancreatic insufficiency (EPI).
 - Large intestinal diarrhea characteristics—small volume, increased frequency, tenesmus, mucus, hematochezia.

Physical Examination Findings

- Patients can vary from stable to unstable.
- Common findings—dehydration, hypovolemia, abdominal pain, nausea, fluid-gas interface on intestinal palpation, increased borborygmi.
- Rectal examination may reveal melena, hematochezia, steatorrhea.

CAUSES

- Extra-GI causes:
 - Common—hepatobiliary disease, pancreatitis, neoplasia (non-GI).
 - Uncommon—endocrine (hypoadrenocorticism, hyperthyroidism), peritonitis, sepsis.
- Intra-GI causes:
 - Infectious—bacterial: *Campylobacter* spp., *E. coli*, *Salmonella* spp., Clostridial enterotoxins; parasitic: many species of ascarids, cestodes, hookworms, whipworms; protozoal: giardiasis, trichomoniasis, coccidiosis; viral: parvovirus, canine distemper virus, corona virus; rickettsial: salmon poisoning (*Neorickettsia*); fungal: histoplasmosis, mycotoxins.
 - Inflammatory (most common cause)—acute enteritis/enterocolitis due to dietary indiscretion or sudden diet change, acute hemorrhagic diarrhea syndrome.
 - Medications/toxins—antibiotics, chemotherapeutic agents, methimazole, nonsteroidal anti-inflammatory drugs (NSAIDs), toxins (corrosive, heavy metals).
 - Motility—obstructive or nonobstructive foreign bodies, intussusception, mesenteric torsion.
 - Neoplasia—primary neoplasia including adenocarcinoma, lymphoma (small cell and large cell) leiomyoma/leiomyosarcoma, mast cell tumor (cats), metastatic.

RISK FACTORS

- Dietary—abrupt diet change or dietary indiscretion.
- Medications—many medications can cause acute diarrhea (see Causes).
- Infectious—geographic distribution effect.

ACUTE DIARRHEA

A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Unlikely to be confused with other conditions; however, rarely intestinal bleeding or expulsion of liquid in constipated patient can mimic acute diarrhea.

CBC/BIOCHEMISTRY/URINALYSIS

- Extra-GI etiologies—may reflect etiology:
- Increased hepatic enzyme activity in hepatobiliary diseases.
- Increased hepatic enzyme activity, hypoalbuminemia, inflammatory leukogram in pancreatitis.
- Hypoalbuminemia, decreased Na : K ratio in hypoadrenocorticism.
- Intra-GI causes of diarrhea—often normal.
- Parvoviral enteritis causes significant neutropenia.
- As result of diarrhea, following may be present:
 - Hemoconcentration.
 - Prerenal azotemia.
 - Hypokalemia.
 - Hypoalbuminemia, hypcholesterolemia.
 - Hypoglycemia—toy breed puppies with GI signs predisposed.

OTHER LABORATORY TESTS

- Extra-GI interrogation:
 - Baseline cortisol or adrenocorticotropic hormone (ACTH) stimulation test in dogs.
 - T₄ in cats.
- Quantitative pancreatic lipase immunoreactivity if EPI suspected.
- Intra-GI interrogation:
 - Parvovirus ELISA should be immediately performed in any suspect so isolation protocols may be initiated as soon as possible.
 - Fecal flotation, fecal direct smear cytology, *Giardia* ELISA.
 - Diarrhea PCR panel may be useful for specific pathogens (i.e., *Salmonella*), but note there is controversy about some bacteria on this panel causing clinical signs.

IMAGING

Abdominal Radiography

- Survey abdominal radiographs interrogate mainly extra-GI causes of diarrhea.
- Acute enteritis/enterocolitis—mild gas and/or fluid dilation of stomach/intestine.
- Pancreatitis—widened gastroduodenal angle, focal decreased serosal detail at proximal duodenal flexure.

Abdominal Ultrasonography

- Abdominal ultrasonography may be useful in interrogation of intra- and extra-GI causes of diarrhea, such as pancreatitis.
- Emergency cage-side focused ultrasonographic examination of abdomen is indicated in patients with acute abdominal pain, to evaluate for etiologies that are surgical emergencies, such as septic or bile peritonitis.
- If peritoneal effusion is seen, abdominocentesis and immediate in-house cytology are indicated (+/- culture).

DIAGNOSTIC PROCEDURES

Endoscopy rarely indicated in acute diarrhea, except for patients with melena where gastroduodenal ulceration is suspected.

ACUTE DIARRHEA

(CONTINUED)

PATHOLOGIC FINDINGS

Dependent on underlying etiology.



TREATMENT

APPROPRIATE HEALTH CARE

- Stable patients, mild diarrhea—outpatient medical care. Careful assessment of young patients should be made, as they can become unstable with mild signs.
- Unstable patients, hypovolemic or acute abdominal pain—inpatient medical care.

NURSING CARE

- Isolation protocols should be instituted immediately for any patient that may have a contagious etiology of diarrhea, i.e., patients that are unvaccinated, fed raw diets, come from housing situations with many other animals, or if multiple animals in same household are exhibiting same clinical signs.
- Fluid therapy as mandated by hydration/perfusion status and ongoing losses.
- Most hyporexic patients with dehydration/hypovolemia need isotonic crystalloids to replenish losses and provide maintenance.
- Potassium supplementation may be needed.

ACTIVITY

Activity restriction only required in post-operative care of surgical patients.

DIET

Feeding bland, highly digestible diet is indicated for 3–5 days, then gradual reintroduction of patient's routine diet.

CLIENT EDUCATION

Client education on dietary indiscretion, gradual diet changes, routine deworming, and vaccination may be appropriate.

SURGICAL CONSIDERATIONS

Surgery rarely may be indicated to treat etiology, such as mechanical obstruction.



MEDICATIONS

DRUG(S) OF CHOICE

- In acute diarrhea caused by stress or antibiotics, veterinary-grade probiotics may be useful.
- Antibiotics not indicated in acute diarrhea patients, and should be avoided in accordance with antibiotic stewardship, unless specifically indicated with known bacterial etiology, or in cases where bacterial translocation and sepsis are of concern (e.g., parvoviral enteritis with neutropenia).
- Gastric antacids not indicated unless concurrent vomiting and/or regurgitation.
- Anti-diarrheal medications like loperamide not indicated in

acute diarrhea, as usually self-limiting; if diarrhea persists beyond 5–7 days, further etiologic investigation and appropriate treatment are warranted.

- Anthelmintics (e.g., fenbendazole 50 mg/kg PO q24h for 5 days) are recommended for empiric treatment of parasitic enteritis.
- Antiprotozoal or coccidiostatic medication should be used if fecal analysis warrants.

CONTRAINdications

- Prokinetic medications should not be given to patients with diarrhea.
- Anti-diarrheal medications like loperamide should not be given to breeds with possible ABCB-1/MDR-1 mutation.

PRECAUTIONS

- For puppies and kittens, see manufacturer's instructions regarding age and safety labeling.
- Many drugs such as antibiotics and anti-diarrheal medications can perpetuate diarrhea.
- Metronidazole can cause neurologic toxic effects with high dose and/or chronic use.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Continuation of diarrhea for 3–5 days is to be expected, but should be continual improvement in signs.
- If diarrhea not improving, or getting more severe, further diagnostics are warranted.
- If diarrhea persists beyond 7 days or recurs despite appropriate therapy, consider chronic diarrhea etiologies.

PREVENTION/AVOIDANCE

Avoid rapid diet changes and dietary indiscretion, and institute prophylactic deworming and vaccinations.

POSSIBLE COMPLICATIONS

- Dehydration and hypovolemia.
- Hypoalbuminemia and subsequent cavitary effusion.

EXPECTED COURSE AND PROGNOSIS

- Mild acute diarrhea usually self-limiting.
- Other prognoses etiology dependent.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Acute vomiting.
- Hypoxia.

AGE-RELATED FACTORS

Younger patients more likely to have infectious etiologies.

ZOONOTIC POTENTIAL

Parasitic, protozoal, and bacterial etiologies (e.g., *Ancylostoma*, *Campylobacter*, *Giardia*, *Salmonella*).

PREGNANCY/FERTILITY/BREEDING

Varies with treatment.

SYNONYMS

N/A

SEE ALSO

- Acute Vomiting.
- Diarrhea, Chronic—Cats.
- Diarrhea, Chronic—Dogs.
- Gastroenteritis, Acute Hemorrhagic Diarrhea Syndrome.
- Pancreatitis—Cats.
- Pancreatitis—Dogs.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- EPI = exocrine pancreatic insufficiency.
- GI = gastrointestinal.
- NSAID = non-steroidal anti-inflammatory.

INTERNET RESOURCES

- <https://www.avma.org/practicemanagement/clientmaterials/pages/default.aspx>
- <https://veterinarian.vin.com>

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Acknowledgment The author and editor acknowledge the prior contribution of Erin Portillo.



Client Education Handout
available online

ACUTE KIDNEY INJURY



BASICS

DEFINITION

- Acute kidney injury (AKI) represents a continuum of renal injury, from mild, clinically inapparent, nephron loss to severe acute renal failure.
- AKI is likely underrecognized. Any increase in serum creatinine >0.3 mg/dL from hydrated baseline is considered an AKI.
- The spectrum of injury is highly variable and may range from mild subclinical to severe damage, requiring renal replacement therapy.
- Patients with AKI have the potential for recovery of renal function.

PATHOPHYSIOLOGY

- AKI may be categorized as prerenal, intrinsic renal, or postrenal based on underlying etiology. Pre- and postrenal causes may progress to intrinsic renal damage.
- Patients with preexisting chronic kidney disease (CKD) are very predisposed to development of clinical AKI due to decreased renal reserve. Special care must be taken in patients with existing CKD to minimize predisposing factors: volume depletion, nephrotoxic medications, etc.

SYSTEMS AFFECTED

- Renal/urologic.
- Uremia may affect all body systems.

INCIDENCE/PREVALENCE

- Prevalence is lower than for CKD.
- Prevalence may increase in environments that support *Leptospira*.
- Ureteral obstruction is most common cause of severe acute uremia in cats.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

None

Mean Age and Range

- 6–8 years peak prevalence.
- Older animals at greater risk due to decreased renal reserve (AKI on CKD).

SIGNS

Historical Findings

Sudden onset of anorexia, listlessness, depression, vomiting or diarrhea (\pm blood), halitosis, ataxia, seizures, known toxin or drug exposure, recent medical or surgical procedure.

Physical Examination Findings

Normal body condition and hair coat, depression, dehydration (or iatrogenic overhydration), scleral injection, oral ulceration, necrosis of tongue, uremic breath, hypothermia, fever, tachypnea, bradycardia, nonpalpable urinary bladder, and asymmetric, enlarged, painful, or firm kidneys.

CAUSES

Hemodynamic/Hypoperfusion

Shock, trauma, thromboembolism (e.g., disseminated intravascular coagulation [DIC]), vasculitis, transfusion reaction), heatstroke, excessive vasoconstriction (e.g., administration of nonsteroidal anti-inflammatory drugs [NSAIDs]), adrenal insufficiency, excessive vasodilation (e.g., angiotensin-converting enzyme inhibitors [ACEIs] or antihypertensive drugs), prolonged anesthesia, significant hypertension, heart failure.

Nephrotoxic

Grape or raisin ingestion (dogs), lily ingestion (cats), ethylene glycol, aminoglycoside, amphotericin B, chemotherapeutic agents, NSAIDs, radiographic contrast agents, heavy metals, insect or snake venom, heme pigment, and many others. Patients with ethylene glycol toxicity may be exposed from other sources than antifreeze, such as some paints, freezer packs, catering heat sources, etc.

Intrinsic and Systemic Disease

Leptospirosis, immune-mediated glomerulonephritis, pancreatitis, septicemia, DIC, hepatic failure, heat stroke, transfusion reaction, bacterial endocarditis, pyelonephritis, lymphoma, and ureteral obstruction.

RISK FACTORS

- Endogenous—preexisting CKD, pancreatitis, dehydration, sepsis, hypovolemia, hypotension, advanced age, concurrent disease.
- Exogenous—drugs, prolonged anesthesia, trauma, multiple organ disease, high environmental temperature.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prerenal azotemia—oliguria correctable with fluid repletion. Typically hypersthenuric, but consider ability to concentrate urine: preexisting kidney disease, endocrine disorders, medications, and diet may all affect concentrating ability.
- Postrenal azotemia—anuria, dysuria, stranguria, painful or asymmetric kidneys, ureteral/urethral obstruction, enlarged prostate, urethral tear, uroperitoneum.
- CKD—polyuria, polydipsia, history of chronic illness, loss of body condition, anemia.
- Hypoadrenocorticism—hyponatremia, hyperkalemia, low serum cortisol.
- Pancreatitis—cranial abdominal pain, hyperbilirubinemia, increase in liver enzyme activity.

CBC/BIOCHEMISTRY/URINALYSIS

- Variable packed cell volume (PCV), leukocytosis, or lymphopenia.
- Variable increases in blood urea nitrogen (BUN), creatinine, phosphorus, potassium, and glucose; and variably low bicarbonate and calcium.

- Urine specific gravity (USG) ≤ 1.020 , mild to moderate proteinuria, glucosuria, casts, pyuria, hematuria, and tubular epithelial cells; variable bacteriuria and crystalluria.

OTHER LABORATORY TESTS

- Metabolic acidosis—mixed disorders may occur.
- Leptospirosis testing.
- Ethylene glycol testing.
- Canine pancreatic lipase immunoreactivity (cPLI) for pancreatitis.

IMAGING

- Survey and contrast radiography—kidneys normal to large with smooth contours; asymmetric in cats (“big kidney–little kidney” syndrome) with ureteral obstruction, uroliths may be seen.
- Antegrade nephropelography for ureteral obstruction.
- Ultrasonography—evidence of pancreatitis, marked cortical hyperechogenicity may suggest ethylene glycol toxicity. Moderate cortical hyperechogenicity suggests glomerulonephritis or nephrosis. Pelvic and/or ureteral dilation may suggest outflow obstruction.

DIAGNOSTIC PROCEDURES

- Monitor urine output (UOP): anuria (≤ 0.25 mL/kg/h), oliguria, polyuria (≥ 2 mL/kg/h). Avoid urinary catheterization due to infection risk. Assess UOP with serial body weights, ultrasound bladder assessment, weigh bedding, etc.
- Fine-needle aspiration may diagnose lymphoma.
- Renal biopsy may help identify underlying cause and prognosticate recovery.

PATHOLOGIC FINDINGS

Nephrosis or nephritis, glomerulonephritis, calcium oxalate crystals, interstitial edema, and lack of interstitial fibrosis, variable tubular regeneration.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient management—eliminate inciting causes; discontinue nephrotoxic drugs; maintain hemodynamic stability; ameliorate life-threatening fluid imbalances, biochemical abnormalities, and uremic complications.

NURSING CARE

- Hypovolemia—correct estimated fluid deficits with balanced isotonic solution within 2–4 hours if patient condition permits; once hydrated, ongoing fluid requirements are provided by 5% dextrose for insensible losses (-20 – 25 mL/kg/day) and balanced electrolyte solution equal to sensible losses; avoid overhydration.
- Hypervolemia—stop fluid administration and eliminate excess fluid by diuretics or dialysis.

ACUTE KIDNEY INJURY

(CONTINUED)

- Monitor body weight and blood pressure several times daily and adjust fluids to maintain stable weight once rehydrated.

DIET

- Nutritional support should be provided within 3 days using moderately protein-restricted diets.
- Caloric and protein requirements supplied by blended renal diets, liquid enteral solutions, or formulated diets delivered by enteral feeding tube. Parenteral nutrition may be needed in some cases.

CLIENT EDUCATION

- Depending on inciting cause, prognosis for recovery of renal function is variable. Average recovery for all causes of AKI is 50%. Likelihood of some degree of persistent kidney damage.
- Potential for complications of treatment (e.g., fluid overload, pancreatitis, sepsis, and multiple organ failure); expense of prolonged hospitalization; options for continued care if conventional medical management fails (hemodialysis, peritoneal dialysis); zoonotic potential of leptospirosis.

SURGICAL CONSIDERATIONS

- See Ureterolithiasis.
- Renal transplantation may provide long-term survival for cats with severe, nonrecovered AKI.

Peritoneal or Hemodialysis

- Dialysis can stabilize the patient to allow time for renal recovery. Without, most oliguric patients die before sufficient renal repair occurs.
- Indications—oliguria or anuria, life-threatening fluid overload or acid-base/electrolyte disturbances, BUN \geq 100 mg/dL, serum creatinine \geq 5 mg/dL, clinical course refractory to conservative treatment, perioperative stabilization, and poisoning/overdosage with dialyzable toxin/drug.



MEDICATIONS

DRUG(S) OF CHOICE

Inadequate Urine Production

- Avoid overhydration. Once fluid replete, administer diuretics.
- Hypertonic mannitol (20%)—0.5 g/kg IV over 15–30 minutes; if effective, continue IV bolus q6h.
- Furosemide—1–4 mg/kg IV; if effective, continue at 0.5 mg/kg/h or 2 mg/kg q6h.
- Dopamine—potential side effects and lack of efficacy contraindicate its use except for pressor control. Fenoldopam may be more efficacious.
- Dialysis for refractory cases.

Metabolic Disorders, Acid-Base Disorders

Administer bicarbonate if serum bicarbonate \leq 16 mEq/L; bicarbonate replacement: mEq = bicarbonate deficit \times body weight (kg) \times 0.3;

give half IV over 30 minutes and remainder over 2–4 hours, then reassess.

Hyperkalemia

- Correct dehydration with potassium-free fluids.
- Minimize potassium intake.
- Discontinue medications that promote hyperkalemia.
- Loop diuretics—furosemide 1–2 mg/kg IV.
- Sodium bicarbonate—correct bicarbonate deficit, if bicarbonate status unknown 1–2 mEq/kg IV.
- Dextrose \pm insulin—1–2 mL/kg of 50% dextrose diluted to 25% IV or regular insulin 0.1–0.2 U/kg IV bolus followed by 1–2 g dextrose/unit insulin.
- Calcium gluconate 10%—0.5–1.0 mL/kg IV over 10–15 minutes (cardioprotective, does not alter serum potassium).
- Refractory hyperkalemia—dialysis.

Vomiting

- Reduce gastric acid production—pantoprazole (1 mg/kg IV q12h), famotidine CRI.
- Mucosal protectant for gastrointestinal (GI) ulceration—sucralfate (0.25–1 g PO q6–8h).
- Antiemetics—maropitant (1 mg/kg SC/IV q24h); ondansetron (0.2–1 mg/kg IV q8–12h).

PRECAUTIONS

Modify dosages of drugs requiring renal metabolism or elimination.



FOLLOW-UP

PATIENT MONITORING

Fluid, electrolyte, and acid-base balances; body weight; blood pressure; UOP; and clinical status.

PREVENTION/AVOIDANCE

- Anticipate AKI in aged patients or those with systemic disease, sepsis, trauma, hemodynamic instability, receiving nephrotoxic drugs, multiple organ failure, or undergoing prolonged anesthesia.
- Monitor urine production, BUN, and creatinine in high-risk patients.

POSSIBLE COMPLICATIONS

Seizures, coma, cardiac arrhythmias, hypo- or hypertension, congestive heart failure, pulmonary edema, uremic pneumonitis, GI bleeding, sepsis, cardiopulmonary arrest, and death.

EXPECTED COURSE AND PROGNOSIS

- Prognosis depends on underlying cause, extent of renal injury, concomitant disease or organ failure, and response to therapy.
- Survival rate ~50%, but depends on cause: <20% for advanced ethylene glycol toxicosis, >80% for acute leptospirosis.
- Polyuric AKI—typically milder than oliguric; recovery may occur over 2–6 weeks, but prognosis remains guarded.
- Oliguric AKI—extensive kidney injury, difficult to manage, and has poor prognosis for recovery without dialysis; recovery may be

signaled by sudden (and often excessive) polyuria and sluggish and possibly incomplete return of renal function over 4–12 weeks; dialysis extends potential for renal regeneration and repair.

- Anuric AKI—poor prognosis without dialysis. Anuria is not prognostic and does not impact ability for renal recovery, if hemodialysis is available to maintain patient during recovery period.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Leptospirosis

PREGNANCY/FERTILITY/BREEDING

A rare complication of pregnancy; promoted by acute metritis, pyometra, and postpartum sepsis or hemorrhage.

SYNONYMS

- Acute renal failure.
- Acute tubular necrosis.
- Acute uremia.

SEE ALSO

- Azotemia and Uremia.
- Hyperkalemia.
- Hypertension, Systemic Arterial.
- Leptospirosis.
- Ureterolithiasis.

ABBREVIATIONS

- ACEI = angiotensin-converting enzyme inhibitors.
- AKI = acute kidney injury.
- BUN = blood urea nitrogen.
- CKD = chronic kidney disease.
- cPLI = canine pancreatic lipase immunoreactivity.
- DIC = disseminated intravascular coagulation.
- GI = gastrointestinal.
- NSAID = nonsteroidal anti-inflammatory drug.
- PCV = packed cell volume.
- UOP = urine output.
- USG = urine specific gravity.

Suggested Reading

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Client Education Handout
available online

ACUTE RESPIRATORY DISTRESS SYNDROME



BASICS

DEFINITION

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

PATHOPHYSIOLOGY

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

SYSTEMS AFFECTED

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

GENETICS

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

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat.

Breed Predilections

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

Mean Age and Range

Unknown

SIGNS

Historical Findings

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

Physical Examination Findings

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

CAUSES

Primary Pulmonary Causes

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

Nonpulmonary Causes

- Systemic inflammatory response syndrome (SIRS). • Sepsis. • Neoplasia. • Pancreatitis.
- Severe trauma and shock. • Severe bee sting envenomation.

RISK FACTORS

- SIRS. • Sepsis. • Severity of illness. • Multiple transfusions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

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

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis or leukopenia. • Other changes dependent on underlying disease process.

OTHER LABORATORY TESTS

- Arterial blood gases—low PF ratio (where PaO_2 is measured in mmHg and FiO_2 is

0.21–1.0). Normal PF ratio = 500; comparison of this ratio allows evaluation of severity of lung disease and direct comparison of blood gases taken at different FiO_2 . PaCO_2 is often low; hypercapnia tends to be late (preterminal) development. • Total protein of airway edema fluid compared with serum total protein—ratio of edema fluid to serum total protein <0.5 supportive of low-protein hydrostatic pressure pulmonary edema (e.g., heart failure, fluid overload); edema fluid/serum total protein ratio >0.7 suggests high-protein, increased permeability pulmonary edema such as ARDS and pneumonia. • Coagulation panel may reveal hypocoagulable state supportive of disseminated intravascular coagulation (DIC) or cause of pulmonary hemorrhage.

IMAGING

Thoracic Radiographs

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

Echocardiography

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

DIAGNOSTIC PROCEDURES

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

PATHOLOGIC FINDINGS

Gross Pathology

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

Histopathology

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



TREATMENT

APPROPRIATE HEALTH CARE

- No specific therapy; general aims to maintain tissue oxygenation and minimize iatrogenic lung injury while treating underlying disease.
- Oxygen therapy—no more than required to maintain $\text{PaO}_2 > 60$ –80 mmHg to minimize oxygen toxicity. • Positive-pressure ventilation (PPV) essential in management of ARDS patients; indicated in patients that are hypoxic despite

oxygen therapy, patients requiring high levels of inspired oxygen for prolonged periods, or patients working so hard to breathe that at risk of exhaustion. • ARDS thought to be exacerbated by ventilator-induced lung injury associated with alveolar overdistension compounded by cyclic opening and collapse of atelectatic alveoli; therefore, lung-protective strategies of PPV with moderate to high PEEP, low tidal volumes, and permissive hypercapnia recommended to minimize ventilator-induced lung injury; tidal volumes of 6 mL/kg have been found to increase survival significantly in human ARDS patients compared to tidal volumes of 12 mL/kg. • Recruitment maneuvers and high levels of PEEP can both cause significant hemodynamic compromise and patients should have constant direct arterial blood pressure monitoring. • Intensive supportive care of cardiovascular system and other organ systems is vital, as these patients at high risk for development of multiple organ dysfunction.

NURSING CARE

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

ACTIVITY

If not anesthetized for ventilation, strict cage confinement.

DIET

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

CLIENT EDUCATION

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

SURGICAL CONSIDERATIONS

Underlying disease may require surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- No specific drug therapy. • Antibiotics for underlying disease where indicated.

- Vasoactive drugs to maintain blood pressure. • Anesthetic drugs to allow PPV.
- Analgesia as appropriate. • Low-dose corticosteroid—use remains controversial, with conflicting reports of efficacy for low-dose steroids in early or late ARDS.

ALTERNATIVE DRUG(S)

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



FOLLOW-UP

PATIENT MONITORING

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

PREVENTION/AVOIDANCE

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

POSSIBLE COMPLICATIONS

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

EXPECTED COURSE AND PROGNOSIS

- Mortality in human patients remains at 40–60%. • Mortality in veterinary patients is likely greater than 90%.



MISCELLANEOUS

ASSOCIATED CONDITIONS

SIRS, multiple organ dysfunction syndrome, sepsis.

SYNOMYMS

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

SEE ALSO

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

ABBREVIATIONS

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

INTERNET RESOURCES

www.ardsnet.org

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BASICS

DEFINITION

Vomiting of fewer than 7 days' duration.

PATHOPHYSIOLOGY

- Vomiting is a reflex initiated by the vomiting center in the medulla, triggered by three major mechanisms—gastric/duodenal mucosal irritation, gastric/duodenal distention, or the chemoreceptor trigger zone (CRTZ).
- Mucosal irritation or gastric/duodenal distention signal the vomiting center via sympathetic and vagal afferent innervation. Anti-peristaltic waves force intestinal contents back to the duodenum, then distention becomes the main trigger for the vomiting reflex.
- The CRTZ can directly trigger the vomiting center via receptor activation or vestibular input; known receptors are α_2 , D₂, H1, M1, NK₁, 5HT₃.
- Cerebral cortex and vestibular apparatus can also directly stimulate the vomiting center.
- The vomiting center initiates an autonomic motor reaction via spinal nerves to diaphragmatic and abdominal muscles, and cranial nerves 5, 7, 9, 10, and 12 to the upper gastrointestinal (GI) tract.
- The reflex involves a deep breath, opening the upper esophageal sphincter, closing the glottis, strong diaphragmatic and abdominal muscle contractions, and lower esophageal sphincter relaxation, leading to expulsion of contents.

SYSTEMS AFFECTED

- Cardiovascular**—fluid losses can be significant, with progressive dehydration to hypovolemia; vagal stimulation can lead to bradycardia, and rarely syncope.
- GI**—esophagitis.
- Metabolic**—vomiting of mixed small intestinal and gastric contents results in isotonic electrolyte losses; pyloric obstruction results in metabolic alkalosis; hypokalemia is common with concurrent hypoxemia.
- Respiratory**—aspiration pneumonitis/pneumonia.

GENETICS

N/A

INCIDENCE/PREVALENCE

Increased incidence of infectious causes and dietary indiscretion in young patients.

GEOGRAPHIC DISTRIBUTION

Some infectious etiologies have specific geographic distributions.

SIGNALMENT

- Species**—dog and cat.
- No breed, age, or sex predilections.

SIGNS

Historical Findings

- Care should be taken to differentiate vomiting from regurgitation.
- Dietary indiscretion, foreign body, and medication/

toxin history should be investigated.

- Nausea and hypersalivation.
- Varying amounts, frequency, and severity of vomiting.
- Varying activity levels can be seen, from normal to lethargic.
- Hematemesis may be seen.

Physical Examination Findings

- Dehydration/hypovolemia, cranial abdominal pain, nausea, fluid-gas interface on intestinal palpation, increased borborygmi.
- Careful sublingual examination for anchored linear foreign bodies.
- Careful abdominal palpation for mechanical obstruction.
- Rectal examination for melena or concurrent diarrhea.

CAUSES

- Extra-GI causes:**
 - Common—hepatobiliary disease, kidney disease, pancreatitis, neoplasia (non-GI).
 - Uncommon—CNS, cardiac, endocrine (hypoadrenocorticism, hyperthyroidism, diabetic ketoacidosis), respiratory disease, peritonitis, sepsis.
- Intra-GI causes:**
 - Congenital/genetic—hiatal hernia.
 - Infectious—parasitic, protozoal, viral (parvovirus, canine distemper virus, corona virus), fungal, bacterial (*Campylobacter*, *Salmonella*).
 - Inflammatory (most common cause)—acute gastritis/gastroenteritis due to dietary indiscretion or sudden diet change, acute hemorrhagic diarrhea syndrome.
 - Mechanical obstruction—foreign body, intussusception, obstructive mass (granuloma, neoplasia, pyloric hypertrophy, trichobezoar), torsion/volvulus (gastric, mesenteric).
 - Medications/toxins— α_2 agonists, antibiotics, apomorphine, chemotherapeutic agents, methimazole, nonsteroidal anti-inflammatory drugs (NSAIDS), opioids, toxins (corrosive, heavy metals).
 - Neoplasia—primary such as adenocarcinoma, lymphoma, leiomyoma/leiomyosarcoma, gastrointestinal stromal tumor, mast cell tumor (cats), metastatic.
 - Ulcers—gastric and/or duodenal ulceration is usually secondary: NSAIDS, neoplasia (primary GI, mast cell tumor, gastrinoma), hypoadrenocorticism, uremia, infectious (controversial—*Helicobacter*), stress.

RISK FACTORS

- Dietary**—abrupt diet change or dietary indiscretion.
- Medications**—many medications can cause acute vomiting.
- Infectious**—geographic distribution effect.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vomiting can be mistaken for regurgitation.
- Vomiting—prodromal nausea (hypersalivation), retching, abdominal contractions.
- Regurgitation—no prodromal nausea, passive expulsion of fluid/food.
- Vomiting can lead to

regurgitation via esophagitis, so if both signs are present, it is important to establish chronology.

- In cats, vomiting can be mistaken for coughing.
- Coughing involves extension of neck and elbows.
- Physical exam findings may differentiate.
- Videos can be helpful to differentiate.

CBC/BIOCHEMISTRY/URINALYSIS

- Extra-GI causes:**
 - Increased hepatic enzyme activity in hepatobiliary diseases.
 - Renal azotemia in kidney disease.
 - Increased hepatic enzyme activity, hypoalbuminemia, inflammatory leukogram in pancreatitis.
 - Hypoalbuminemia, decreased Na : K ratio in hypoadrenocorticism.
 - Intra-GI causes—often normal.
 - As result of vomiting, following may be present:
 - Hemoconcentration.
 - Prerenal azotemia.
 - Hypokalemia, hypochloremia.
 - Hypoalbuminemia, hypcholesterolemia.
 - Hypoglycemia—toy-breed puppies predisposed.

OTHER LABORATORY TESTS

- Extra-GI interrogation**—baseline cortisol or adrenocorticotropic hormone (ACTH) stimulation test in dogs, T₄ in cats, quantitative pancreatic lipase immunoreactivity.
- Intra-GI interrogation**—fecal flotation, fecal direct smear cytology.

IMAGING

Abdominal Radiography

- Survey abdominal radiographs** indicated in most acutely vomiting patients to evaluate potential surgical emergencies, like mechanical obstructions and sepsis. Survey abdominal radiographs also interrogate many extra-GI causes of vomiting.
- Acute gastritis/gastroenteritis**—mild gas and/or fluid dilation of stomach/intestine.
- Mechanical obstruction**—foreign body may be radiopaque, or two populations of bowel may be seen, one distended orad to the obstruction, and one normal aborad to the obstruction.
- If foreign body is suspected, but no radiographic evidence, serial radiographs every 6 hours or contrast radiography may be considered.
- Gastric dilatation and volvulus**—malpositioned pylorus on right lateral radiograph.
- Pancreatitis**—widened gastro-duodenal angle, focal decreased serosal detail at proximal duodenal flexure.

Abdominal Ultrasonography

- Abdominal ultrasonography** may be useful in interrogation of intra- and extra-GI causes of vomiting, such as pancreatitis and intussusception.
- Emergency cage-side focused ultrasonographic examination** of abdomen is indicated in patients with acute abdominal pain, to evaluate for etiologies that are surgical emergencies, such as septic or bile peritonitis.
- If peritoneal effusion seen, abdominocentesis and immediate in-house cytology are indicated (+/- culture).

DIAGNOSTIC PROCEDURES

- Endoscopy rarely indicated in acute vomiting, except for gastric foreign bodies or gastric ulceration.
- Exploratory celiotomy may be considered with high suspicion for mechanical obstruction, even when not confirmed with imaging.

PATHOLOGIC FINDINGS

Dependent on underlying etiology.

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

- Stable patients, mild vomiting—outpatient medical care. Careful assessment of young patients should be made, as they can become unstable with mild signs.
- Unstable patients, hypovolemic or acute abdominal pain—inpatient medical care.
- Emergency surgery may be indicated—mechanical obstruction, septic or bile peritonitis, volvulus.

NURSING CARE

- Fluid therapy as mandated by hydration/perfusion status.
- Most patients with dehydration/hypovolemia need isotonic crystalloids to replenish losses and provide maintenance.
- Nothing PO—only indicated in patients with mechanical obstruction, severe intractable vomiting, or patients with high risk of aspiration.

ACTIVITY

Activity restriction only required in postoperative care of surgical patients.

DIET

Once vomiting resolves, gradual reintroduction of small amounts of water, then small, frequent meals of bland, highly digestible diet is indicated for 3–5 days, then gradual reintroduction of patient's routine diet and feeding schedule.

CLIENT EDUCATION

Client education on dietary indiscretion, gradual diet changes, and foreign body avoidance may be appropriate.

SURGICAL CONSIDERATIONS

Surgery may be indicated to treat etiology, such as mechanical obstruction.

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

- Anti-emetics not usually needed for mild acute vomiting, but may be needed in more severe cases—5HT₃ antagonists such as ondansetron (0.2–1 mg/kg SC/IV q8h), NK₁ antagonist maropitant (1 mg/kg SC q24h or 2 mg/kg PO q24h), dopamine antagonist and prokinetic metoclopramide (0.2–0.5 mg/kg

SC/PO q6–8h, or 1–2 mg/kg/day as CRI), phenothiazine derivative chlorpromazine (0.5 mg/kg SC q8h). • Refractory vomiting patients (i.e., pancreatitis) may need multi-modal anti-emetics that act on different receptors. • Gastric/duodenal ulcers—proton pump inhibitor such as pantoprazole IV or omeprazole PO (1 mg/kg IV/PO q12h) is preferred treatment. Sucralfate, while used conventionally in ulcers, has only been shown to help cats with esophagitis, and due to impaired absorption of concurrently given medications, and q8 dosing, is of questionable efficacy. • NSAID-induced ulceration—consider misoprostol. • Vestibular mediated—H₁ antagonist like diphenhydramine (2–4 mg/kg PO/IM q6–8h).

CONTRAINdications

- Prokinetic medications should not be given to patients with mechanical obstruction.
- Phenothiazine derivatives—caution in patients with seizures or hypovolemia/hypotension.
- Anticholinergics should not be given, as exacerbation of signs from ileus can result.

PRECAUTIONS

Anti-emetic medications should not be given to patient receiving outpatient care, unless mechanical obstruction has been ruled out.

POSSIBLE INTERACTIONS

Ondansetron IV can react with other medications and precipitate.

ALTERNATIVE DRUGS

Dolasetron, famotidine.

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

- If patient receives anti-emetic with outpatient medical care, and continues to vomit—hospitalize for further diagnostics and inpatient medical care.
- If vomiting not improving, or getting more severe, further diagnostics are warranted.
- If vomiting persists beyond 7 days or recurs despite appropriate therapy, consider chronic vomiting etiologies.

PREVENTION/AVOIDANCE

Avoid rapid diet changes and dietary indiscretion, and institute prophylactic deworming and vaccinations.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia.
- Esophagitis.
- Dehydration and hypovolemia.

EXPECTED COURSE AND PROGNOSIS

- Mild acute vomiting from acute gastritis/gastroenteritis usually self-limiting.
- Mechanical obstruction from foreign bodies has good prognosis with rapid recognition and treatment.
- Other prognoses etiology dependent.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Acute diarrhea, hyporexia.

AGE-RELATED FACTORS

Younger patients more likely to have ingested foreign body or have infectious etiologies.

ZOONOTIC POTENTIAL

Parasitic, protozoal, and bacterial etiologies (*Ancylostoma*, *Campylobacter*, *Giardia*, *Salmonella*).

PREGNANCY/FERTILITY/BREEDING

Misoprostol for treatment of NSAID-induced ulcers is contraindicated in pregnant animals and humans.

SYNONYMS

Emesis

SEE ALSO

- Acute Diarrhea.
- Gastroduodenal Ulcer/Erosion.
- Gastroenteritis, Acute Hemorrhagic Diarrhea Syndrome.
- Pancreatitis – Cats.
- Pancreatitis – Dogs.
- Vomiting, Chronic.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- CRTZ = chemoreceptor trigger zone.
- GI = gastrointestinal.
- NSAID = nonsteroidal anti-inflammatory drug.

INTERNET RESOURCES

- <https://www.avma.org/practicemanagement/clientmaterials/pages/default.aspx>
- <https://veterinarian.vin.com>

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Acknowledgment The author and editor acknowledge the prior contribution of Erin Portillo.



Client Education Handout
available online

ALKALINE HYPERPHOSPHATASEMIA IN DOGS



BASICS

DEFINITION

Increase in serum alkaline phosphatase (ALP) activity above reference interval.

PATHOPHYSIOLOGY

- ALPs are heterogeneous group of isoenzymes that catalyze hydrolysis of organic phosphate esters in extracellular space.
- Membrane-bound enzymes present in liver, bone, placenta, intestine, and kidney.
- Total serum ALP attributed to liver (L-ALP), bone (B-ALP), and glucocorticoid-induced (G-ALP) isoenzymes; proportion of each isoenzyme changes with age in normal dogs.
- Serum ALP activity increases with cholestatic, necroinflammatory, and neoplastic injury; many hepatic and nonhepatic causes; affected dogs often asymptomatic.
- Anticonvulsants (phenobarbital, primidone, phenytoin) and steroids can induce L-ALP synthesis; steroids, inflammation, and chronic disease can induce G-ALP synthesis.
- ALP has high sensitivity but poor specificity for hepatobiliary disease; reflects common induction of enzyme synthesis due to nonhepatic causes, i.e., “reactive hepatopathy.”
- Increased ALP activity with concurrent increase in GGT activity increases specificity for hepatobiliary disease.

SYSTEMS AFFECTED

- Multiple organ systems can influence ALP synthesis.
- Increased ALP activity does not cause direct damage to other organ systems.

GENETICS

- Benign familial alkaline hyperphosphatasemia in Siberian huskies—presumed autosomal.
- Vacuolar hepatopathy of Scottish terriers—breed relationship.

INCIDENCE/PREVALENCE

Increased ALP activity is common biochemical abnormality in dogs.

SIGNALMENT

- Any age, breed, or sex.
- Young dogs, <1 year of age—increased B-ALP activity.
- Siberian huskies and Scottish terriers.
- Older dogs—conditions causing increased L-ALP, G-ALP, and/or B-ALP activity.

SIGNS

General Comments

- Many dogs with increased ALP activity are asymptomatic.
- Dogs with hepatic or nonhepatic disorders causing increased ALP may be asymptomatic or have clinical signs related to underlying disorder.
- Dogs with drug-induced elevations of ALP may have clinical signs related to drug side effects.

Historical Findings

- Dependent on cause.
- Medication history important, including exposure to topical/ocular medications used by humans.

Physical Examination Findings

- Highly variable depending on cause; often normal.
- Hepatomegaly or microhepatica.
- Jaundice.
- Abdominal pain.
- Musculoskeletal—pendulous abdomen, muscle atrophy, lameness, difficulty walking, palpable bony swelling.
- Dermatologic—alopecia, cutaneous hyperpigmentation, comedones, thin skin, pyoderma, calcinosis cutis.

CAUSES

- Age and breed (see Signalment).
- Drug induced.
- Bone-related disorders—neoplasia, osteomyelitis, hyperparathyroidism (primary or secondary), healing fractures.
- Chronic stress, acute-phase response (endogenous cortisol).
- Endocrinopathies (hyperadrenocorticism, diabetes mellitus, hypothyroidism).
- Primary hepatobiliary disorders.
- Extrahepatic disorders—extrahepatic biliary obstruction (EHBO), pancreatic/intestinal/other inflammation, neoplasia.
- Infection—Leptospirosis, sepsis, viral.
- Systemic inflammation/infection causing ischemic injury/cholestasis.
- Hepatic or nonhepatic neoplasia (e.g., benign or malignant mammary tumors).

RISK FACTORS

- Age (young).
- Breed—Siberian husky, Scottish terrier.
- Breed association to conditions causing alkaline hyperphosphatasemia (e.g., Shetland sheepdog predisposition to gallbladder mucocele).



DIAGNOSIS

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Corticosteroids, certain anticonvulsants.

Disorders That May Alter Laboratory Results

- Severe hemolysis (>500 hemolysis index) can falsely elevate ALP.
- Lipemia and icterus have no significant effect on ALP.

CBC/BIOCHEMISTRY/URINALYSIS

- Thrombocytosis possible with hyperadrenocorticism and pancreatic, gastrointestinal disease.
- Thrombocytopenia possible with leptospirosis, hepatic failure, neoplasia.
- Leukocytosis or leukopenia with left shift, monocytosis with sepsis, systemic inflammation.
- Stress leukogram with hyperadrenocorticism.
- Concurrent elevation of other liver enzyme activities including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and/or gamma glutamyltransferase (GGT), depending on underlying cause.
- ± markers of hepatic synthetic dysfunction (hypalbuminemia, hypoglycemia, hypcholesterolemia, decreased blood urea nitrogen [BUN]); many primary hepatic disorders.

- Hyperbilirubinemia in EHBO, end-stage chronic hepatopathies, acute hepatic toxicities, infections.
- Hypercholesterolemia with many causes of cholestasis, endocrinopathies.
- Urinalysis—proteinuria with hyperadrenocorticism, other liver disorders; dilute urine, bacteriuria, pyuria with endocrinopathies; glucosuria with diabetes mellitus, copper-associated hepatopathy; ammonium biurate crystalluria with portosystemic vascular anomaly (PSVA; young dogs).
- Conditions with often sole increase in serum ALP include idiopathic vacuolar hepatopathy, hepatic nodular hyperplasia, drug-induction breed-related disorders, some hepatic neoplasias, sudden acquired retinal degeneration (SARDs).
- Hyperphosphatemia, hypercalcemia (young growing dogs, usually mild).
- Hyperglycemia—mild with hyperadrenocorticism.
- Azotemia—prerenal or renal with pancreatitis, pyelonephritis, Leptospirosis.

OTHER LABORATORY TESTS

- Serum bile acids; redundant test if hepatic hyperbilirubinemia.
- Testing for endocrine disorders—hypothyroidism or hyperadrenocorticism based on clinical signs, physical exam findings, and associated laboratory abnormalities.
- Infectious disease testing—leptospirosis PCR, microagglutination test (MAT), immunoglobulin (Ig) M; urine, bile cultures; tick-borne disease screening.
- Blood pressure measurement.
- Urine protein qualitative; quantitative with protein; creatinine if inactive sediment and culture negative.

IMAGING

- Radiographs—for liver most useful for hepatomegaly, microhepatica; nonhepatic findings may also be identified (pancreatitis, ascites, cystoliths, pyometra, pleural effusion).
- Sonographic evaluation for hepatic parenchymal abnormalities (hyper- or hypoechoic nodules, heterogeneity, hyper- or hypoechoic hepatic echogenicity; changes in echodensity, echotexture; microhepatica, hepatomegaly, hepatic masses), biliary tract (gallbladder mucocele, gallbladder wall abnormalities, cholelithiasis, choledochitis, biliary tract neoplasia), pancreas, adrenal enlargement, neoplasia.
- Abdominal CT ± angiography may be useful if suspicion of pancreatitis, gallbladder disease, or hepatic vascular disorders.

DIAGNOSTIC PROCEDURES

- Hepatic fine-needle aspirate (FNA) for cytology; caution as cytologic and histologic agreement may be as low as 30%; cytology is not diagnostic for many hepatobiliary conditions.
- FNA of liver tends to agree with histology in cases of vacuolar hepatopathy, hepatic lipidosis, and some neoplasias (e.g., lymphoma).
- If primary hepatobiliary

ALKALINE HYPERPHOSPHATASEMIA IN DOGS

(CONTINUED)

disease suspected after elimination of other causes, hepatic biopsy may be warranted; biopsy at least three liver lobes; laparoscopic or wedge samples preferred; Tru-Cut® needle biopsy may be too small, use 14–16G needle.

PATHOLOGIC FINDINGS

Variable depending on cause; see specific chapters for pathologic findings.



TREATMENT

APPROPRIATE HEALTH CARE

- Dictated by underlying disorder.
- Asymptomatic dogs often do not require any specific treatment.

NURSING CARE

Variable as above.

ACTIVITY

Alteration of activity typically unnecessary.

DIET

- Dietary alteration unnecessary in most cases.
- Dietary fat restriction in some cases (pancreatitis, hypertriglyceridemia, obesity, chronic EHBO).
- Commercial liver diets rarely indicated (see Portosystemic Vascular Anomaly, Congenital; Hepatic Encephalopathy).

CLIENT EDUCATION

- Dictated by underlying disorder.
- Clients with asymptomatic dogs should be counseled on potential for subsequent development of endocrine disease, neoplasia (Scottish terriers), other causes.
- Liver biopsy necessary for definitive diagnosis if other underlying causes are ruled out and/or if ALP value continues to elevate; rarely pursued initially in asymptomatic dogs without other underlying disorder.

SURGICAL CONSIDERATIONS

- Refractory hypotension is common peri- and postoperative complication in dogs with obstructive cholestasis (see EHBO).
- Dogs with end-stage hepatic disease (cirrhosis) may have alterations of coagulation and/or higher anesthetic risk.



MEDICATIONS

DRUG(S) OF CHOICE

- Specific for underlying cause.
- Certain drugs/supplements have general hepatobiliary protective effects; see Hepatosupportive Therapies.

CONTRAINdications

Depending on cause, drugs requiring hepatic metabolism or capable of causing hepatotoxicity should be limited or avoided when possible.

PRECAUTIONS

Drugs known to induce elevation of ALP may confuse monitoring of underlying condition.



FOLLOW-UP

PATIENT MONITORING

- Dependent on the underlying cause.
- Suspected benign causes of ALP elevation can be monitored for elevations in other serum liver enzyme activities, further elevation in ALP, and/or synthetic hepatic function tests.

EXPECTED COURSE AND PROGNOSIS

- Dependent on underlying cause.
- Increased ALP activity for which underlying cause cannot be found after complete diagnostic evaluation may be benign.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Elevation of other serum liver enzymes, hyperbilirubinemia, alterations in hepatic synthetic function tests.

AGE-RELATED FACTORS

Young dogs (see Signalment).

ZOONOTIC POTENTIAL

Leptospirosis has high zoonotic potential; see Leptospirosis.

PREGNANCY/FERTILITY/BREEDING

Placental ALP can increase in late-term pregnant cats; not reported in dogs.

SYNONYMS

- Elevated ALP.
- Serum alkaline phosphatase (SAP).

SEE ALSO

- Bile Duct Obstruction (Extrahepatic).
- Cholangitis/Cholangiohepatitis Syndrome.
- Cholecystitis and Choledochitis.
- Cholelithiasis.
- Copper Associated Hepatology.
- Glycogen-Type Vacuolar Hepatopathy
- Hepatic Failure, Acute.
- Hepatic Nodular Hyperplasia and Dysplastic Hyperplasia.
- Hepatitis, Chronic.
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs.
- Leptospirosis.
- Pancreatitis—Dogs.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- AST = aspartate aminotransferase.
- B-ALP = bone isoform.
- BUN = blood urea nitrogen.
- G-ALP = glucocorticoid isoform.
- EHBO = extrahepatic biliary obstruction.
- FNA = fine-needle aspirate.
- GGT = gamma glutamyltransferase.
- Ig = immunoglobulin.
- L-ALP = liver isoform.
- MAT = microagglutination test.
- PSVA = portosystemic vascular anomaly.
- SAP = serum alkaline phosphatase.
- SARDS = sudden acquired retinal degeneration.

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BASICS

DEFINITION

A process in the body that leads to an increase in pH above the reference interval. An increase in blood pH is specifically termed alkalemia. Associated with an increase in plasma bicarbonate concentration (HCO_3^- ; dogs, >24 mEq/L; cats, >22 mEq/L) and base excess (BE; >4 mmol/L) with a compensatory increase in carbon dioxide tension (PCO_2).

PATHOPHYSIOLOGY

- Metabolic alkalosis may develop from either a *gain of bicarbonate* or a *loss of acid*:
- *Bicarbonate gain* subsequent to: contraction alkalosis due to free water deficit; iatrogenic administration of alkalinizing therapy (e.g., NaHCO_3); metabolism of organic ions (lactate, citrate, acetate, and ketones); hypokalemia; and renal ammoniogenesis.
- *Acid loss* subsequent to: gastric or renal acid loss (loop or thiazide diuretic); mineralocorticoid excess; presence of nonreabsorbable anions; decreased weak acids (hypalbuminemia, hypophosphatemia). ◦ Renal HCO_3^- excretion very efficient in eliminating an excess HCO_3^- load, but hindered by decreased effective circulating volume; hypokalemia, hypochloremia, and hyperaldosteronism; metabolic alkalosis persists only if renal excretion of HCO_3^- is impaired, which primarily occurs from continued high rate of alkali administration, or some stimulus for kidneys to retain Na^+ in presence of a relative Cl^- deficit. • *Hypochloremic (corrected)* metabolic alkalosis results from loss of fluid rich in Cl^- and hydrogen ion (H^+), primarily from alimentary tract or kidneys; loss of Cl^- and H^+ associated with increase in plasma HCO_3^- concentration; with Cl^- loss and volume depletion, kidneys reabsorb Na^+ with HCO_3^- instead of Cl^- , perpetuating metabolic alkalosis. Hypochloremic alkalosis divided into *chloride-responsive* and *chloride-resistant*:
- *Chloride-responsive* results primarily from loss of Cl^- rich fluid and characterized by decreased extracellular fluid volume, hypochloremia, and low urinary Cl^- concentration; this type of alkalosis responds to administration of chloride salt. ◦ *Chloride-resistant* characterized by excessive mineralocorticoid leading to increased effective circulating volume and is not responsive to chloride salt. • *Hypokalemia* may contribute to metabolic alkalosis by shifting H^+ intracellularly; stimulating apical H^+/K^+ ATPase in collecting duct; stimulating renal ammoniogenesis; impairing Cl^- reabsorption in distal nephron; and reducing glomerular filtration rate (GFR), which decreases filtered load of HCO_3^- and, in presence of volume depletion, impairs renal excretion of excess HCO_3^- . • *Hypoalbuminemic* alkalosis is due to

decrease in plasma albumin concentration; plasma albumin is a weak acid. • *Compensatory* metabolic alkalosis occurs in response to respiratory acidosis; this is associated with low pH and increased PCO_2 .

SYSTEMS AFFECTED

- Nervous—muscle twitching and seizures occur rarely in dogs. Metabolic alkalosis and associated hypokalemia may precipitate hepatic encephalopathy in patients with liver failure.
- Urinary—kidneys rapidly and effectively excrete excessive alkali. In patients with Cl^- deficiency and volume depletion, kidneys cannot excrete excess alkali. Therefore, metabolic alkalosis is maintained. In these patients, Cl^- administration is required for renal compensation to occur. Volume expansion will hasten compensation. Patients with mineralocorticoid excess have excessive Cl^- loss. Therefore, Cl^- administration does not lead to hyperchloremia and correction of metabolic alkalosis (so-called chloride-resistant metabolic alkalosis). • Respiratory—low $[\text{H}^+]$ (increased pH) decreases alveolar ventilation. Hypoventilation increases PCO_2 and helps offset the effects of high plasma HCO_3^- on pH. In dogs, for each 1 mEq/L increase in plasma HCO_3^- there is an expected increase of approximately 0.7 mmHg in PCO_2 . Limited data available for cats, but degree of respiratory compensation appears to be similar.

SIGNALMENT

Any breed, age, or sex of dog and cat.

SIGNS

Historical Findings

- Administration of loop diuretics (e.g., furosemide) or thiazides. • Vomiting.

Physical Examination Findings

- Signs related to underlying disease or accompanying potassium depletion (e.g., weakness, cardiac arrhythmias, ileus).
- Muscle twitching caused by low ionized calcium concentration. • Dehydration in volume-depleted patients. • Muscle twitching and seizures in patients with neurologic involvement (rare).

CAUSES

- *Chloride-responsive*—gastrointestinal losses (e.g., gastric vomiting, nasogastric tube suctioning); renal losses (diuretic therapy); and rapid correction of chronic hypercapnia (respiratory acidosis). • *Chloride-resistant*—hyperadrenocorticism and primary hyperaldosteronism. • *Oral administration of alkalinizing agents*—sodium bicarbonate or other organic anions with Na^+ (e.g., lactate, acetate, gluconate); administration of cation-exchange resin with nonabsorbable alkali (e.g., phosphorus binders).
- *Hypoalbuminemia*—liver disease, protein-losing nephropathy, protein-losing enteropathy.
- *Free water deficit*—diabetes insipidus; water

deprivation; postobstructive diuresis; polyuric renal failure. • *Hypokalemia*.

RISK FACTORS

- Administration of loop or thiazide diuretics.
- Vomiting. • Stomach drainage. • Diseases associated with hypoalbuminemia (e.g., protein-losing nephropathy, liver failure).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

High plasma HCO_3^- and hypochloremia may also occur in animals compensating for chronic respiratory acidosis, in which PCO_2 is high and pH is low despite high HCO_3^- and low Cl^- concentration; blood gas determination is required to differentiate.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

None

Disorders That May Alter Laboratory Results

- Too much heparin (>10% of sample) decreases pH, PCO_2 , and HCO_3^- . • Blood samples stored at room temperature for more than 15 minutes have low pH because of increased PCO_2 . • Exposure to room air decreases PCO_2 . • Venous samples may have pH 0.5–1 unit lower and PCO_2 5–10 mmHg higher than arterial sample.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- High total CO_2 (total CO_2 in samples handled aerobically closely approximates HCO_3^-). • Low blood ionized calcium concentration. • Serum electrolyte abnormalities vary with underlying cause.
- *Hypochloremia*—consider hypochloremic metabolic alkalosis, the most common reason for metabolic alkalosis in dogs and cats, which usually results from diuretic administration or vomiting of stomach contents. • High Na^+ but normal Cl^- concentration—consider chloride-resistant metabolic alkalosis (e.g., hyperadrenocorticism or primary hyperaldosteronism) or administration of alkali. • *Hypoalbuminemia*—consider hypoalbuminemic metabolic alkalosis (e.g., liver failure, protein-losing enteropathy, and protein-losing nephropathy). In vitro, a 1 g/dL decrease in albumin concentration is associated with an increase in pH of 0.093 in cats and 0.047 in dogs. • *Hypokalemia*—likely results from intracellular potassium shifting due to metabolic alkalosis or underlying problem (e.g., vomiting of stomach contents or loop diuretic administration). • *Urinary Cl^- concentrations*—chloride-responsive metabolic alkalosis characterized by urine Cl^- concentrations <10 mEq/L, whereas

ALKALOSIS, METABOLIC

(CONTINUED)

chloride-resistant metabolic alkalosis associated with urine Cl^- concentrations $>20 \text{ mEq/L}$.

OTHER LABORATORY TESTS

Blood gas analysis reveals high HCO_3^- , PCO_2 , pH, and BE. Unlike HCO_3^- , BE is independent of changes in metabolic acid-base status, and is thus more reliable measure of metabolic acid-base changes.

IMAGING

None

DIAGNOSTIC PROCEDURES

- Blood pressure—combination of hypertension, hypernatremia, and hypokalemia with metabolic alkalosis may indicate presence of hyperaldosteronism.
- Diagnostic testing for hyperadrenocorticism or primary hyperaldosteronism (e.g., plasma renin activity and aldosterone concentration).



TREATMENT

- Acid-base disturbances are secondary phenomena; diagnosis and treatment of underlying disease process are essential to successful resolution of acid-base disorders.
- Severe alkalemia is uncommon, but may be life-threatening. Patients with chronic respiratory disease and respiratory alkalosis are at risk of developing severe alkalemia if they start vomiting or receive diuretics.
- Discontinue drugs that may cause metabolic alkalosis.
- *Chloride-responsive*—fluid of choice for patients with volume depletion is 0.9% saline or balanced isotonic replacement fluid supplemented with KCl; patients with hypokalemia may require large amounts of KCl (see Hypokalemia).
- *Chloride-resistant* metabolic alkalosis can only be corrected by resolution of underlying disease; metabolic alkalosis usually mild in these patients.
- If metabolic alkalosis associated with hypokalemia and total body potassium deficits, correcting deficit with KCl is particularly effective way to reverse alkalosis.

NURSING CARE

Supportive care to maintain normal hydration, plasma volume, and adequate nutrition.



MEDICATIONS

DRUG(S) OF CHOICE

Hypochloremic Alkalosis

- If chloride-responsive alkalosis occurs during edematous state (e.g., congestive heart

failure), oral administration of compounds containing Cl^- without Na^+ is recommended to correct alkalosis; if diuresis needed due to volume overload, carbonic anhydrase inhibitor (e.g., acetazolamide) or potassium-sparing diuretic (e.g., spironolactone, amiloride) can be used to correct alkalosis.

- H₂-blocking agents such as famotidine decrease gastric acid secretion and may be considered as adjunctive therapy if gastric losses are ongoing.
- Antiemetics may help prevent further gastric acid loss.

Hypoalbuminemic Alkalosis

- Treatment for hypoalbuminemic alkalosis should be directed at underlying cause and decreased colloid oncotic pressure.
- Enteral nutrition will facilitate endogenous albumin production.
- Consider species-specific plasma or albumin (e.g., canine albumin) therapy.

CONTRAINDICATIONS

- Avoid chloride-free fluids—they may correct volume depletion, but will not correct hypochloremic alkalosis.
- Avoid using salts of potassium without Cl⁻ (e.g., potassium phosphate)—potassium will be excreted in urine and will correct neither alkalosis nor potassium deficit.

PRECAUTIONS

Do not use distal-acting, potassium-sparing diuretics (e.g., spironolactone) in volume-depleted patients.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

Acid-base status—frequency dictated by underlying disease and patient response to treatment.

POSSIBLE COMPLICATIONS

- Hypokalemia.
- Neurologic signs.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypokalemia.
- Hypochloremia.

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYNS

- Nonrespiratory alkalosis.
- Chloride-responsive metabolic alkalosis—metabolic alkalosis that responds to Cl⁻ administration.
- Chloride-resistant alkalosis—metabolic alkalosis secondary to increased mineralocorticoid activity that does not respond to Cl⁻ administration.
- Hypochloremic alkalosis—metabolic alkalosis caused by low Cl⁻ concentration.
- Hypoalbuminemic alkalosis—metabolic alkalosis caused by low albumin concentration.
- Concentration alkalosis—metabolic alkalosis resulting from decreased free water in plasma.
- Contraction alkalosis—metabolic alkalosis formerly attributed to volume contraction, but now known to be caused by Cl⁻ depletion; volume depletion is common but not essential feature.

SEE ALSO

- Hypochloremia.
- Hypokalemia.

ABBREVIATIONS

- BE = base excess.
- GFR = glomerular filtration rate.
- H⁺ = hydrogen ion.
- HCO_3^- = bicarbonate.
- PCO_2 = carbon dioxide tension.

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Consulting Editor J.D. Foster

Acknowledgment The authors and editors acknowledge the prior contribution of Lee E. Palmer.



BASICS

DEFINITION

Common problem, seen as abnormal lack of hair coat.

PATHOPHYSIOLOGY

Specific and unique for each cause.

SYSTEMS AFFECTED

- Endocrine/metabolic.
- Hemic/lymphatic/immune.
- Skin/exocrine.

SIGNALMENT

- Age, breed, or sex predilections specific to each condition.
- Neoplastic- and paraneoplastic-associated alopecias generally recognized in older cats.

SIGNS

Depends on specific diagnosis. Knowing whether cat is pruritic is a very important part of workup for alopecia.

CAUSES

- Infectious—dermatophytosis, parasitic (mites, fleas), superficial and deep bacterial infections, viral: herpesvirus, papillomaviral plaques, feline immunodeficiency virus (FIV)—and feline leukemia virus (FeLV)—associated giant cell dermatosis.
- Hypersensitivity—atopy/allergy, oral medication reaction, topical medication reaction.
- Disorders of hair follicle cycling—telogen effluvium, Cushing's (iatrogenic and hyperadrenocorticism), hypothyroidism (iatrogenic).
- Congenital—hair follicle dystrophy, alopecia universalis (normal in sphynx cats), feline hypotrichosis (Siamese and Rex cats), pinnal hypotrichosis.
- Environmental—solar damage, burns, frostbite, scarring.
- Ischemic—post matting alopecia, post traumatic.
- Autoimmune—alopecia areata, pemphigus foliaceus.
- Neoplastic—epitheliotropic lymphoma, mastocytosis, squamous cell carcinoma in situ.
- Manifestation of internal disease—sebaceous adenitis (thymoma-associated exfoliative dermatitis), paraneoplastic alopecia, mural lymphocytic folliculitis, hyperthyroidism, hyperadrenocorticism, diabetes.
- Psychogenic—compulsive disorder.

RISK FACTORS

FeLV/FIV—reported risk for demodicosis (not all cases associated with viral infection).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Infectious

- Dermatophytosis.
- Parasites
 - Mites—*Demodex gatoi*, *cheyletiella*, *nothoedres* are often pruritic and scaly; *Demodex cati* cause hair loss with minimal inflammatory change in many cases.
 - Fleas can cause alopecia if patient is hypersensitive and pruritic; severe on caudal dorsum, abdomen, and around ears.
 - Tick attachment sites can cause alopecic granuloma.
- Bacterial:
 - Alopecia secondary to deep bacterial infection.
 - Superficial bacterial infections secondary to underlying cause.
- Viral:
 - Herpesvirus can cause neuralgia, pruritus, alopecia, and ulcerated eosinophilic skin lesions, most commonly on the face.
 - FIV- and FeLV-associated giant cell dermatosis.
 - Papillomaviral plaques in older cats may transform to squamous cell carcinoma.

Hypersensitivities

- Food, flea bites, or environmental allergens (atopy)—ears, face, and abdomen are most affected.
- Oral medication reactions—severe facial pruritus caused by methimazole: symptoms resolve when medication discontinued.
- Topical parasite preventives—rare cause of alopecia at site of application; usually temporary.

Disorders of Hair Follicle Cycling

- Telogen effluvium:
 - Caused by severe stressful situation or hormonal change such as anesthesia/surgery, parturition, severe illness, drugs.
 - Sudden onset of large symmetric areas of hair thinning or alopecia.
 - Hair regrows over weeks.
- Cushing's syndrome:
 - Long-term (months) corticosteroid administration, oral or injectable.
 - Megestrol acetate administration.
 - Hyperadrenocorticism from adrenal tumor or pituitary tumor.
 - Causes symmetric alopecic and atrophic thin skin, sometimes skin fragility/tearing, ear tips droop.
- Hypothyroidism—iatrogenic is most common cause, due to treatment of hyperthyroidism.

Congenital

- Hair follicle dystrophy/sebaceous gland dystrophy can cause thin hair diffusely or waxy accumulations on the hairs.

- Alopecia universalis (normal in sphynx cats):
 - Hereditary, complete absence of primary hairs; decreased secondary hairs.
 - Sebaceous and apocrine ducts open onto skin surface; oily feel to skin.
 - Wrinkled foreheads; gold eyes; no whiskers; downy fur on paws, tip of tail, and scrotum.
 - Comedones with or without secondary folliculitis.

- Feline hypotrichosis:
 - Siamese and Devon Rex cats (autosomal recessive alopecia).
 - Poorly developed primary telogen hair follicles.
 - Born with normal coat, which becomes thin and sparse as young adult.

Environmental

- Solar damage—skin can be damaged with prolonged sun exposure; most common in outdoor light-colored cats. Areas with thin hair most affected: ears, eyes, and nose; early signs alopecia, scaling, and erythema; can transform to squamous cell carcinoma.
- Burns/frostbite—burns are location dependent sometimes have a drip-like pattern if caused by hot liquid; affect pressure points if due to heating pad. Third-degree burns will have permanent scars. Frostbite commonly affects ear tips and causes alopecia and necrosis.
- Scarring is loss of hair follicles and usually pigment from area of skin.

Ischemic

- Post matting/traction—caused by loss of blood supply to hair follicle due to tight prolonged matting or pulling of hair; usually hair regrows with time.
- Post traumatic—rare, alopecia with little inflammation can be seen with injuries where nerve or blood supply interrupted to the skin.

Autoimmune

- Alopecia areata—rare, alopecia with little outward inflammation, most common on face and head.
- Pemphigus foliaceus—crusting and alopecia on ears, sometimes nose, feet, and other areas; pruritus variable.

Neoplastic

- Epitheliotropic lymphoma—scaly alopecia, eventually plaques and nodules.
- Squamous cell carcinoma in situ—papillomaviral plaques: in older cats, scaly, crusty, often pigmented, multifocal, sometimes pruritic.

Manifestation of Internal Disease

- Thymoma-associated exfoliative dermatitis:
 - Nonpruritic dramatic scaling dermatitis that starts on head and neck.
 - Surgical removal of thymoma resolves dermatitis over 4–5 months.

- Paraneoplastic alopecia:
 - Most cases associated with pancreatic adenocarcinomas, bile duct carcinomas.
 - Nonpruritic alopecia has acute onset, progresses rapidly; bilaterally symmetric, ventrally distributed (also located along bridge of nose and periocular); hair epilates easily; dry fissuring footpads; skin often thin and hypotonic; rapid weight loss.
- Mural lymphocytic folliculitis—sometimes paraneoplastic: alopecia of face, eyelids, muzzle; skin has thick, waxy feel; histologic lymphocytic invasion of follicular outer root sheath and epidermis.
- Hyperthyroidism—alopecia due to self-barbering; can see weight loss as well.
- Hyperadrenocorticism—symmetric, nonpruritic; older cat if natural, any age if iatrogenic; can have severe skin fragility.
- Diabetes—unkempt and unhealthy coat, skin infections.

Psychogenic

Although anxiety may make overgrooming worse from any underlying condition, a pure compulsive disorder is very rare; all other causes of alopecia must be ruled out prior to considering.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities may be noted with diabetes mellitus, hyperadrenocorticism, and hyperthyroidism.

OTHER LABORATORY TESTS

- FeLV and FIV—risk factors for demodicosis and other infections.
- Thyroid hormones—document hyperthyroidism/hypothyroidism.

IMAGING

- Abdominal ultrasound—assess adrenals in hyperadrenocorticism and look for neoplasia in animals with paraneoplastic syndrome.
- Chest radiographs/ultrasound to rule out thymoma.
- CT scan—look for pituitary or other neoplasia tumors in animals with hyperadrenocorticism.

DIAGNOSTIC PROCEDURES

- Skin scrapes.
- Dermatophyte culture.
- Parasite treatment trials, since negative skin scrapes do not rule out all parasites.
- Skin biopsy.
- Shirts/collar to prove self-trauma if pruritus is questioned.
- Food elimination trials if parasites and dermatophytes are ruled out.
- Intradermal allergy testing.



TREATMENT

- See specific chapters for full list of medications, doses, and other therapies.
- If pet is compliant, shampoo and topical therapy may relieve secondary problems such as hyperkeratosis, crusting, or secondary bacterial infections.



MEDICATIONS

DRUG(S) OF CHOICE

- Demodicosis—fluralaner topically as per label every 3 months; lime sulfur dips at weekly intervals for six dips; other mites and fleas also respond to appropriate topical or oral treatments.
- Allergic dermatitis—antihistamines only rarely helpful; novel restricted-ingredient diet; corticosteroids; cyclosporine (5–7 mg/kg/day initially); allergen-specific immunotherapy; ectoparasite control.
- Hyperthyroidism—methimazole, thyroidectomy, or radioactive iodine therapy.
- Diabetes mellitus—regulation of glucose levels (insulin, weight loss, diet).
- Hyperadrenocorticism—discontinue glucocorticoids if iatrogenic; if natural, trilostane, mitotane, and surgery are options.
- Paraneoplastic alopecia—surgical excision of neoplasia; but neoplasia often fatal.
- Epitheliotropic lymphoma—corticosteroids, lomustine.
- Sebaceous adenitis—surgical removal of thymoma, corticosteroids, cyclosporine.
- Squamous cell carcinoma in situ—surgical excision, retinoids (topical and oral), topical imiquimod cream.

PRECAUTIONS

Toxicity with griseofulvin and itraconazole (see Dermatophytosis).



FOLLOW-UP

PATIENT MONITORING

Determined by specific diagnosis.

PREVENTION/AVOIDANCE

Determined by specific diagnosis.

POSSIBLE COMPLICATIONS

Determined by specific diagnosis.

EXPECTED COURSE AND PROGNOSIS

Determined by specific diagnosis.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Dermatophytosis—can cause skin lesions in humans.
- Cheyletiellosis—can cause irritation in humans.

SEE ALSO

- Cheyletiellosis.
- Demodicosis.
- Dermatophytosis.
- Diabetes Mellitus Without Complication—Cats.
- Feline Paraneoplastic Alopecia.
- Flea Bite Hypersensitivity and Flea Control.
- Hyperadrenocorticism (Cushing's Syndrome)—Cats.
- Hyperthyroidism.
- Lymphoma, Cutaneous Epitheliotropic.
- Pemphigus.
- Sebaceous Adenitis, Granulomatous.
- Squamous Cell Carcinoma, Skin.
- Thymoma.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.

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Author Melissa N.C. Eisenschenk
Consulting Editor Alexander H. Werner Resnick

Acknowledgment The author and editors acknowledge the prior contribution of Karen Helton Rhodes.



Client Education Handout
available online



BASICS

DEFINITION

- Common disorder.
- Characterized by complete or partial loss of hair in areas where it is normally present.
- May be associated with multiple causes, be the primary problem, or be secondary to an underlying cause.

PATHOPHYSIOLOGY

- Multiple causes.
- Represents removal of hair or disruption in the growth of the hair from hypersensitivity, infection, genetic abnormality, trauma, immunologic attack, mechanical “plugging,” endocrine abnormalities, neoplasia, drug reaction, and/or blockage of receptor sites for stimulation of hair growth cycle.

SYSTEMS AFFECTED

- Endocrine/metabolic.
- Hemic/lymphatic/immune.
- Skin/exocrine.

SIGNALMENT

Age, breed, and sex predilections are specific to each cause listed.

SIGNS

- May be acute in onset or slowly progressive.
- Multifocal patches of alopecia are associated with folliculitis caused by demodicosis, dermatophytosis, or, most commonly, staphylococcus infection.
- Large, more diffuse areas of alopecia may indicate follicular dysplasia or metabolic component.
- Pattern and degree of hair loss, along with presence of pruritus, are important for establishing differential diagnoses.

CAUSES

- Infectious—dermatophytosis, parasitic (mites, fleas), superficial and deep bacterial infections.
- Hypersensitivity/reaction—atopy/allergy, oral medication reaction, topical medication reaction.
- Disorders of hair follicle cycling—telogen effluvium, Cushing's (iatrogenic and hyperadrenocorticism), hypothyroidism (iatrogenic), alopecia X, seasonal flank alopecia.
- Congenital—hair follicle dystrophy.
- Environmental—solar damage, burns, frostbite, scarring.
- Ischemic—post-matting alopecia, barrette or rubber band too tight, dermatomyositis, post vaccine, vasculitis.
- Autoimmune—alopecia areata, pemphigus foliaceus, sebaceous adenitis, vasculitis.
- Neoplastic—epitheliotropic lymphoma.
- Manifestation of internal disease—hypothyroidism, hyperadrenocorticism.

RISK FACTORS

Chronic corticosteroid use causes hair cycle arrest with other signs of iatrogenic Cushing's.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Multifocal Alopecia

- Demodicosis—partial to complete alopecia with erythema, comedones, and mild scaling; lesions may become inflamed and crusted.
- Dermatophytosis—partial to complete alopecia with scaling, with or without erythema, not usually ring-like.
- Staphylococcal folliculitis—circular patterns of alopecia with epidermal collarettes, erythema, crusting, and hyperpigmented macules.
- Injection/topical medication reactions—inflammation with alopecia and/or cutaneous atrophy from scarring.
- Rabies vaccine vasculitis—well-demarcated patch of alopecia observed 1–3 months post vaccination. Small-breed dogs more predisposed.
- Alopecia areata—noninflammatory areas of complete alopecia.
- Sebaceous adenitis of short-coated breeds—annular to polycyclic areas of alopecia and scaling.

Symmetric Alopecia

- Hyperadrenocorticism—truncal alopecia associated with atrophic skin, comedones, and pyoderma, as well as other systemic signs.
- Hypothyroidism—thinning of truncal haircoat; generalized alopecia is uncommon presentation; alopecic “rat” tail.
- Noninflammatory alopecia (alopecia X)—symmetric truncal alopecia associated with hyperpigmentation; alopecia often starts along collar area of neck; Pomeranian, chow chow, Akita, Samoyed, Keeshonden, Alaskan Malamute, and Siberian husky.
- Hyperestrogenism (females)—symmetric alopecia of flanks and perineal and inguinal regions with enlarged vulva and mammary glands; may also be associated with exogenous hormone exposure.
- Male feminization from Sertoli cell tumor—alopecia of perineum and genital region with gynecomastia.
- Seasonal/cyclic/flank alopecia—common, serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
- Color mutant/dilution alopecia—brittle or coarse hair, thinning of blue or fawn-colored hair coat, and secondary folliculitis; other colors of hair normal.
- Follicular dysplasia—slowly progressive alopecia affecting one color of hair.
- Anagen defluxion and telogen defluxion—acute onset of alopecia due to stressful event.

- Epitheliotropic lymphoma—diffuse, generalized truncal alopecia with scaling and intense erythema; later nodule and plaque formation.

- Pemphigus foliaceus—hair loss associated with scale and crust formation.

- Sebaceous adenitis—hair straightening, thinning, with dry hyperkeratosis; standard poodles and crosses, Havanese, other breeds.

- Allergic dermatitis with secondary infections and self-trauma due to pruritus.

Specific Locations

- Pinnal alopecia/pattern baldness—miniaturization of hairs and progressive alopecia; dachshund, greyhound, American water spaniel, Portuguese water spaniel, Boston terrier, Manchester terrier, whippet, Italian greyhound, Chihuahua.
- Pinnal alopecia with crusting or necrosis—consider vasculitis, which can have many triggers.
- Traction alopecia—hair loss secondary to having barrettes or rubber bands applied to the hair, or prolonged tight matting of the hair.
- Post-clipping alopecia—failure to regrow after clipping associated with slow or arrested hair cycle.
- Melanoderma (alopecia of Yorkshire terriers)—symmetric alopecia of pinnae, bridge of nose, tail, and feet.
- Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
- Black hair follicular dysplasia—alopecia of black-haired areas only.
- Dermatomyositis—alopecia of face, tip of ears, tail, and digits; associated with scale crusting and scarring.

Breed-Related Alopecia

- Alopecia breeds—Chinese crested, Mexican hairless, Inca hairless, Peruvian Inca orchid, American hairless terrier (often associated with comedones, folliculitis, and furunculosis).
- Congenital hypotrichosis—cocker spaniel, Belgian shepherd, poodle, whippet, beagle, French bulldog, Yorkshire terrier, Labrador retriever, bichon frise, Lhasa apso, basset hound.
- Color dilution alopecia—blue or fawn Doberman pinscher, silver Labrador, cream chow chow, blond Irish setter, blue pit bull terrier, other breeds with dilute coat colors.
- Melanoderma with alopecia—Yorkshire terrier.
- Seasonal/cyclic/canine flank alopecia—serpiginous flank alopecia with hyperpigmentation; boxer, English bulldog, Airedale terrier.
- Pinnal alopecia/pattern baldness—miniaturization of hairs and progressive alopecia; dachshund, greyhound, American water spaniel, Portuguese water spaniel, Boston

terrier, Manchester terrier, whippet, Italian greyhound, Chihuahua.

- Noninflammatory alopecia (alopecia X)—symmetric truncal alopecia associated with hyperpigmentation; alopecia often starts along collar area of neck; Pomeranian, chow chow, Akita, Samoyed, keeshond, Alaskan Malamute, Siberian husky.

CBC/BIOCHEMISTRY/URINALYSIS

Rule out metabolic causes such as hyperadrenocorticism.

OTHER LABORATORY TESTS

- Thyroid panel—do not rely on low T_4 (total thyroxine) alone; diagnose hypothyroidism.
- Adrenocorticotrophic hormone (ACTH)-response test, low-dose dexamethasone-suppression test (LDDST), and high-dose dexamethasone-suppression test (HDDST)—evaluate for hyperadrenocorticism.
- Sex hormone profiles (questionable validity, often not useful for diagnosis or therapy).

IMAGING

Ultrasonography—evaluate adrenal glands for evidence of hyperadrenocorticism.

DIAGNOSTIC PROCEDURES

- Cytology.
- Skin scraping.
- Fungal culture.
- Skin biopsy—very useful to evaluate status of follicle/hair growth as well as epidermal changes associated with specific conditions.



TREATMENT

- Treatments depend on the underlying causes of alopecia; see specific chapters for each condition.
- Bathing can be useful as adjunctive therapy for many conditions.



MEDICATIONS

DRUG(S) OF CHOICE

- Demodicosis or other external parasites—isoxazoline antiparasitics as per label.

- Dermatophytosis—terbinafine, ketoconazole, fluconazole, itraconazole, lime sulfur dips, griseofulvin.
- Staphylococcal folliculitis—investigate and treat underlying cause, shampoo and antibiotic therapy.
- Sebaceous adenitis—topical therapy, essential fatty acid supplementation, cyclosporine.
- Iatrogenic Cushing's—stop all glucocorticoids.
- Natural hyperadrenocorticism—trilostane, mitotane, surgical removal of tumor.
- Hypothyroidism—levothyroxine supplementation.
- Follicular dysplasia—control concurrent allergies and infections.
- Alopecia X and seasonal flank alopecia—sometimes responds to melatonin.
- Ischemic lesions—consider pentoxifylline.

CONTRAINDICATIONS

N/A

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

Determined by cause.

POSSIBLE COMPLICATIONS

N/A



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Dermatophytosis can cause skin lesions in humans.

PREGNANCY/FERTILITY/BREEDING

Avoid retinoids and griseofulvin in pregnant animals.

SEE ALSO

- Demodicosis.
- Dermatophytosis.
- Flea Bite Hypersensitivity and Flea Control.
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs.
- Hypothyroidism.
- Lymphoma, Cutaneous Epitheliotropic.
- Pemphigus.
- Sebaceous Adenitis, Granulomatous.
- Sertoli Cell Tumor.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- HDDST = high-dose dexamethasone-suppression test.
- LDDST = low-dose dexamethasone-suppression test.
- T_4 = Total thyroxine.

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Acknowledgment The author and editor acknowledge the prior contribution of Karen Helton Rhodes.



Client Education Handout available online



BASICS

OVERVIEW

- Anal sacs are reservoirs for secretions normally evacuated by compression during defecation.
- Normal gland secretions vary widely in consistency and color.
- Disorders include impaction, infection/sacculitis, and neoplasia.
- Treatment options include manual expression, flushing, antibiotics, and surgical excision.

SIGNALMENT

Impaction/Infection

- Dogs and cats (rarely)—no age or sex predisposition.
- Breeds predisposed (impaction)—smaller breeds (miniature/toy poodle, Chihuahua, American cocker and English springer spaniel).

Neoplasia

- Adenocarcinoma—English cocker spaniel most commonly reported.

SIGNS

Impaction/Infection

- Anal/perianal pruritus—often manifested by “scooting.”
- Hesitancy to defecate.
- Tenesmus.
- Tail chasing.
- Foul-smelling, nonfeces anal discharge.
- Refusal to sit and/or lift tail.
- Cats—excessive licking of the ventral abdomen and tail head.
- Abscess—often unilateral; localized pain and discharge.

Neoplasia

- Mass or swelling in perianal region.
- Tenesmus, constipation, polyuria/polydipsia (due to hypercalcemia with adenocarcinoma).
- L4-Cd myelopathy reported in one cat (adenocarcinoma).

CAUSES & RISK FACTORS

Impaction/Infection

- Predisposing factors—changes in muscle tone, fecal form (soft stool/diarrhea), secretion character/volume leading to decreased/lack of expression; intestinal disease, obesity, endocrine disease.
- Infection/abscess—chronic or recurrent impactions.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Impaction/Infection/Neoplasia

- Hypersensitivity (flea, atopy, food).
- Tapeworm infestation.
- Tail fold bacterial folliculitis.
- Malassezia dermatitis.

- Compulsive disorder (anal licking).
- Colitis or other intestinal disorder.
- Keratinization disorder.
- Anal sac neoplasia (adenocarcinoma, squamous cell carcinoma, melanoma).
- Perianal adenoma, adenocarcinoma.
- Perianal fistulae.

CBC/BIOCHEMISTRY/URINALYSIS

Impaction/Infection

Usually normal.

Neoplasia

Hypercalcemia—anal sac adenocarcinoma.

OTHER LABORATORY TESTS

None unless indicated by an underlying cause.

IMAGING

None unless indicated by an underlying cause.

DIAGNOSTIC PROCEDURES

- Digital palpation of anal sacs—should not be palpable externally.
- Expression of anal sac contents—varies widely in gross appearance and microscopic characteristics.
- Cytology (normal dogs/cats)—one study reports Gram-positive cocci/rods, Gram-negative cocci/rods, yeast, nondegenerate neutrophils without phagocytosis, mononuclear cells, and corneocytes; erythrocytes uncommonly found in dogs, rare in cats. Another study had similar findings but with intracellular bacteria in clinically normal dog anal sacs.

Impaction/Infection

- Cytology—no statistically significant difference in bacterial counts or inflammatory cells found between normal dogs and those with clinical signs of anal sac disease.
- Bacterial culture and susceptibility—*Bacillus*, *Escherichia coli*, *Micrococcus*, *Proteus mirabilis*, *Streptococcus* spp., others possible.

Neoplasia

- Surgical excision with histopathology.



TREATMENT

Impaction/Infection

- Gentle manual expression and/or flushing of contents. Sedation may be necessary to flush severely impacted or painful anal sacs.
- Feeding high-fiber diets may help natural expression of anal sacs.
- Identification of underlying causes of predisposing disease.
- Chronic disease—anal sac excision.
- Infection—infusion of antibiotic and/or corticosteroid medications directly into the anal sacs, drainage of abscesses, use of appropriate oral antibiotics and/or antiyeast medication.

Neoplasia

- Surgical excision and staging; combine with chemotherapy.



MEDICATIONS

DRUG(S) OF CHOICE

Infection

Use of appropriate oral antibiotics: cephalixin (dog, 22–30 mg/kg q12h), amoxicillin trihydrate-clavulanate potassium (dog, 13.75 mg/kg q12h; cat, 62.5 mg/cat q12h), clindamycin (dog, 11–22 mg/kg q24h; cat, 11–30 mg/kg q24h), trimethoprim-sulfamethoxazole (dog, 15 mg/kg q12h); metronidazole (dog, 15–25 mg/kg q12–24h), enrofloxacin (dog, 10–20 mg/kg q24h), orbifloxacin (dog/cat, 5 mg/kg q24h).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Trimethoprim-sulfamethoxazole—Dobermanns highly susceptible to type III hypersensitivity reactions.



FOLLOW-UP

Impaction/Infection

- Reassess patients weekly initially, then as necessary to monitor healing.
- Manually express anal sac contents and/or flush contents until sacs empty without intervention.
- Trimethoprim-sulfamethoxazole—monitor tear production, liver function; affects thyroid serum values.



MISCELLANEOUS

SEE ALSO

- Adenocarcinoma, Anal Sac
- Perianal Fistula

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Acknowledgment The author acknowledges the prior contribution of Alexander H. Werner Resnick.

ANEMIA OF CHRONIC KIDNEY DISEASE



BASICS

OVERVIEW

- Progressive decrease in packed cell volume (PCV), red blood cell (RBC) count, and hemoglobin, and hypoplasia of erythroid elements of bone marrow are predictable features of chronic kidney disease (CKD).
- Anemia is normocytic, normochromic, nonregenerative, and proportional to stage of CKD; underlying cause of anemia is multifactorial.
- Gastrointestinal (GI) blood loss, reduced RBC survival, deficiencies in iron and/or folate, cytokines, and inflammatory mediators may be involved; however, primary cause of anemia in CKD is inadequate production of erythropoietin (EPO) by the kidneys.
- EPO is hormone that regulates bone marrow RBC generation and is produced in peritubular interstitial cells in response to decreased tissue oxygen.

SIGNALMENT

Any patient with advanced CKD—juvenile or acquired.

SIGNS

- Anemia contributes to anorexia, weight loss, fatigue, lethargy, depression, weakness, and behavior changes characterizing CKD.
- Pallor.
- Tachypnea.
- Tachycardia.
- Systolic murmur.

CAUSES & RISK FACTORS

- All inherited, congenital, and acquired forms of CKD.
- Exacerbated by iron deficiency, inflammatory or neoplastic disease, GI bleeding, hemolysis, and myeloproliferative disorders.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Anemia of chronic infectious, inflammatory, or neoplastic disease; myeloproliferative disease; chronic blood loss; aplastic anemia; endocrine disease; drug reaction; chronic immune-mediated, toxic, viral, rickettsial, or parasitic anemia; hemodilution.
- Regenerative anemia excludes diagnosis of anemia of CKD.

CBC/BIOCHEMISTRY/URINALYSIS

- Normocytic, normochromic, hypoproliferative anemia.
- Reticulocytes—low corrected indices and absolute counts ($\leq 10,000/\mu\text{L}$).
- Typically, IRIS stage 3 or greater CKD.

- High blood urea nitrogen (BUN) : creatinine ratio may predict concurrent GI bleeding.

OTHER LABORATORY TESTS

- Serum iron—normal or variably low.
- Transferrin saturation—normal or variably low (<20%).
- Feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), mycoplasma, or rickettsial testing to exclude infection-induced myelodysplasia.
- Serum EPO—inappropriately normal or low.

IMAGING

- Small, irregular kidneys with loss or disruption of renal architecture often seen.
- Less commonly enlarged, polycystic, hydronephrotic, infiltrative.

DIAGNOSTIC PROCEDURES

Bone marrow cytology—erythroid hypoplasia; myeloid : erythroid ratio normal or high; stainable iron normal or low.



TREATMENT

- Stabilize azotemia in patients with uremic crisis.
- Ensure adequate nutrition.
- Stabilize any metabolic derangement (e.g., acidosis) that could contribute to shortened RBC lifespan.
- Minimize micronutrient deficiencies that could reduce RBC production.
- Identify and manage GI bleeding.
- Parenteral iron supplementation if needed.
- Correct systemic hypertension.



MEDICATIONS

DRUG(S) OF CHOICE

Blood Transfusion

- Short-term, rapid correction needed if hypoxic distress (typically PCV $\leq 15\%$)—give compatible packed RBCs.
- May transfuse intermittently for prolonged management, although compatibility issues are likely to occur.
- Preferred treatment is EPO support for progressive or symptomatic anemia.

EPO Replacement

- Darbepoetin alfa (Aranesp[®])—an analogue of recombinant human EPO (r-HuEPO) with prolonged half-life and sustained effects; very effective with less tendency for antibody induction; should be used preferentially to epoetin alfa.
- Target PCV—dogs, 30–35%; cats, 30%.

- Dosage—0.8–1.0 $\mu\text{g}/\text{kg}$ SC once weekly until PCV reaches low end of target, then decrease to q2–4 weeks as needed to maintain target; check PCV first to avoid overtreatment.

- If PCV exceeds target, discontinue until upper target range is achieved, then increase dosing interval.

- Iron dextran (5–10 mg/kg IM) should be administered as needed to normalize serum iron and transferrin saturation before initiating and during EPO treatment; injectable iron more effective than oral preparations.

- r-HuEPO—original synthetic erythropoiesis-stimulating protein, replica of human EPO (Epogen[®] and Procrit[®]); higher potential for anti-r-HuEPO antibody production and pure red cell aplasia (PRCA); use no longer recommended,

Anabolic Steroids

Not indicated.



FOLLOW-UP

PATIENT MONITORING

- PCV and blood pressure.
- Iron and transferrin saturation—at 1, 3, and 6 months, then semiannually.
- Discontinue EPO if patient develops evidence of polycythemia, local or systemic sensitivity, PRCA, or refractory hypertension.

POSSIBLE COMPLICATIONS

EPO Related

- Development of polycythemia, seizures, hypertension, iron depletion, injection pain, and mucocutaneous reactions.
- Development of PRCA during epoetin alfa treatment suggests formation of anti-r-HuEPO antibodies, which neutralize r-HuEPO and native EPO, causing severe anemia in 20–30% of animals; often reversible with cessation of treatment.
- Development of anti-r-HuEPO antibodies occurs in <10% of patients receiving darbepoetin alfa.
- Signs associated with production of anti-r-HuEPO antibodies include decreasing PCV, erythroid hypoplasia, reticulocyte count nearing zero, and myeloid : erythroid ratio ≥ 8 .
- EPO replacements should be used cautiously or withheld if hypertension or iron deficiency develops; treatment can be reinstated once hypertension or iron deficiency is corrected.

Transfusion Related

- Incompatibility reaction.
- Circulatory or iron overload.
- Systemic hypertension.
- Transmissible infection.

EXPECTED COURSE AND PROGNOSIS

- Correction of anemia increases appetite, activity, and quality of life.

(CONTINUED)

- Use of EPO replacement agents requires careful assessment of risks and benefits.
- Short-term prognosis depends on severity of CKD.
- Long-term prognosis is guarded to poor because of underlying CKD.



MISCELLANEOUS

ABBREVIATIONS

- BUN = blood urea nitrogen.
- CKD = chronic kidney disease.
- EPO = erythropoietin.
- FeLV = feline leukemia virus.

- FIV = feline immunodeficiency virus.
- GI = gastrointestinal.
- PCV = packed cell volume.
- PRCA = pure red cell aplasia.
- RBC = red blood cell.
- r-HuEPO = recombinant human erythropoietin.

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Consulting Editor J.D. Foster

Acknowledgment The authors and book editors acknowledge the prior contribution of Ilaria Lippi.

ANEMIA, APLASTIC



BASICS

OVERVIEW

• A disorder of hematopoietic precursor cells characterized by replacement of normal bone marrow with adipose tissue. There is decreased production of granulocytes, erythrocytes, and platelets, resulting in pancytopenia in the peripheral blood. The disease is sometimes also referred to as aplastic pancytopenia. • In the acute form, neutropenia and thrombocytopenia predominate because of the shorter life spans of these cells; in the chronic form, nonregenerative anemia also occurs. In both forms, the bone marrow exhibits variable degrees of panhypoplasia. • Precipitating causes can include infectious diseases, drug or toxin exposure, and starvation; immune-mediated mechanisms are often suspected. • Hemic/lymphatic/immune systems affected.

SIGNALMENT

Dogs and cats, no apparent breed or sex predilection. In one study, the mean age of nine affected dogs was 3 years.

SIGNS

• Acute form—fever, petechial hemorrhages, epistaxis, hematuria, melena; i.e., signs due to neutropenia and thrombocytopenia. • Chronic form—pale mucous membranes, weakness, lethargy; i.e., signs due to anemia, in addition to signs observed in acute forms.

CAUSES & RISK FACTORS

Often not identified.

Infectious Agents

• Feline leukemia virus (FeLV), feline immunodeficiency virus (FIV). • Canine and feline parvovirus. • Rickettsial organisms (e.g., *Ehrlichia* spp.).

Drugs and Chemicals

• Estrogen (exogenous administration, Sertoli and interstitial cell tumors). • Methimazole (cats). • Chemotherapeutic drugs, including azathioprine, cyclophosphamide, cytosine arabinoside, doxorubicin, vinblastine, and hydroxyurea. • Antibiotics, including trimethoprim-sulfadiazine, cephalosporins, and chloramphenicol. • Griseofulvin. • Nonsteroidal anti-inflammatory drugs (NSAIDs), including phenylbutazone and meclofenamic acid. • Fenbendazole, albendazole. • Captopril. • Quinidine. • Thiacetarsamide. • Ionizing radiation. • Mycotoxins (cats).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Causes of pancytopenia with normal to increased bone marrow cellularity (e.g., myelodysplastic syndromes, leukemias, myelofibrosis).

CBC/BIOCHEMISTRY/URINALYSIS

• Leukopenia characterized by neutropenia with or without lymphopenia. • Normocytic, normochromic, nonregenerative anemia. • Thrombocytopenia.

OTHER LABORATORY TESTS

• Immunologic tests for infectious diseases, e.g., serologic titers, ELISA, immunofluorescent antibody (IFA). • PCR for infectious agents. • Positive tests for antierythrocyte antibodies (Coombs' test) and/or antinuclear antibody (ANA) may indicate immune-mediated mechanisms.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

• Bone marrow aspiration—frequently an inadequate or fatty sample is obtained because of decreased hematopoietic tissue and replacement by adipocytes. • Bone marrow core biopsy—permits an evaluation of architecture and reveals hypoplasia of cell lines and replacement by adipose tissue.



TREATMENT

Supportive treatment, antibiotics, blood component therapy, as dictated by clinical condition and results of infectious disease testing.



MEDICATIONS

DRUG(S) OF CHOICE

• Cyclosporine A—10–25 mg/kg PO q12h (dogs), 4–5 mg/kg PO q12h (cats). • Mycophenolate mofetil—10 mg/kg PO/IV q12h. • Recombinant hematopoietic growth factors, e.g., recombinant human granulocyte colony-stimulating factor (rhG-CSF) 5 µg/kg/day SC. • Androgen and corticosteroid administration have been largely unsuccessful.

Other Drugs

• Antibiotics to treat secondary infections if fever and neutropenia present. • Whole or component blood transfusion if indicated.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

• Daily physical examination. • CBC every 3–5 days. • Repeat bone marrow evaluation if necessary.

PREVENTION/AVOIDANCE

• Castration of cryptorchid males (to prevent development of Sertoli or interstitial cell tumors). • Vaccination for infectious diseases. • Frequent monitoring of CBC in cancer patients receiving chemotherapy or radiation.

POSSIBLE COMPLICATIONS

• Sepsis. • Hemorrhage.

EXPECTED COURSE AND PROGNOSIS

• Guarded to poor. • Recovery of hematopoiesis may take weeks to months, if it occurs at all. • Spontaneous recovery occasionally occurs, especially in younger animals.



MISCELLANEOUS

SEE ALSO

Pancytopenia.

ABBREVIATIONS

- ANA = antinuclear antibody.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- IFA = immunofluorescent antibody (test).
- NSAID = nonsteroidal anti-inflammatory drug.
- rhG-CSF = recombinant human granulocyte colony-stimulating factor.

Suggested Reading

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BASICS

OVERVIEW

- Heinz bodies occur in red blood cells (RBCs) following damage from chemical or dietary oxidants, can cause hemolytic anemia.
- When oxidants overwhelm protective reductive pathways in RBCs, denaturation of hemoglobin (Hb) causes precipitation and attachment to cell membrane.
- RBCs with Heinz bodies are removed by splenic macrophages, and occasionally undergo intravascular lysis, forming ghost cells.
- The spleen may occasionally remove Heinz bodies, resulting in spherocytes.
- Cats more susceptible to Heinz body formation because have less reductive enzymatic capacity and closed splenic circulation, preventing macrophages from removing Heinz bodies.
- Healthy cats may have low numbers of Heinz bodies without anemia.
- Heinz bodies reported in patients with hyperthyroidism, lymphoma, and diabetes mellitus.
- Heinz bodies may be accompanied by methemoglobinemia (Hb containing Fe³⁺) and/or eccentrocytes (indicating oxidative damage to RBC membranes).

SIGNALMENT

No species, sex, breed, or age disposition.

SIGNS

Historical Findings

- Oxidant exposure.
- Sudden onset of weakness, lethargy, or anorexia secondary to anemia.
- Signs related to underlying disease if present.

Physical Examination Findings

- Pale, occasionally icteric mucous membranes, dark or chocolate-colored if methemoglobinemia.
- Tachypnea, tachycardia.

CAUSES & RISK FACTORS

- Dietary—onions (raw, cooked, dehydrated, powdered), garlic, propylene glycol (cats).
- Drugs—acetaminophen, phenacetin (cats), phenazopyridine (cats), methylene blue, vitamin K1 or K3 (dogs), DL-methionine (cats), benzocaine, phenylhydrazine (dogs), propofol (cats).
- Miscellaneous—zinc (bolts, pennies minted after 1982, dermatologic or sun creams), naphthalene (mothballs), skunk musk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Immune-mediated or hemoparasitic hemolysis.

CBC/BIOCHEMISTRY/URINALYSIS

- Diagnosis of Heinz body anemia requires regenerative anemia, evidence of hemolytic process, presence of Heinz bodies in peripheral blood, and elimination of other causes of hemolysis or blood loss.
- Regenerative anemia; severity depends on dose and duration of oxidant exposure.
- Hb concentration and mean corpuscular hemoglobin concentration (MCHC) may be falsely increased due to Heinz body interference with measurement.
- Heinz bodies on routinely stained blood smear appear as small, nonstaining to pale red, round inclusions that may protrude from RBC surface.
- Single, small (<0.5 µm) Heinz bodies may be found in cats without anemia, but large or multiple Heinz bodies in anemic cat suggest hemolytic anemia.
- Dogs may have concurrent eccentrocytosis.
- Hyperbilirubinemia, bilirubinuria, hemoglobinemia, and hemoglobinuria possible with intravascular hemolysis.

OTHER LABORATORY TESTS

- New methylene blue stains Heinz bodies blue, making them easy to identify and quantify on a blood smear.
- Measure methemoglobin or perform spot test if blood is dark or chocolate-colored.
- Serum zinc concentration.

IMAGING

Abdominal radiographs may reveal metallic foreign bodies contributing to zinc toxicity.

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Immediate identification and removal of oxidant may be sufficient, though often takes several days after exposure for severity of anemia to reach nadir.
- Treatment depends on severity and may include IV fluids, RBC transfusions, oxygen, and restricted activity.
- Endoscopy or surgery to remove metallic items in gastrointestinal tract.



MEDICATIONS

DRUG(S) OF CHOICE

- Acetaminophen toxicity in cats—N-acetylcysteine (Mucomyst®) 140 mg/kg PO/IV, followed by seven additional treatments of 70 mg/kg PO/IV q8h.
- Ascorbic acid (vitamin C) 30 mg/kg PO q6-12h, to reduce methemoglobin concentrations.

Alternative Drug(s)

Use of dietary antioxidants (e.g., bioflavonoids) is controversial, but may help prevent further formation of Heinz bodies.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Administration of methylene blue to treat methemoglobinemia may exacerbate Heinz body formation.



FOLLOW-UP

PATIENT MONITORING

Serial CBCs and review of blood smears to assess RBC regeneration and disappearance of Heinz bodies.

PREVENTION/AVOIDANCE

Counsel clients about identifying and preventing exposure to oxidant compounds.

POSSIBLE COMPLICATIONS

Without proper treatment and removal of oxidant, condition can be fatal.

EXPECTED COURSE AND PROGNOSIS

Prognosis is good with removal of oxidant and supportive care once hemolytic crisis is over.



MISCELLANEOUS

SEE ALSO

- Acetaminophen (APAP) Toxicosis.
- Methemoglobinemia.
- Zinc Toxicosis.

ABBREVIATIONS

- Hb = hemoglobin.
- MCHC = mean corpuscular hemoglobin concentration.
- RBC = red blood cell.

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Jennifer S. Thomas.

A ANEMIA, IMMUNE-MEDIATED



BASICS

DEFINITION

Accelerated removal or hemolysis of red blood cells (RBCs) due to a type II hypersensitivity reaction.

PATHOPHYSIOLOGY

- Antibodies form against endogenous RBC antigens (primary/nonassociative immune-mediated hemolytic anemia [IMHA]), or RBC membrane antigens, or antigens altered by infectious organisms, drugs, or neoplasia (secondary/associative IMHA).
- Immunoglobulin deposited on RBC membrane, causing either direct intravascular hemolysis or accelerated extravascular removal by monocyte/macrophage system.
- Intravascular hemolysis occurs when adsorbed antibodies (especially immunoglobulin [Ig] M) activate complement.
- Extravascular removal of RBCs occurs when RBCs coated with antibodies (especially IgG) are engulfed by splenic macrophages.
- RBC agglutination occurs when IgM or high titers of IgG causes RBC bridging.
- Nonregenerative IMHA caused by immune-mediated destruction of RBC precursors in bone marrow.

SYSTEMS AFFECTED

- Hemic/lymphatic/immune—destruction of RBCs, release of proinflammatory mediators, disseminated intravascular coagulation (DIC).
- Cardiovascular—signs of anemia, thromboembolism.
- Hepatobiliary—hyperbilirubinemia, icterus, bilirubinuria; centrilobular necrosis.
- Respiratory—tachypnea (secondary to anemia or inflammation), hypoxemia (pulmonary thromboembolism [PTE]).
- Integument—rare: cold-type IMHA causes necrosis of extremities and ear tips.

GENETICS

Cocker spaniels are at increased risk.

INCIDENCE/PREVALENCE

Most common hemolytic anemia of dogs, relatively rare in cats.

GEOGRAPHIC DISTRIBUTION

Secondary IMHA may have higher prevalence where associated infectious diseases endemic; incidence may vary seasonally.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Cocker spaniel, English springer spaniel, Old English sheepdog, Doberman pinscher, collie, bichon frise, miniature pinscher, Finnish spitz.
- Domestic shorthair cats.

Mean Age and Range

- Dogs—mean age 5–6 years (range: 1–13 years).
- Cats—mean age 2 years (range: 0.5–9 years).

Predominant Sex

- Female dogs at higher risk.
- Male cats overrepresented.

SIGNS

Historical Findings

- Lethargy/weakness/collapse.
- Anorexia.
- Dyspnea, tachypnea.
- Vomiting and/or diarrhea.
- Pigmenturia.
- Pica (cats).

Physical Examination Findings

- Pale mucous membranes, tachycardia, tachypnea.
- Splenomegaly/hepatomegaly.
- Icterus and pigmenturia (hemoglobin or bilirubin).
- Fever/lymphadenopathy.
- Systolic heart murmur.
- Petechia, ecchymoses, or melena (if concurrent thrombocytopenia or DIC).
- Other findings possible (e.g., joint pain) when IMHA is component of systemic lupus erythematosus (SLE).
- Necrosis of extremities and ear tips in cold-type IMHA (rare).

CAUSES & RISK FACTORS

Primary IMHA

Poorly characterized immune dysregulation.

Secondary IMHA

- Infectious causes—hemotrophic *Mycoplasma* spp., *Ehrlichia* spp., *Anaplasma phagocytophilum*, *Anaplasma platys*, *Babesia* spp., *Leishmaniaisis*, *Dirofilaria immitis*, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), chronic bacterial infection.
- Neoplasia—lymphoma, lymphoid leukemia, hemangiosarcoma, hemophagocytic histiocytic sarcoma.
- Drugs—penicillins, cephalosporins, propylthiouracil, methimazole, sulfonamides.
- SLE.
- Neonatal isoerythrolysis.
- Dog erythrocyte antigen (DEA) incompatible blood transfusion.
- Vaccination, surgery, hormonal changes, or other stressful events hypothesized as potential triggers.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Toxicity (zinc, onions, garlic, naphthalene, skunk musk).
- Snake/spider envenomation (coral snakes, recluse spiders).
- Severe hypophosphatemia.
- Anemia due to hemorrhage, hemoperitoneum.
- Microangiopathic anemia due to splenic neoplasia or torsion.
- Pyruvate kinase or phosphofructokinase deficiency.

Cats

- Toxicity (acetaminophen, zinc, onions, garlic).
- Severe hypophosphatemia.
- Congenital feline porphyria.
- Increased osmotic fragility (Abyssinian, Somali).

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—anemia, normal to high mean cell volume (MCV), spherocytosis, polychromasia, ghost cells, leukocytosis with neutrophilia and left shift, monocytosis; anemia nonregenerative in 30% of dogs and 50% of cats.
- Serum biochemistry—hyperbilirubinemia, high alanine aminotransferase (ALT).
- Urinalysis—hemoglobinuria, bilirubinuria.

OTHER LABORATORY TESTS

- Positive saline agglutination test.
- Direct antiglobulin (Coombs') test—positive in up to 75% of animals with IMHA.
- Reticulocytosis if regenerative.
- Thrombocytopenia—60% of dogs.
- Prolonged activated partial thromboplastin time (APTT), ± prolonged prothrombin time (PT), increased fibrin degradation products (FDP) and d-dimer, decreased antithrombin in animals with DIC.
- Blood smear—evidence of hematologic parasites.
- Infectious disease testing—especially *Babesia* spp. (serology, PCR), *Mycoplasma hemofelis* (PCR), other vector-borne pathogens.

IMAGING

Abdominal radiography, ultrasonography—hepatomegaly/splenomegaly, neoplasia.

DIAGNOSTIC PROCEDURES

Bone marrow aspirate to identify nonregenerative (RBC precursor-directed) IMHA or myelofibrosis in chronic cases.

PATHOLOGIC FINDINGS

- Hepatosplenomegaly, centrilobular hepatic necrosis.
- Splenic and hepatic extramedullary hematopoiesis.
- PTE and DIC.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient intensive care during acute hemolytic crisis and if complications such as DIC, PTE, thrombocytopenia, gastrointestinal (GI) bleeding, or need for multiple transfusions occur.
- Outpatient when PCV stable, hemolysis controlled, and clinical signs of anemia resolved.

NURSING CARE

- Fluid therapy as needed.
- Packed RBCs (or whole blood), fresh frozen plasma (FFP) if coagulopathic.
- Oxygen therapy as needed.
- Monitor for complications.

(CONTINUED)

ANEMIA, IMMUNE-MEDIATED**A****ACTIVITY**

Cage rest.

DIET

N/A

CLIENT EDUCATION

- IMHA can be fatal and difficult to treat, with guarded prognosis.
- Lifelong maintenance therapy may be needed; side effects may be severe.
- Disease may recur.

SURGICAL CONSIDERATIONS

Splenectomy can be considered if medical management fails.

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

- Corticosteroids—prednisone 2–3 mg/kg/day PO; dexamethasone sodium phosphate (0.2–0.4 mg/kg IV q24h) can be used in patients unable to take oral medication.
- Adjunctive immunosuppressants (if poor response to corticosteroids or to avoid side effects of prednisone)—cyclosporine 5 mg/kg PO q12h, cats: 0.5–3 mg/kg PO q12h; mycophenolate mofetil 8–12 mg/kg PO/IV q12h; azathioprine 2 mg/kg PO q24h, can decrease to 0.5–1.0 mg/kg PO q48h after 3 weeks or if bone marrow suppression occurs, monitor for side effects; *do not use in cats*.
- Once PCV above 30%, decrease prednisone dosage to 1 mg/kg PO q12h; then taper by maximum rate of 25–50% per month over 3–6-month period, depending upon PCV and severity of side effects; additional immunosuppressant drugs may be tapered as well.
- For prevention of thromboembolism consider unfractionated heparin 150–300 U/kg SC q6–8h (dose adjusted based on APTT prolongation or measurement of anti-Xa activity) and/or clopidogrel 1–2 mg/kg PO q24h; low molecular weight heparins (enoxaparin 0.8 mg/kg SC q6–8h or dalteparin 150 U/kg SC q8h) or rivaroxaban (0.5–1.0 mg/kg PO q24h) may be considered in lieu of unfractionated heparin.
- Address underlying cause (secondary IMHA).
- Therapeutic plasma exchange/plasmapheresis may be useful adjunctive therapy.

CONTRAINDICATIONS

Anticoagulant medications should be used cautiously in patients with thrombocytopenia (<40,000 platelets/ μ L).

PRECAUTIONS

- Prednisone/prednisolone can cause signs of hyperadrenocorticism and may increase risk of PTE, pancreatitis, diabetes mellitus, secondary infection, gastric ulcers (consider gastric protectants).
- Immunosuppressive drugs can

cause bone marrow suppression, secondary infection, pancreatitis (azathioprine), GI upset (cyclosporine, azathioprine, mycophenolate mofetil), gingival hyperplasia, papillomatosis (cyclosporine), infertility.

ALTERNATIVE DRUG(S)

- Chlorambucil—for cats, 0.1–0.2 mg/kg PO q24h initially, then q48h.
- Human IV immunoglobulin (hIVIG; 0.5–1 g/kg IV) in dogs not responding to other therapies.

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

- Monitor heart rate, respiratory rate, body temperature frequently.
- Monitor for adverse reactions to treatment.
- If PTE suspected, CT angiography indicated for diagnosis; oxygenation can be assessed with pulse oximetry or arterial blood gas analysis.
- Initially, check packed cell volume (PCV) daily until stable, then every 1–2 weeks for 2 months; if still stable, recheck monthly for 6 months, then 2–4 times/year.
- CBC and reticulocyte count at least monthly; if neutrophil count falls <3,000 cells/ μ L, discontinue cytotoxic drugs until count recovers; reinstitute at lower dosage.

PREVENTION/AVOIDANCE

Consider need for vaccination on case-by-case basis in dogs with IMHA; measurement of titers prior to elective vaccinations may be indicated.

POSSIBLE COMPLICATIONS

- Pulmonary/multiorgan thromboembolism.
- DIC.
- Centrilobular hepatic necrosis and renal tubular necrosis secondary to hypoxia.
- Infection secondary to immunosuppressive therapy.
- GI ulceration due to high-dose glucocorticoids.
- Iatrogenic hyperadrenocorticism.

EXPECTED COURSE AND PROGNOSIS

- Mortality—30–70% (dog), 24% (cat).
- Hyperbilirubinemia >5 mg/dL, autoagglutination, intravascular hemolysis, severe thrombocytopenia, hypoalbuminemia associated with poorer prognosis.
- Response to treatment may take weeks to months; nonregenerative IMHA may have more gradual onset than typical IMHA and be slower to respond to treatment. Most patients receive immunosuppressive therapy for 4–8 months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

See above.

ZOONOTIC POTENTIAL

None

SYNOMYNS

- Autoimmune hemolytic anemia.
- Immune-mediated anemia.

SEE ALSO

- Anemia, Regenerative.
- Cold Agglutinin Disease.

ABBREVIATIONS

- ALT = alanine aminotransferase.
- APTT = activated partial thromboplastin time.
- DEA = dog erythrocyte antigen.
- DIC = disseminated intravascular coagulation.
- FDP = fibrin degradation products.
- FeLV = feline leukemia virus.
- FFP = fresh frozen plasma.
- FIV = feline immunodeficiency virus.
- GI = gastrointestinal.
- hIVIG = human IV immunoglobulin.
- Ig = immunoglobulin.
- IMHA = immune-mediated hemolytic anemia.
- MCV = mean cell volume.
- PCV = packed cell volume.
- PT = prothrombin time.
- PTE = pulmonary thromboembolism.
- RBC = red blood cell.
- SLE = systemic lupus erythematosus.

Suggested Reading

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ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats. J Vet Intern Med 2019, 33(2):313–334.

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Acknowledgment The author and book editors acknowledge the prior contribution of J. Catharine R. Scott-Moncrieff.



**Client Education Handout
available online**

ANEMIA, IRON-DEFICIENCY



BASICS

OVERVIEW

Caused by chronic external blood loss or iron-limited erythropoiesis.

SIGNALMENT

- Fairly common in adult dogs, rare in adult cats.
- Transient neonatal iron-deficiency anemia may occur at 5–10 weeks of age in kittens.

SIGNS

- Signs of anemia (e.g., lethargy, weakness, tachypnea, pale mucous membranes).
- Cardiovascular—bounding pulses, tachycardia, systolic heart murmur.
- Gastrointestinal—intermittent melena or hematochezia, diarrhea.
- Integumentary—heavy hematophagous parasite burden (e.g., fleas), wounds.

CAUSES & RISK FACTORS

- Chronic external blood loss.
- Gastrointestinal—hookworms, lymphoma or other neoplasia, ulceration (related to medications, [e.g., non-steroidal anti-inflammatories] or disease [e.g., renal disease]).
- Less common—severe flea infestation, urinary tract hemorrhage.
- Iatrogenic—blood donor overuse, excessive diagnostic blood sampling.
- Inappropriate home-cooked diet (low dietary iron).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any cause of anemia, especially hemorrhage.
- Microcytic anemia in portosystemic shunt disease may or may not be due to iron deficiency.
- Anemia of inflammatory disease—iron-limited erythropoiesis.

CBC/BIOCHEMISTRY/URINALYSIS

- Packed cell volume (PCV) variably decreased; may be within reference interval.
- Regenerative or nonregenerative anemia.
- Microcytosis—low normal or low mean cell volume (MCV), low mean reticulocyte volume (MCVr), anisocytosis, widened erythrocyte histogram, or increased red cell distribution width (RDW). Decreased mean cell hemoglobin concentration (MCHC) not sensitive or specific.
- Red blood cell (RBC) morphology—microcytosis, hypochromia, keratocyte (indicating oxidative damage), and schistocyte formation.

- Reticulocyte indices reticulocyte corpuscular hemoglobin concentration mean (CHCMr), reticulocyte hemoglobin content (CHr), hypochromic reticulocyte RBCs (%HYPOr), and %LowCHr are sensitive for detecting iron-limited erythropoiesis, but not specific.
- Lab tests indicating iron-limited erythropoiesis do not differentiate true from functional iron deficiency. Clinical findings of inflammatory disease are required to differentiate iron-limited erythropoiesis. Inflammatory disease and true iron deficiency may also occur concurrently.
- Thrombocytosis due to chronic blood loss.
- Hypoproteinemia—from blood loss.

OTHER LABORATORY TESTS

- Hypoferremia (serum iron <70 µg/dL) and transferrin saturation <15% support diagnosis.
- Serum iron values may be normal during iron repletion if blood loss is intermittent.
- Fecal exam for hookworms.
- Fecal examination for occult blood or melena.

IMAGING

Abdominal radiography, ultrasonography—abnormalities in gastrointestinal tract causing blood loss.

DIAGNOSTIC PROCEDURES

- Bone marrow aspirate, staining with Prussian blue (dogs only) to indicate body iron stores.
- Gastrointestinal endoscopy to identify sites of gastrointestinal blood loss.



TREATMENT

- Identify/correct cause of blood loss, treat underlying disease.
- Administer iron until hematologic features of iron deficiency resolve.
- If severe anemia (i.e., PCV <15%), transfusion may be required, using whole blood (10–30 mL/kg IV) or packed RBC (10 mL/kg IV).



MEDICATIONS

DRUG(S) OF CHOICE

Parenteral Iron Supplementation

- Iron therapy should begin with injectable iron.
- Iron dextran—10–20 mg/kg IM (dog), 50 mg IM (cat), followed by oral supplementation.

Oral Iron Supplementation—Dogs Only

- Animals with severe iron deficiency may have impaired intestinal iron absorption,

making oral therapy of little value until partial iron repletion has occurred.

- Oral iron supplementation should continue 1–2 months, or until resolved.
- Ferrous sulfate powder—place in food or drinking water, 100–300 mg PO q24h.
- Ferrous gluconate—325 mg PO q24h.

CONTRAINdications/POSSIBLE INTERACTIONS

- Oral iron is associated with unexplained death in kittens and should be avoided.
- Kittens undergo spontaneous iron repletion beginning at 5–6 weeks of age.



FOLLOW-UP

- Monitor CBC every 1–4 weeks, more frequently as needed.
- Effective treatment associated with an increase in MCV and reticulocyte volume.
- Erythrocyte histogram—effective treatment reduces microcytic subpopulation over time (2–3 months).



MISCELLANEOUS

ABBREVIATIONS

- CHCMr = mean reticulocyte corpuscular hemoglobin concentration.
- CHr = reticulocyte hemoglobin content.
- HYPOr = hypochromic reticulocyte RBCs.
- MCHC = mean cell hemoglobin concentration.
- MCV = mean cell volume.
- MCVr = mean reticulocyte volume.
- PCV = packed cell volume.
- RBC = red blood cell.
- RDW = red cell distribution width.

Suggested Reading

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Authors Glade Weiser and Melinda S. Camus
Consulting Editor Melinda S. Camus



BASICS

DEFINITION

Low red blood cell (RBC) mass due to low erythroid production, without evidence of polychromasia or reticulocytosis in peripheral blood. Anemia with reticulocyte counts $<80 \times 10^3/\mu\text{L}$ (dog) or $60 \times 10^3/\mu\text{L}$ (cat) considered nonregenerative. Caused by altered erythropoiesis or bone marrow injury.

PATHOPHYSIOLOGY

- Alterations in erythropoiesis include deficient erythropoietin (EPO) production, nutritional deficiency, cytokine-mediated iron sequestration, disturbed metabolism in or destruction of RBC precursors (e.g., immune-mediated).
- Bone marrow injury usually caused by toxins, infection, or infiltrative processes.
- Anemia of inflammatory disease results from increased hepcidin production and release of cytokines from white blood cells (WBCs) leading to iron sequestration and decreased iron absorption. Low serum iron and transferrin, increased ferritin, decreased EPO production, shortened RBC lifespan result in anemia.

SYSTEMS AFFECTED

- Cardiovascular—shock from decreased systemic oxygen delivery.
- Hemic/lymph/immune.
- Hepatobiliary—from hypoxic injury.

SIGNALMENT

- Nonregenerative immune-mediated hemolytic anemia (IMHA)—middle-aged female dogs and male cats <3 years old.
- Congenital cobalamin malabsorption reported in Komondor, beagle, giant schnauzer, Australian shepherd, border collie, shar-pei.

SIGNS

General Comments

Usually secondary; signs associated with primary disease often precede signs of anemia.

Historical Findings

- Lethargy, exercise intolerance, inappetence, pica.
- Other findings reflect primary condition—polyuria/polydipsia (chronic kidney disease [CKD]), old paint exposure (lead poisoning), estrogen therapy or feminization in male dogs, failure to thrive (hereditary cobalamin malabsorption).

Physical Examination Findings

- Pallor, heart murmur (due to anemia), tachycardia, tachypnea, shock.
- Digital rectal examination may reveal melena if gastrointestinal (GI) blood loss.

- Signs reflecting primary condition—oral ulcerations (CKD), cachexia, organomegaly, GI or nervous system abnormalities (cobalamin malabsorption, lead poisoning), symmetric alopecia (hypothyroidism, hyperestrogenism).

CAUSES

Nonregenerative Anemia without Other Cytopenias

- Anemia of inflammatory disease (AID)—most common cause of mild nonregenerative anemia (also anemia of chronic disease).
- CKD—decreased EPO production by kidneys; uremic toxins shorten RBC lifespan and impair bone marrow response to EPO.
- Chronic liver disease—shortened RBC survival due to changes in RBC membrane lipids; functional iron deficiency due to decreased transferrin synthesis and impaired mobilization of hepatic iron.
- Hypothyroidism, hypoadrenocorticism—thyroid hormones and cortisol stimulate erythropoiesis.
- Immune-mediated destruction of precursors—spectrum from nonregenerative IMHA to pure red cell aplasia.

Nutritional or Mineral Deficiency/Toxicity

- Iron deficiency—usually due to chronic external blood loss.
- Copper deficiency—secondary to chelation therapy.
- Cobalamin (vitamin B₁₂) and/or folate deficiency—rare; can be caused by dietary insufficiency, malabsorption, congenital defects in cobalamin absorption.
- Disruption of precursor metabolism—chronic lead toxicity and possibly high concentrations of aluminum, arsenic, and cadmium inhibit heme synthesis; cadmium and lead cause renal toxicity, impaired EPO production.

Nonregenerative Anemia with Other Cytopenias

- Toxicities—drugs or chemicals, hormones (e.g., estrogen).
- Infections—feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), ehrlichiosis, babesiosis, *Cytauxzoon felis*, parvovirus (occasionally just erythroid line affected).
- Infiltrative processes—myelodysplasia, myeloproliferative and lymphoproliferative diseases, histiocytic sarcoma, metastatic neoplasia, myelofibrosis, osteosclerosis.

RISK FACTORS

- CKD.
- Inflammatory or chronic disease.
- Multicat household/cattery (infectious disease risk).
- Daily exposure to toxins (e.g., old homes with lead paint, environmental pollution).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Regenerative anemia can initially appear nonregenerative (especially in cats); exacerbation of chronic condition may produce appearance of acute onset.

CBC/BIOCHEMISTRY/URINALYSIS

CBC and Blood Smear

- Packed cell volume (PCV), hematocrit (HCT), RBC count, and hemoglobin concentration low.
- Anemia usually normocytic, normochromic, with normal mean cell volume (MCV) and mean corpuscular hemoglobin concentration (MCHC); occasionally severe vitamin B₁₂ deficiency; characteristic large erythrocytes can be masked by presence of misshapen and/or small RBCs, giving normal MCV but widened red cell distribution.
- Macrocytosis (high MCV)—without polychromasia suggests nuclear maturation defect; seen in cats with FeLV.
- Microcytosis suggests maturation complete; iron deficiency most common cause; in late stages concurrent hypochromasia common in dogs.
- Characteristic RBC morphologies—schistocytes ± hypochromic RBCs common with iron deficiency; acanthocytes with liver disease; target cells with iron deficiency, liver disease, hypothyroidism.
- Inflammatory leukogram supports AID.
- Thrombocytosis common in iron deficiency.
- High number of nucleated red blood cells (NRBCs) without polychromasia or disproportionate to degree of anemia and polychromasia seen with lead toxicity, extramedullary hematopoiesis (EMH), heat stroke, bone marrow injury.
- RBC or WBC precursors in peripheral blood without orderly progression to more mature forms suggest myelodysplasia or myeloproliferative disease.
- Cobalamin malabsorption characterized by normocytic anemia, neutropenia, hypersegmented neutrophils; megaloblastic changes possible in marrow.
- RBC inclusions may be visible on blood smear with some infectious diseases (e.g., *C. felis*).

Serum Biochemistry and Urinalysis

- CKD—azotemia with isosthenuria, possible proteinuria, hypokalemia.
- Liver disease—elevated alanine aminotransferase (ALT) ± alkaline phosphatase (ALP) activities, elevated total bilirubin, bile acids, ammonia concentrations, hypoglycemia, hypoalbuminemia.
- Hypothyroidism—hypercholesterolemia (>500 mg/dL).

A ANEMIA, NONREGENERATIVE

(CONTINUED)

- Hypoadrenocorticism—hyponatremia, hyperkalemia, lymphocytosis, eosinophilia.

OTHER LABORATORY TESTS

- Reticulocyte count.
- Spherocytosis, autoagglutination, or positive Coombs' test supports immune-mediated destruction of erythroid precursors.
- Serum iron profile—with iron deficiency both serum iron and ferritin low, while total iron-binding capacity varies; with AID, serum iron low but serum ferritin high.
- Serum lead—indicated when NRBCs present; >30 µL/dL (0.3 ppm) strongly supports lead intoxication.
- Serologic testing—FeLV, FIV in cats; *Ehrlichia canis*, *Anaplasma phagocytophilia* in dogs, particularly if anemia with thrombocytopenia.
- Endocrine testing—adrenocorticotrophic hormone (ACTH) stimulation test or thyroid function testing to rule out hypoadrenocorticism or hypothyroidism, respectively.
- Serum cobalamin, homocysteine, methylmalonic acid ± urine methylmalonic acid concentrations—to diagnose hereditary cobalamin malabsorption.

DIAGNOSTIC PROCEDURES

Cytologic Examination of Bone Marrow and Core Biopsy

- Cytologic examination of bone marrow aspirate indicated in all patients unless primary cause apparent, and bone marrow core biopsy useful in evaluation of bone marrow architecture and overall cellularity.
- Erythroid hypoplasia or aplasia confirms pure red cell aplasia; erythroid hyperplasia suggests IMHA; increased erythropagia or incomplete maturation sequence suggests immune-mediated or toxic injury to specific maturation stage, or incomplete recovery from previous injury.
- Expanded erythron and high numbers of metarubricytes suggest iron deficiency; absence of iron stores supportive in dogs, but not cats.
- Disorderly maturation and atypical cellular morphology suggest myelodysplastic syndrome.
- Hypercellular marrow with increased blast cells consistent with hematopoietic neoplasia; immunophenotyping can identify affected cell line.
- Hypocellular sample can suggest aplastic marrow or myelofibrosis.

Abdominal Radiographs, Ultrasound

As part of evaluation for underlying causes such as neoplasia, CKD, or GI blood loss.



TREATMENT

- Anemia usually resolves with resolution of underlying disease.
- Conditions associated with severe anemia or pancytopenia often carry guarded to poor prognosis and may involve long-term treatment with incomplete resolution.
- Mild to moderate anemia (PCV >20%) generally requires no immediate supportive intervention.
- Patients with severe anemia (PCV <12–15%) require transfusion for stabilization (e.g., 6–10 mL/kg packed RBCs or 10–20 mL/kg whole blood).
- Determine blood type prior to transfusion (imperative for cats, ideal for dogs).
- If blood volume and tissue perfusion compromised by concurrent blood loss or shock, administer isotonic crystalloid solution (10–20 mL/kg IV, repeat as necessary) or isotonic colloid solution (2–5 mL/kg IV, to total 20 mL/kg/24h). See Shock, Hypovolemic.
- With chronic anemia, animals may be hypervolemic, and volume overload may be a concern during blood and fluid therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- EPO or darbopoetin in patients with anemia of CKD.
- Iron supplementation in patients with iron deficiency anemia.
- Immunosuppressive drugs.
- May supplement with cobalamin (vitamin B₁₂) at rate of 100–200 mg PO q24h (dogs) or 50–100 mg PO q24h (cats); parenteral cyanocobalamin administration (50 µg/kg SC/IM weekly to monthly) needed in dogs with inherited cobalamin malabsorption.

PRECAUTIONS

Monitor for transfusion reactions.



FOLLOW-UP

PATIENT MONITORING

- With severe anemia—serial physical examinations, PCV/CBC, blood smear examination every 1–2 days.
- Stable animals with chronic or slowly improving disease course—reevaluate every 1–2 weeks.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Pregnant animals have mildly low PCV.

SEE ALSO

- Anemia, Immune-Mediated.
- Anemia, Iron-Deficiency.
- Blood Transfusion Reactions.
- Shock, Hypovolemic.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- AID = anemia of inflammatory disease.
- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- CKD = chronic kidney disease.
- EMH = extramedullary hematopoiesis.
- EPO = erythropoietin.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- GI = gastrointestinal.
- HCT = hematocrit.
- IMHA = immune-mediated hemolytic anemia.
- MCHC = mean corpuscular hemoglobin concentration.
- MCV = mean cell volume.
- NRBC = nucleated red blood cell.
- PCV = packed cell volume.
- RBC = red blood cell.
- WBC = white blood cell.

Suggested Reading

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ANEMIA, REGENERATIVE



BASICS

DEFINITION

Decreased circulating red blood cell (RBC) mass (indicated by low packed cell volume [PCV] or hematocrit [HCT], hemoglobin, and total RBC count) accompanied by appropriate, compensatory increase in RBC production by the bone marrow.

PATHOPHYSIOLOGY

- Caused by blood loss or hemolysis.
- Hemolysis—caused by intrinsic RBC defects (e.g., congenital RBC membrane defects or enzyme deficiencies) or extrinsic factors (e.g., RBC parasites, oxidative injury, hemolysins, osmotic changes, immune-mediated RBC destruction, hemophagocytic neoplasia, heat stroke, and severe hypophosphatemia).

SYSTEMS AFFECTED

- Cardiovascular—murmurs with marked anemia; tachycardia.
- Hemic/lymph/immune—erythroid hyperplasia in bone marrow; splenic extramedullary hematopoiesis (EMH).
- Hepatic—decreased oxygen delivery causes centrilobular degeneration of liver.
- Renal—severe intravascular hemolysis rarely leads to pigmentary nephropathy and acute renal failure.
- Musculoskeletal—progressive osteoclerosis seen in pyruvate kinase (PK)-deficient dogs.

SIGNALMENT

- PK deficiency—basenji, beagle, cairn terrier, Chihuahua, dachshund, Labrador retriever, labradoodle, miniature poodle, pug, West Highland white terrier, and American Eskimo; Somali, Abyssinian, domestic shorthair cats.
- PFK deficiency—Australian labradoodle, English springer spaniel, American cocker spaniel, cockapoo, English cocker spaniel, whippet, wachtelhund, and mixed breed dogs with spaniel parentage.
- Marked RBC osmotic fragility—English springer spaniel; Abyssinian, Somali, Siamese, and domestic shorthair cats.
- Feline congenital porphyria—Siamese and domestic shorthair cats.
- Heritable coagulopathies (e.g., factor VIII or IX deficiency), von Willebrand disease.
- Immune-mediated hemolytic anemia (IMHA)—middle-aged female dogs, especially American cocker spaniels, English springer spaniels, Irish setters, Old English sheepdogs, poodles, and Shetland sheepdogs.
- Hemophagocytic histiocytic sarcoma—Bernese mountain dog, Rottweiler, golden retriever, and flat-coated retriever.

SIGNS

- Pallor.
- Weakness, exercise intolerance, collapse.
- Anorexia.
- Possible heart murmur, tachycardia, bounding pulses (unless hemorrhage is present).
- Possible jaundice and hemoglobinuria.
- Petechiae, epistaxis, melena suggest blood loss due to vasculitis or thrombopathia.
- Hematomas or cavity bleeds suggest coagulation factor inhibition or deficiency.
- Clinical signs depend on degree of anemia and rapidity of onset.
- Rapid loss of 15–25% blood volume or acute hemolysis results in shock.
- With chronic anemia, compensatory increases in heart rate, and eventually heart size, occur; hemoglobin can drop to as low as 50% of minimum normal value without overt signs of shock or decreased oxygen delivery.

CAUSES

- Immune-mediated (IMHA).
- RBC toxins—snake venom and bee stings may cause RBC hemolysis; oxidants can cause Heinz body formation.
- Erythrocyte parasites—cats: *Mycoplasma* spp., *Cytauxzoon felis* (may be nonregenerative); dogs: *Mycoplasma haemocanis*, *Babesia* spp.
- Mechanical RBC fragmentation—caused by vasculitis, thromboembolic disease, or disease of any vascular organ; rare cause of significant anemia unless accompanied by hemorrhage.
- Inherited RBC abnormalities:
 - PK deficiency.
 - Phosphofructokinase (PFK) deficiency.
 - Increased RBC osmotic fragility (unknown RBC defect), leads to recurrent severe anemia and splenomegaly.
 - Feline congenital porphyria—enzyme deficiency in heme synthetic pathway leads to accumulation of heme precursors, hemolytic anemia, and brown-red discoloration of teeth and bones; Siamese tend to have severe hemolytic anemia, while domestic shorthair cats have less severe autosomal dominant trait that causes mild anemia.
- Hypophosphatemia—severe hypophosphatemia impairs adenosine triphosphate (ATP) production, leading to increased erythrocyte fragility and hemolysis; seen with refeeding syndrome and insulin administration.
- Blood loss:
 - Trauma.
 - Bleeding neoplasms.
 - Coagulopathies (e.g., warfarin toxicity, hemophilia, thrombocytopenia).
 - Blood-feeding parasites.
 - Gastrointestinal ulcers.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiated from nonregenerative anemia by a reticulocyte count above the regenerative threshold for that species, generally above $80 \times 10^3/\mu\text{L}$ in dogs and $60 \times 10^3/\mu\text{L}$ in cats.

LABORATORY FINDINGS

Disorders That May Alter Laboratory Results

- Lipemia can cause mild in vitro hemolysis, without appreciable anemia, and may falsely elevate mean corpuscular hemoglobin concentration (MCHC).
- Autoagglutination may falsely decrease RBC count and increase MCV.
- Exercise and excitement can increase RBC count, PCV, and reticulocyte count through splenic contraction, masking severity of anemia.

Valid If Run in Human Laboratory?

- Dogs—yes.
- Cats—yes, if hematology instrument uses species-specific parameters; instruments designed for analysis of human specimens may undercount small feline RBCs and be unable to distinguish between erythrocytes and platelets.

CBC/BIOCHEMISTRY/URINALYSIS

- PCV, RBC count, and hemoglobin are below the reference interval.
- Total protein is often low with blood loss anemia and may be the only sign with acute blood loss due to splenic contraction, which elevates the circulating RBC count.
- RBC indices vary depending on the cause of anemia and degree of regenerative response:
 - Mean cell volume (MCV) is normal to high with regeneration, but low with iron deficiency.
 - MCHC is normal to low in most patients, low with iron deficiency, and artificially high with hemolysis.
- Specific RBC morphologies may suggest the cause of hemolysis:
 - Marked spherocytosis suggests immune-mediated disease in dogs.
 - Heinz bodies or eccentrocytes suggest oxidant injury.
 - Numerous schistocytes suggest microangiopathy.
 - RBC parasites may be found on or within RBC.
- Agglutinated RBCs indicate anemia is immune mediated; distinguish autoagglutination from rouleaux by saline agglutination test (see Appendix X).
- Hemolysis is often accompanied by an inflammatory leukogram.

(CONTINUED)

- Animals with IMHA often have a concurrent thrombocytopenia, while iron deficiency is often accompanied by thrombocytosis.
- Hyperbilirubinemia and bilirubinuria accompany marked hemolysis; hemoglobinemia and hemoglobinuria can be seen following intravascular hemolysis.

OTHER LABORATORY TESTS

- Reticulocytosis may be absent in the first 3–5 days after onset of blood loss or hemolysis.
- Direct antiglobulin test (Coombs' test) is indicated when IMHA is suspected, in the absence of agglutination; a positive test is confirmatory.
- The rapid osmotic fragility test detects erythrocyte membrane defects and can help to discriminate hemolytic from nonhemolytic conditions.
- Coagulation testing may be indicated in cases of blood loss.
- PCR is more sensitive for diagnosis of *Babesia* and hemotropic *Mycoplasma* than microscopic blood smear exam; can differentiate between species.
- PCR for PK deficiency.
- PCR for PFK deficiency.

DIAGNOSTIC PROCEDURES

Fine-needle aspiration and cytologic exam of abnormal spleen, lung, or lymph nodes may help to diagnose hemophagocytic histiocytic sarcoma.

**TREATMENT**

- Emergency if anemia is severe or has developed rapidly.
- Massive hemorrhage leads to hypovolemic shock and decreased oxygen delivery to tissues; acute hemolysis also leads to decreased oxygen content in the blood.
- In cases of massive hemorrhage, crystalloid fluids can rapidly correct hypovolemia and restore circulation, but RBC replacement (and resolving the source of hemorrhage) is necessary for definitive therapy.

- RBC replacement (packed RBCs or whole blood) indicated with severe anemia (PCV <15%) or rapid drops (>15%) in HCT. Initial dosage depends on product selected; 1 mL/kg of packed RBCs will raise the HCT by approximately 1%; 3 mL/kg of whole blood will raise the PCV by approximately 1%, both depending on the PCV of the donor product.
- In cases of hemorrhage or coagulopathy, fresh whole blood will also provide volume expansion and coagulation factor replacement, compared to packed RBCs.
- Determine blood type prior to transfusion, especially in cats (who have preexisting autoantibodies to opposite blood types). Cross-match against donor blood if blood typing reagents not available, or if patient requires second transfusion more than 4 days after first transfusion.
- Animals with chronic blood loss or hemolytic anemias are generally normovolemic with increased cardiac output, therefore attention should be paid to transfusion volumes and rates.

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

- Iron may benefit animals with chronic blood-loss anemia (see Anemia, Iron-Deficiency).
- Hemolytic anemias—varies with cause of hemolysis.

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

- Initially, monitor PCV and morphologic features of RBCs on a blood smear every 24 hours to evaluate effectiveness of treatment and bone marrow responsiveness; polychromasia may be seen as regenerative response starts.
- As regeneration becomes apparent, recheck every 3–5 days.

- During and following transfusion, monitor for transfusion reactions (see Blood Transfusion Reactions).

**MISCELLANEOUS****SEE ALSO**

- Anemia, Heinz Body.
- Anemia, Immune-Mediated.
- Anemia, Iron-Deficiency.
- Babesiosis.
- Bartonellosis.
- Blood Transfusion Reactions.
- Cytauxzoonosis.
- Phosphofructokinase Deficiency.
- Pyruvate Kinase Deficiency.
- Von Willebrand Disease.
- Zinc Toxicosis.

ABBREVIATIONS

- ATP = adenosine triphosphate.
- EMH = extramedullary hematopoiesis.
- HCT = hematocrit.
- IMHA = immune-mediated hemolytic anemia.
- MCHC = mean corpuscular hemoglobin concentration.
- MCV = mean cell volume.
- PCV = packed cell volume.
- PFK = phosphofructokinase.
- PK = pyruvate kinase.
- RBC = red blood cell.

Suggested Reading

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ANOREXIA



BASICS

DEFINITION

Anorexia is the lack or loss of appetite for food. Hyporexia is a reduction in appetite, while dysrexia is a change in appetite or lack of consistent appetite. Anorexia results in decreased food intake, which then leads to weight loss, dehydration, nutritional deficiencies, and/or sarcopenia.

PATHOPHYSIOLOGY

- The control of appetite is a complex interaction between the central nervous system, the environment, and the gastrointestinal (GI) tract.
- The hypothalamus and brainstem contain feeding-regulatory neurons that act as input stations for sensory and metabolic signals. These cell populations project to several brain regions and interconnect extensively.
- Sensory signals that affect appetite include the odor, taste, texture, and temperature of food, as well as gastric and duodenal distention.
- Metabolic signals for hunger and satiety include a variety of peptides and hormones released during the fasting and fed states, as well as plasma concentrations of glucose, amino acids, and fatty acids.
- Insulin, glucagon, somatostatin, cholecystokinin, peptide tyrosine tyrosine (PYY), and pancreatic peptide decrease hunger centrally.
- Leptin, produced primarily by adipocytes, acts on specific hypothalamic receptors to increase metabolism and decrease appetite.
- Neuropeptide Y, released from the GI tract after food restriction, induces hunger and decreases energy expenditure.
- Ghrelin, produced by the stomach, is a prokinetic and increases appetite; it decreases leptin and increases neuropeptide Y production.
- Serotonin is an important central mediator and acts via a serotonergic tract that passes near the ventromedial hypothalamic nuclei (satiety center).
- Dopaminergic tracts in the hypothalamus help regulate food intake and are closely associated with the lateral hypothalamic nuclei (feeding center).
- Environmental factors including the location and timing of meals, as well as learned behaviors and circadian rhythms, modulate appetite.
- Brain lesions that affect the hypothalamus can decrease or increase appetite; any disorder that decreases cerebral arousal will potentially decrease food intake.
- Inflammatory and neoplastic diseases can cause hyporexia by the release of proinflammatory cytokines.
- The expected upregulation of dietary intake in response to increased energy expenditure is frequently absent in patients with neoplastic and advanced cardiac diseases.
- Exogenous and endogenous toxins (e.g., renal and liver failure) cause hyporexia.
- Neoplasia, metabolic disorders, pancreatitis, and primary GI diseases are associated with hyporexia.
- Fear, pain, and stress may decrease appetite.

SYSTEMS AFFECTED

All body systems.

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat.

Breed Predilections

N/A

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

Historical Findings

- Refusal to eat is a common presenting complaint and causes owners significant distress.
- Weight loss may be reported.

Physical Examination Findings

- Findings vary depending on the underlying cause.
- Low body condition score and muscle wasting may be evident depending upon the duration of decreased food intake.
- Pseudoanorectic patients commonly display halitosis, excessive drooling, difficulty with prehension or mastication, and odynophagia (painful swallowing).

CAUSES

Anorexia/Hyporexia/Dysrexia

- Possible manifestations of a myriad of systemic disorders.
- Psychological—food aversion, stress, alterations in routine or environment.
- Pain.
- Toxicities and drug adverse effects.
- GI and pancreatic diseases.
- Acid-base disorders.
- Organ failure—e.g., cardiac, renal, hepatic.
- Endocrine and metabolic diseases.
- Neoplasia.
- Infectious diseases.
- Immune-mediated diseases.
- Respiratory diseases.
- Musculoskeletal diseases.
- Neurologic diseases.
- Miscellaneous (e.g., motion sickness, high environmental temperature).

Pseudoanorexia

Any disease causing painful or dysfunctional prehension, mastication, or swallowing.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pseudoanorexia is a term describing patients who are hungry but are unable to eat due to disorders causing dysfunction or pain of the face, neck, oropharynx, and esophagus.

- Animals lacking a sense of smell (anosmia) often show a lack of interest in food.

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormalities vary with different underlying diseases.
- May be normal.

OTHER LABORATORY TESTS

- Additional diagnostic tests may be necessary to investigate specific diseases suggested by history, physical examination, and preliminary tests.
- Heartworm serology, tick serology, retrovirus serology, thyroid level, and histologic/cytologic examination of tissue/cell samples may be required to make a definitive diagnosis.
- A baseline cortisol or an adrenocorticotrophic hormone (ACTH) stimulation test to rule out hypoadrenocorticism is warranted even when there are no significant laboratory changes.

IMAGING

- Thoracic and abdominal imaging (radiographs and ultrasound) studies are often included in the minimum database to detect anatomic or functional abnormalities.
- Videofluoroscopy and endoscopy may be indicated to specifically evaluate pharyngeal, esophageal, and GI function and appearance.

DIAGNOSTIC PROCEDURES

- Perform a nutritional assessment; collect a thorough dietary history, evaluate food intake, and obtain body and muscle condition scores.
- Elicit a thorough history regarding the patient's environment, changes in routine, people, or other pets, to help identify potential sources of psychologic stress.
- Observe the patient's interest in food and ability to prehend, masticate, and swallow food.
- Complete a thorough physical examination including ophthalmic, oropharyngeal, neurologic, orthopedic, thoracic, abdominal, and rectal exam to determine the presence of disease.

PATHOLOGIC FINDINGS

Dependent on underlying disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Assisted feeding (enteral and/or parenteral feeding) should be considered immediately for significantly malnourished patients ($\geq 10\%$ body weight loss, hypoalbuminemia, poor body condition score, evidence of muscle wasting, and/or chronic disease processes). In well-conditioned patients with decreased appetite, assisted feeding should be considered if food consumption is less than the resting energy requirement [RER = $70 \times (\text{body weight}_{\text{kg}}^{0.75})$] for 3–5 days without trends toward improvement.
- Force feeding should be avoided, particularly in cats, considering the association with conditioned food aversions.

(CONTINUED)

ANOREXIA**A****NURSING CARE**

- Medications the patient is receiving should be reviewed for possible side effects leading to reduced appetite.
- Provide comfort and nutrition to the patient while efforts are directed at identifying and correcting the underlying disease so that more specific treatment can be provided.
- Symptomatic therapy includes correcting fluid deficits and electrolyte derangements, control of pain and/or nausea, reduction in environmental stressors, and modification of the diet to improve palatability.

ACTIVITY

N/A

DIET

- Palatability can be improved by adding flavored toppings such as low-sodium broth, increasing the moisture, fat, or protein content of the food, and warming the food to body temperature.
- When learned food aversion is suspected, food should be removed immediately at the first signs of aversion.

CLIENT EDUCATION

Depends on specific diagnosis.

SURGICAL CONSIDERATIONS

N/A

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

- Pharmacologic interventions aimed at improving appetite should not replace diagnostic efforts to identify the specific cause(s) of decreased appetite.
- Mirtazapine antagonizes inhibitory, presynaptic, α_2 -adrenergic receptors, facilitating release of norepinephrine and serotonin (5-HT). It is also a 5-HT2 and 5-HT3 antagonist on the postsynaptic neuron. Stimulation of 5-HT1 produces antidepressant effects, while inhibition of 5-HT2 and 5-HT3 produces anti-emetic and appetite-stimulating effects. Canine dosing is 0.5 mg/kg q24h. Mirataz® is FDA approved for use in cats, with a recommended dose of a 1.5 in. strip applied to the inner pinna once daily for 14 days. Alternatively, 1.88 mg/cat PO q24–48h (for cats with chronic kidney disease) can be given to stimulate appetite.
- Capromorelin is a ghrelin receptor agonist that stimulates appetite centrally in the hypothalamus. Entyce® is capromorelin, approved by the FDA for dogs as an appetite stimulant. A trial in healthy laboratory beagles demonstrated significant increases in food consumption and weight compared to placebo, and a clinical field trial in inappetent client-owned dogs demonstrated increases in appetite and body weight compared to placebo. Dosing at 3 mg/kg PO q24h is safe for long-term administration. Capromorelin is not approved for cats, though a safety trial has been published and clinical trials are underway.
- Diazepam (0.1 mg/kg IV q24h) is a short-acting appetite stimulant with sedative properties. Oral

diazepam should be avoided in cats due to possible idiosyncratic hepatotoxicosis.

- Cyproheptadine (0.2–0.4 mg/kg PO, 10–20 minutes prior to feeding), an antihistamine with antiserotonergic properties, has been used as an appetite stimulant with mixed success.
- Prokinetics such as metoclopramide (0.2–0.4 mg/kg SC/PO q8–12h), ranitidine (2 mg/kg SC/IV/PO q12h), or erythromycin (0.5–1 mg/kg PO q8–12h) are useful if anorexia is associated with ileus.
- Antiemetics are useful in decreasing nausea or vomiting, but are not appetite stimulants. Ondansetron (0.5–1.0 mg/kg SC/IV/PO q12h) and dolasetron (0.6–1.0 mg/kg SC/IV/PO q24h) are potent antiemetics as 5-HT3 antagonists. Maropitant is a substance P analogue, which binds neurokinin-1 receptors in the chemoreceptor trigger zone (CRTZ) and vomiting center, inhibiting vomiting. Cerenia® is maropitant, approved by the FDA for dogs and cats as an antiemetic (dogs: 1 mg/kg SC/IV or 2 mg/kg PO q24h; cats: 1 mg/kg SC/IV/PO q24h).
- Omega-3 fatty acids can reduce inflammatory cytokines and have modest benefit for appetite.

CONTRAINdications

Avoid antiemetics and prokinetics if GI obstruction is present or suspected.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

Mirtazapine should not be combined with drugs that interact with or affect serotonergic systems including monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), and selective serotonin reuptake inhibitors (SSRIs). Ondansetron and dolasetron, as well as metoclopramide, are 5-HT3 antagonists, and care should be used with combining these drugs with mirtazapine.

ALTERNATIVE DRUG(S)

N/A

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

- Body weight, body and muscle condition score, and hydration assessment.
- Monitor caloric intake to ensure return of appetite is sufficient to meet nutritional needs.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Dehydration, malnutrition, cachexia, and sarcopenia are sequelae of prolonged anorexia/hyporexia/dysrexia; these exacerbate the underlying disease.
- A loss of more than 25–30% of body protein compromises the immune system and muscle strength, and death results from infection and/or cardiopulmonary failure.
- Hepatic lipidosis is a possible complication of anorexia, particularly in cats.

- Breakdown of the intestinal mucosal barrier further compromises debilitated patients.

EXPECTED COURSE AND PROGNOSIS

Depends on the underlying cause(s).

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

Nutritional support and glucose-containing fluids may be necessary to treat or prevent hypoglycemia in anorectic puppies and kittens.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

N/A

SEE ALSO

Weight Loss and Cachexia.

ABBREVIATIONS

- 5-HT = 5-hydroxytryptamine (serotonin).
- ACTH = adrenocorticotrophic hormone.
- CRTZ = chemoreceptor trigger zone.
- GI = gastrointestinal.
- MAOI = monoamine oxidase inhibitor.
- PYY = peptide tyrosine tyrosine.
- RER = resting energy requirement.
- SSRI = selective serotonin reuptake inhibitor.
- TCA = tricyclic antidepressant.

INTERNET RESOURCES

<https://entyce.aratana.com/resources/clinical-references>

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Acknowledgment The author and book editors acknowledge the prior contribution of Kathryn E. Michel.



**Client Education Handout
available online**



BASICS

DEFINITION

Osteoarthritis (OA) or degenerative joint disease is a chronic and progressive disease that leads to loss of articular cartilage and ultimately failure of the joint. OA is characterized as a noninfectious disorder of diarthrodial (synovial) joints, such that the disease process involves the entire joint, not just the articular cartilage. It is due to both primary (idiopathic) and secondary causes.

PATOPHYSIOLOGY

- Ebb and flow characterization with periods of calmness followed by periods of exacerbation of clinical signs (flare-ups).
- OA initiated by mechanical stress—traumatic injury, instability, abnormal conformation, abnormal activity, etc.
- Inflammatory mediators and free radicals such as metalloproteinases, serine proteases, cysteine protease enzymes, and reactive oxygen species are released from damaged chondrocytes and synovium, resulting in breakdown of extracellular matrix of articular cartilage, causing collagen degradation and loss of collagen cross-linking.
- Collagen synthesis is altered, resulting in decreased collagen/proteoglycan interaction and reduced hydrophilic matrix properties.
- Extracellular matrix further compromised by increased breakdown of proteoglycans along with manufacture of poorer-quality proteoglycans.
- Nitric oxide released along with other free radicals, which mediates cartilage breakdown and supports chronic inflammation. Chondrocyte apoptosis facilitated by cyclooxygenase-2 enzymes and oxidative stress.
- Synovitis is driving force of the inflammatory cascade in OA, in addition to resulting in decreased viscosity of synovial fluid, reducing lubrication.
- Poorer-quality synovial fluid reduces oxygen and nutrient supply to chondrocytes as well as waste removal.
- Subchondral bone becomes sclerotic, worsening loading qualities of bone and overlying cartilage.
- Pain of OA results from distention of the joint capsule and stimulation of pain receptors, inflammation of synovium, increased mechanical loading of subchondral bone, alteration of function of surrounding tendons and ligaments, as well as development of periarticular fibrosis.
- The result of these processes is progressive cartilage degradation ranging from fibrillation to deep fissuring of cartilage. Full-thickness cartilage loss can eventually occur.
- Periarticular fibrosis occurs, resulting in a reduction of joint motion (and pain), leading

to poorer vascularity of synovial membrane as well as lack of functionality of synovium due to lack of motion in joint.

- Osteophytes and enthesiophytes develop around and within joint to increase load-bearing surface area.
- These changes reduce functionality and may eventually lead to ankylosis.

SYSTEMS AFFECTED

Musculoskeletal—diarthrodial joints.

GENETICS

- Primary OA rare, occurring more commonly in cats or in smaller (manus, pes) joints of dogs.
- Dogs—causes of secondary OA are varied, including hip and elbow dysplasia, osteochondritis dessicans (OCD), patellar luxations, congenital shoulder luxation, Legg-Perthes, cranial cruciate ligament rupture, intra-articular fractures, obesity, as well as many other causes.
- Cats—causes of secondary OA are patellar luxation, hip dysplasia, obesity, and arthropathy.

INCIDENCE/PREVALENCE

- Dog—very common; 20% of dogs older than 1 year have some degree of OA.
- Cat—90% of cats over 12 years of age had evidence of OA on radiographs.
- Clinical problems are more prevalent in larger, overweight, and very active animals.
- Primary OA is rare.

SIGNALMENT

Species

Dog and cat.

Mean Age and Range

- Secondary OA due to congenital disorders (OCD, hip dysplasia) seen in immature animals; some present with OA signs when mature (hip and elbow dysplasia).
- Secondary to trauma—any age.

SIGNS

Historical Findings

- Dogs—decreased activity level, unwilling to perform certain tasks; intermittent lameness or stiff gait that slowly progresses; possible history of joint trauma, OCD, or developmental disorders; may be exacerbated by exercise, long periods of recumbency, and cold weather.
- Cats—overt lameness may not be seen. Reduction in activity, reluctance to jump, unkempt appearance, difficulty accessing litter box, and increased irritability.

Physical Examination Findings

- Stiff-legged or altered gait or nonuse of leg.
- Decreased range of motion.
- Crepitus.
- Joint swelling (effusion and/or thickening of the joint capsule).
- Joint pain.

- Joint instability.

CAUSES

- Primary—no known cause.
- Secondary—results from initiating cause: abnormal wear on normal cartilage (e.g., joint instability, joint incongruity, trauma to cartilage or supporting soft tissues, obesity) or normal wear on abnormal cartilage (e.g., osteochondral defects).

RISK FACTORS

- Working, athletic, and obese dogs place more stress on their joints.
- Dogs with disorders that affect collagen or cartilage (Cushing's disease, diabetes mellitus, hypothyroidism, hyperlaxity, prolonged steroid use).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplastic (synovial sarcoma; rarely, chondrosarcoma; osteosarcoma).
- Septic arthritis (caused by bacteria; spirochetes; L forms in cats; *Mycoplasma*; *Rickettsia*; *Ehrlichia*; viruses such as feline calicivirus; fungi and protozoa).
- Immune-mediated arthritis (erosive vs. nonerosive).
- Other musculoskeletal conditions that cause lameness.
- Neurologic conditions causing lameness or decreased activity/weakness.

OTHER LABORATORY TESTS

- Coombs' test, antinuclear antibody (ANA), and rheumatoid factor may help to rule out immune-mediated arthritis.
- Serum titers for *Borrelia*, *Ehrlichia*, and *Rickettsia* to evaluate for infectious arthritis.

IMAGING

- Radiographic changes—include joint capsular distention, osteophytosis, enthesophytosis, soft-tissue thickening, and narrowed joint spaces. In severely affected patients: subchondral sclerosis and intra-articular calcified bodies (joint mice).
- Radiographic severity often does not correlate with clinical severity.
- Stress radiography may identify underlying instability and accentuate joint incongruity (e.g., distraction index, passive hip laxity of coxofemoral joint is predictive of hip OA).
- Bone nuclear scintigraphy can assist in localizing subtle OA.
- Arthroscopy can allow direct observation of cartilage and characterization by Modified Outerbridge Score.

DIAGNOSTIC PROCEDURES

- Arthrocentesis and synovial fluid analysis—cell counts are normal or slightly increased (<2,000–5,000 cells/mL) predominantly

ARTHRITIS (OSTEOARTHRITIS)

(CONTINUED)

mononuclear (macrophages) and occasional synovial lining cells.

- Bacterial culture of synovial fluid or synovium—negative.
- Biopsy of synovial tissue to rule out neoplasia or immune-mediated arthropathy (lymphocytic plasmacytic synovitis, systemic lupus erythematosus).

PATHOLOGIC FINDINGS

- Fibrillation or erosion of articular cartilage.
- Eburnation and sclerosis of subchondral bone.
- Thickening and fibrosis of joint capsule.
- Synovial fluid can be grossly normal to thin and watery, usually increased volume.
- Synovial villous hypertrophy and hyperplasia.
- Osteophytes and enthesiophytes at joint capsule attachments and adjacent to the joint.
- Neovascularization or pannus in severe cases over joint surfaces.



TREATMENT

APPROPRIATE HEALTH CARE

- Medical—usually tried initially.
- Surgical options—to improve joint geometry or remove bone-on-bone contact areas through total joint arthroplasty, osteotomy, or joint fusion.

NURSING CARE

- Physical rehabilitation—very beneficial during periods of flare-ups.
- Maintaining or increasing joint motion—active and passive range of motion exercises, stretching, massage, therapeutic exercises, and hydrotherapy.
- Pain management—cold and heat therapy, transcutaneous electrical stimulation (TENS), and acupuncture.
- Muscle tone/strengthening—daily leash walking, incorporation of inclines/declines, stair ascent and stair descent, walking on uneven terrain, open water swimming, underwater and land treadmill.
- Maintenance of a lean body weight through both diet and daily exercise.

ACTIVITY

- During periods of calmness, daily leash walks to work up to twice-daily level flat ground for 20 minutes before incorporation of increased time or terrain.
- Limitation of daily activity that minimizes aggravation of clinical signs during periods of flare-up (avoidance of running, chasing, jumping, and playing).

DIET

- Weight reduction for obese patients—decreases stress placed on arthritic joints. Begin by feeding 60% of calories needed to maintain current body weight.
- Omega n-3 fatty acids decrease production of certain prostaglandins and modulate inflammation. Dosage should be 150–175 mg/kg DHA/EPA daily.

CLIENT EDUCATION

- Medical therapy is palliative and the condition is likely to progress.
- Describe identifying signs of flare-ups and importance of getting it under control quickly.
- Discuss management options, daily exercise, activity level, and diet.

SURGICAL CONSIDERATIONS

- Arthrotomy—used to remove aggravating causes (e.g., fragmented coronoid process, ununited anconeal process, osteochondral flaps).
- Arthroscopy—used to diagnose and remove aggravating causes.
- Reconstructive procedures—used to eliminate joint instability and correct anatomic problems (cruciate ligament rupture, patella luxation, angular deformity).
- Joint removal—femoral head and neck osteotomy, temperomandibular joint arthroplasty.
- Joint replacement—total hip replacement is widely used, total elbow and stifle replacement are used with less frequency, total ankle and shoulder replacement are experimental and used infrequently at this time.
- Joint fusion (arthrodesis)—in selected chronic cases and for joint instability, complete or partial; carpus, hock: generally excellent outcome; shoulder, elbow, stifle: less predictable outcome.



MEDICATIONS

DRUG(S) OF CHOICE

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Inhibit prostaglandin synthesis through cyclooxygenase enzymes.
- Deracoxib (3–4 mg/kg PO q24h, chewable).
- Carprofen (2.2 mg/kg PO q12h or q24h).
- Meloxicam (load 0.2 mg/kg PO, then 0.1 mg/kg PO q24h, liquid).
- Tepoxalin (load 20 mg/kg, then 10 mg/kg PO q24h).
- Cats—meloxicam (0.1 mg/kg PO q24h, liquid) or robenacoxib (1 mg/kg PO q24h for 3 days).
- Inhibit prostaglandin synthesis at receptor specific sites.
- Grapiprant (2.0 mg/kg PO q24h, chewable).

Disease-Modifying Osteoarthritis Agents (DMOAs)

- Host of products, many with little production oversight so effects vary widely. Supply polysulfated glycosaminoglycan (PSGAG) molecules to repair and regenerate cartilage.
- Adequan®—clinical study in dogs with hip dysplasia; 4.4 mg/kg IM every 3–5 days for 8 injections had positive, temporary effect.
- Glucosamine and chondroitin sulfate—oral Cosequin®, oral methylsulfonylmethane

(MSM), mixtures with MSM, or other supplements (e.g., Dasuquin® Advanced, GlycoFlex® 2, Synflex).

CONTRAINdications

- NSAIDs must not be given with steroids.
- Acetaminophen must not be given to cats.

PRECAUTIONS

- NSAIDs may cause gastric ulceration.
- Cyclooxygenase-2 (COX-2)-selective drugs may interfere with liver function when used outside of dosage range
- When switching NSAIDs—wait 3 days for washout before starting new drug.

POSSIBLE INTERACTIONS

Steroids with NSAIDs.

ALTERNATIVE DRUG(S)

- Free-radical scavengers.
- Amantadine (3–5 mg/kg PO q24h)—best used in combination with another analgesic such as NSAID. Only analgesic (other than NSAID) with scientific evidence for usage with OA.
- Gabapentin (5–10 mg/kg PO q8–12h)—no scientific evidence for usage with OA.
- Codeine (1–2 mg/kg PO q 8–12h)—no scientific evidence for usage with OA; suggested for short-term use during flare-ups.
- Glucocorticoids—inhibit inflammatory mediators and cytokines; however, chronic use delays healing and initiates damage to articular cartilage; potential systemic side effects documented; goal is low dose (dogs, 0.5–2 mg/kg; cats, 2–4 mg/kg) q48h.
- Prednisone—initial dose 1–2 mg/kg PO q24h for dogs and 4 mg/kg PO q24h for cats.
- Triamcinolone hexacetonide—intra-articular injection of 5 mg in dogs showed a protective and therapeutic effect in one model.
- Hyaluronic acid—intra-articular injection (15–30 mg/joint) used as a series of 3 separated by 1 week or in combination with an intra-articular steroid.
- Platelet-rich plasma—intra-articular injection to decrease inflammatory mediators; many patients need more than 1 injection separated by 2 weeks; weak scientific evidence for efficacy.



FOLLOW-UP

PATIENT MONITORING

- During flare-up recheck 2 weeks later; pain should be better controlled at this time; then recheck every 4–6 weeks until flare-up under control.
- Recheck OA patients every 4–6 months for life.
- Any clinical deterioration could indicate a flare-up—need to change drug selection or dosage; may indicate need for intra-articular

(CONTINUED)

ARTHRITIS (OSTEOARTHRITIS)**A**

injection, formal rehabilitation therapy, or surgical intervention.

PREVENTION/AVOIDANCE

Early identification of predisposing causes and prompt treatment to help reduce progression of secondary conditions, e.g., surgical removal of osteochondral lesions.

EXPECTED COURSE AND PROGNOSIS

- Slow progression of disease likely.
- Some form of medical or surgical treatment usually allows a good quality of life when managed appropriately and aggressively.

**MISCELLANEOUS****SYNOMYS**

- Degenerative arthritis.
- Degenerative joint disease.
- Osteoarthritis.
- Osteoarthrosis.

ABBREVIATIONS

- ANA = antinuclear antibody.
- COX-2 = cyclooxygenase-2.
- DMOA = disease-modifying osteoarthritis agent.

- MSM = methylsulfonylmethane.
- NSAID = nonsteroidal anti-inflammatory drug.
- OA = osteoarthritis.
- OCD = osteochondritis dessicans.
- PSGAG = polysulfated glycosaminoglycan.

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Consulting Editor Mathieu M. Glassman
Acknowledgment The author and book editors acknowledge the prior contribution of Walter C. Renberg.



**Client Education Handout
available online**

ARTHRITIS, SEPTIC



BASICS

DEFINITION

Pathogenic microorganisms within the closed space of one or more synovial joints.

PATHOPHYSIOLOGY

- Usually caused by contamination associated with traumatic injury (e.g., a direct penetrating injury such as bite, gunshot wound, foreign object), a sequela to surgery, arthrocentesis or joint injection, hematogenous spread of microorganisms from a distant septic focus, or less commonly the extension of primary osteomyelitis.
- Primary sources of hematogenous infection—urogenital, integumentary (including ears and anal sacs), respiratory, cardiac, and gastrointestinal systems.

SYSTEMS AFFECTED

Musculoskeletal—usually affects one joint.

GENETICS

N/A

INCIDENCE/PREVALENCE

Relatively uncommon cause of monoarticular arthritis in dogs and cats.

GEOGRAPHIC DISTRIBUTION

May be an increased incidence in areas with endemic Lyme disease.

SIGNALMENT

Species

- Most common in dogs.
- Rare in cats.

Breed Predilections

Any; medium to large breeds—most commonly German shepherds, Dobermans, and Labrador retrievers.

Mean Age and Range

Any age; usually between 4 and 7 years. Hematogenous—more common in immature animals.

Predominant Sex

Male

SIGNS

General Comments

Always consider the diagnosis in patients with acute, monoarticular lameness associated with soft tissue swelling, heat, and pain.

Historical Findings

- Lameness—acute onset most common, but can present as chronic lameness.
- Lethargy.
- Anorexia.
- May report previous trauma—dog bite, penetrating injury, prior surgery or other invasive procedure of the joint.

Physical Examination Findings

- Monoarticular lameness, rarely polyarticular.
- Joint pain and effusion—commonly carpus, stifle, hock, shoulder, or cubital joint.

- Localized joint heat.
- Decreased range of motion.
- Local lymphadenopathy.
- Pyrexia.

CAUSES

- Aerobic bacterial organisms—most common: *staphylococci*, *streptococci*, *coliforms*, and *Pasteurella*.
- Anaerobic organisms—most common: *Propionibacterium*, *Peptostreptococcus*, *Fusobacterium*, and *Bacteroides*.
- Spirochete—*Borrelia burgdorferi*.
- Mycoplasma*.
- Fungal agents—*Blastomyces*, *Cryptococcus*, and *Coccidioides*.
- Rickettsial*—*Anaplasma*, *Ehrlichia*, *Rickettsia*.
- Leishmania*.
- Feline calicivirus.

RISK FACTORS

- Predisposing factors for hematogenous infection—diabetes mellitus, hypoadrenocorticism (Addison's disease), immunosuppression.
- Penetrating trauma to the joint including surgery.
- Existing osteoarthritis or other joint damage.
- Intra-articular injection, particularly if steroid injected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Osteoarthritis.
- Trauma.
- Immune-mediated arthropathy.
- Postvaccinal transient polyarthritidis.
- Greyhound polyarthritidis.
- Feline progressive polyarthritidis.
- Crystal-induced joint disease.
- Synovial sarcoma.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram—inflammatory left shift in some cases.
- Other results normal.

OTHER LABORATORY TESTS

Serologic testing for specific pathogens.

IMAGING

Radiography

- Early disease—may reveal thickened and dense periarticular tissues; may see evidence of synovial effusion. Often difficult to diagnose early disease radiographically.
- Late disease—reveals bone destruction, osteolysis, irregular joint space, discrete erosions, and periarticular osteophytosis.

DIAGNOSTIC PROCEDURES

Synovial Fluid Analysis

- Increased volume.
- Turbid fluid.
- Decreased viscosity.
- Decreased mucin clot reaction.
- Make slides immediately; if additional fluid is obtained, place in EDTA tube.
- Elevated white blood cell (WBC) count—i.e., >80% neutrophils with $>40,000/\text{mm}^3$ (normal joint fluid <10% neutrophils and $<3,000/\text{mm}^3$).
- Neutrophils may show degenerative changes (chromatolysis, vacuolation, nuclear swelling, loss of segmentation).
- Neutrophils with phagocytosed bacteria—definitive diagnosis or bacteria in the synovial fluid.

Synovial Fluid Culture

- Positive culture is definitive but not necessary for diagnosis; negative culture does not rule out infection.
- Must be collected aseptically; requires heavy sedation or general anesthesia.
- Place fluid sample in aerobic and anaerobic culturets and in blood culture medium.
- Use 1 : 9 dilution of synovial fluid to blood culture media.
- Culturette samples—cultured immediately upon arrival at the laboratory.
- Blood culture medium—reculturing after 24 hours of incubation increases accuracy by 50% and is the preferred method.
- Mycoplasma*, bacterial L-forms, and protozoa require specific culture procedures—contact laboratory prior to sample collection.

Other

- Synovial biopsy—to rule out immune-mediated joint disease; no more effective than incubated blood culture medium for growing bacterial organisms.
- Blood and urine cultures if hematogenous source is suspected.

PATHOLOGIC FINDINGS

- Synovium—thickened; discolored; often very proliferative.
- Histology—evidence of hyperplastic synoviocytes.
- Increased numbers of neutrophils, macrophages, and fibrinous debris.
- Cartilage—loss of proteoglycan, destruction of articular surface, pannus formation.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—initial stabilization; initiate systemic antibiotic therapy as soon as fluid is obtained for bacterial culture; consider joint drainage/lavage as soon as possible to minimize intra-articular injury.
- Analgesia with anti-inflammatory medications if appropriate, and intravenous opioid.
- Identify and treat source if hematogenous spread is suspected.
- Outpatient—long-term management.

NURSING CARE

Alternating heat and cold packing—beneficial in promoting increased blood flow and decreased swelling.

ACTIVITY

Restricted until resolution of symptoms.

DIET

N/A

CLIENT EDUCATION

- Discuss probable cause.
- Warn client about the need for long-term antibiotics and the likelihood of residual degenerative joint disease.

SURGICAL CONSIDERATIONS

- Acute disease with minimal radiographic changes—joint drainage and lavage via needle arthrocentesis, arthroscopic lavage,

(CONTINUED)

or arthrotomy; an irrigation catheter (ingress/egress) can be placed in larger joints. • Chronic disease—may require open arthrotomy with debridement of the synovium and copious lavage; if appropriate, an irrigation catheter (ingress/egress) may be placed to lavage the joint postoperatively. • Lavage—use warmed physiologic saline or lactated Ringer's solution (2–4 mL/kg q8h) until effluent is clear; do not add povidone/iodine or chlorhexidine to lavage fluid. • Effluent fluid—cytologically monitored daily for existence and character of bacteria and neutrophils. • Removal of catheters—when effluent fluid has no bacteria and the neutrophils are cytologically healthy. • Arthroscopy allows for visual assessment of articular cartilage, lavage, and biopsy, and is a less invasive method of thorough joint lavage than arthrotomy. • Recent reports suggest there may be no difference between combined medical and surgical management and medical management alone.



MEDICATIONS

DRUG(S) OF CHOICE

• Pending culture susceptibility data—bactericidal antibiotics, such as first-generation cephalosporin or amoxicillin-clavulanic acid, preferred. • Choice of antimicrobial drugs—primarily depends on in vitro determination of susceptibility of microorganisms; toxicity, frequency, route of administration, and expense also considered; most penetrate the synovium well; need to be given for a minimum of 4–8 weeks. • Nonsteroidal anti-inflammatory drugs (NSAIDs)—may help decrease pain and inflammation.

CONTRAINdications

Avoid fluorinated quinolones in pediatric patients, as their use has induced cartilage lesions experimentally.

PRECAUTIONS

Failure to respond to conventional antibiotic therapy—may indicate anaerobic disease, other unusual cause (fungal, spirochete), or aseptic arthritides.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- If drainage and irrigation catheters have been placed—may be removed after 4–6 days or after reassessment of synovial fluid cytology.
- Duration of antibiotic therapy—2 weeks following resolution of clinical signs; total treatment may be 4–8 weeks or longer, depending on clinical signs and pathogenic organism.
- Persistent synovial inflammation without viable bacterial organisms (dogs)—may be caused by antigenic bacterial fragments or antigen antibody deposition.
- Systemic corticosteroid therapy (after joint sepsis has been resolved) and aggressive physical therapy—may be needed to maximize normal joint dynamics.

PREVENTION/AVOIDANCE

If clinical signs recur, early (within 24–48 hours) treatment provides the greatest benefit.

POSSIBLE COMPLICATIONS

- Chronic disease—severe degenerative joint disease.
- Recurrence of infection.
- Limited range of joint motion.
- Generalized sepsis.
- Osteomyelitis.

EXPECTED COURSE AND PROGNOSIS

- Acutely diagnosed disease (within 24–48 hours) responds well to antibiotic therapy.
- Delayed diagnosis or resistant or highly virulent organisms—guarded to poor prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

- Infectious arthritis.
- Joint ill.

SEE ALSO

- Osteomyelitis.
- Polyarthritis, Erosive, Immune-Mediated.

ARTHRITIS, SEPTIC

ABBREVIATIONS

- NSAID = nonsteroidal anti-inflammatory drug.
- WBC = white blood cell.

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Client Education Handout
available online

ASCITES



BASICS

DEFINITION

The escape of fluid, either transudate or exudate, into the abdominal cavity between the parietal and visceral peritoneum.

PATHOPHYSIOLOGY

- Ascites can be caused by the following:
 - Congestive heart failure (CHF) and associated interference in venous return.
 - Depletion of plasma proteins associated with inappropriate loss of protein from renal or gastrointestinal disease—protein-losing nephropathy or enteropathy, respectively.
 - Obstruction of the vena cava or portal vein, or lymphatic drainage due to neoplastic occlusion.
 - Overt neoplastic effusion.
 - Peritonitis— infective or inflammatory.
 - Electrolyte imbalance, especially hypernatremia.
 - Liver cirrhosis.

SYSTEMS AFFECTED

- Cardiovascular.
- Gastrointestinal.
- Hemic/lymph/immune.
- Renal/urologic.

SIGNALMENT

- Dog and cat.
- No species or breed predisposition.

SIGNS

- Episodic weakness.
- Lethargy.
- Abdominal fullness.
- Abdominal discomfort when palpated.
- Dyspnea from abdominal distension or associated pleural effusion.
- Anorexia.
- Vomiting.
- Weight gain.
- Scrotal or preputial edema.
- Groaning when lying down.

CAUSES

- Nephrotic syndrome.
- Cirrhosis of liver.
- Right-sided CHF.
- Hypoproteinemia.
- Ruptured bladder.
- Peritonitis.
- Abdominal neoplasia.
- Abdominal hemorrhage.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Abdominal Distension without Effusion

- Organomegaly—hepatomegaly, splenomegaly, renomegaly, and hydrometra.
- Abdominal neoplasia.
- Pregnancy.
- Bladder distension.
- Obesity.
- Gastric dilatation.

Differentiating Diseases

- Transudate—nephrotic syndrome, cirrhosis of liver, right-sided CHF, hypoproteinemia, and ruptured bladder.
- Exudate—peritonitis, abdominal neoplasia, and hemorrhage.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis occurs in patients with systemic infection.
- Albumin is low in patients with impaired liver synthesis, gastrointestinal loss, or renal loss.
- Cholesterol is low in patients with impaired liver synthesis.

Liver Enzymes

- Low to normal in patients with impaired liver synthesis.
- High in patients with liver inflammation, hyperadrenocorticism, gallbladder obstruction, and chronic passive congestion.

Total and Direct Bilirubin

- Low to normal in patients with impaired liver synthesis.
- High in patients with biliary obstruction caused by tumor, gallbladder distension, or obstruction.

Blood Urea Nitrogen (BUN)

and Creatinine

- High in patients with renal failure.
- BUN low in patients with impaired liver synthesis or hyperadrenocorticism.

Glucose

Low in patients with impaired liver synthesis.

OTHER LABORATORY TESTS

- To detect hypoproteinemia—protein electrophoresis and immune profile.
- To detect proteinuria—urinary protein : creatinine ratio (normal <0.5 : 1).
- To detect liver ascites—analysis of serum ascites albumin gradient.

IMAGING

- Thoracic and abdominal radiography is sometimes helpful.

• Ultrasonography of the liver, spleen, pancreas, kidney, bladder, and abdomen can often determine cause.

Stages of ascites:

- Stage I—minimal ascites: detected by ultrasound only.
- Stage II—moderate ascites: abdominal distention visible and/or noted on ballottement.
- Stage III—significant ascites: marked abdominal distention; patient uncomfortable, possibly with labored breathing.

DIAGNOSTIC PROCEDURES

Ascitic Fluid Evaluation

Exfoliative cytologic examination and bacterial culture and antibiotic sensitivity—remove approximately 3–5 mL of abdominal fluid via aseptic technique.

Transudate

- Clear and colorless.
- Protein <2.5 g/dL.
- Specific gravity <1.018.
- Cells <1,000/mm³—neutrophils and mesothelial cells.

Modified Transudate

- Red or pink; may be slightly cloudy.
- Protein 2.5–5 g/dL.
- Specific gravity >1.018.
- Cells <5,000/mm³—neutrophils, mesothelial cells, erythrocytes, and lymphocytes.

Exudate (Nonseptic)

- Pink or white; cloudy.
- Protein 2.5–5 g/dL.
- Specific gravity >1.018.
- Cells 5,000–50,000/mm³—neutrophils, mesothelial cells, macrophages, erythrocytes, and lymphocytes.

Exudate (Septic)

- Red, white, or yellow; cloudy.
- Protein >4.0 g/dL.
- Specific gravity >1.018.
- Cells 5,000–100,000/mm³—neutrophils, mesothelial cells, macrophages, erythrocytes, lymphocytes, and bacteria.

Hemorrhage

- Red; spun supernatant clear and sediment red.
- Protein >5.5 g/dL.
- Specific gravity 1.007–1.027.
- Cells consistent with peripheral blood.
- Does not clot.

Chyle

- Pink, straw, or white.
- Protein 2.5–7 g/dL.
- Specific gravity 1.007–1.040 and above.
- Cells <10,000/mm³—neutrophils, mesothelial cells, and large population of small lymphocytes.

(CONTINUED)

- Other—fluid in tube separates into cream-like layer when refrigerated; fat droplets stain with Sudan III.

Pseudochyle

- White.
- Protein >2.5 g/dL.
- Specific gravity 1.007–1.040.
- Cells <10,000/mm³—neutrophils, mesothelial cells, and small lymphocytes.
- Other—fluid in tube does not separate into cream-like layer when refrigerated; does not stain with Sudan III.

Urine

- Clear to pale yellow.
- Protein >2.5 g/dL.
- Specific gravity 1–1.040 and above.
- Cells 5,000–50,000/mm³—neutrophils, erythrocytes, lymphocytes, and macrophages.
- Other—if the urinary bladder ruptured <12 hours before, urinary glucose and protein could be negative; if bladder ruptured >12 hours before, urine becomes a dialysis medium with ultrafiltrate of plasma, and urine contains glucose and protein.

Bile

- Slightly cloudy and yellow.
- Protein >2.5 g/dL.
- Specific gravity >1.018.
- Cells 5,000–750,000/mm³—neutrophils, erythrocytes, macrophages, and lymphocytes.
- Other—bilirubin confirmed by urine dipstick; nonicteric patient may have gallbladder rupture, biliary tree leakage, or rupture in the proximal bowel.

**TREATMENT**

- Can design treatment on an outpatient basis, with follow-up or inpatient care, depending on physical condition and underlying cause.
- If patients are markedly uncomfortable when lying down or become more dyspneic with stress, consider removing enough ascites to reverse these signs.
- Dietary salt restriction may help control transudate fluid accumulation due to CHF, cirrhosis, or hypoproteinemia.
- For exudate ascites control, address the underlying cause; corrective surgery is often indicated, followed by specific therapeutic management (e.g., patient with splenic tumor: tumor removed, abdominal bleeding controlled, blood transfusion administered).

Large-Volume Paracentesis

- Stage III treatment.
- Pretreat patient with hetastarch (6%) @ 1–2 mL/kg for 2 hours.
- Abdominal tap (paracentesis), until drainage slows.
- Post-treat patient with hetastarch (6%) @ 1–2 mL/kg for 4 hours.

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

- Patients with liver insufficiency or CHF—restrict sodium and give a diuretic combination of furosemide (1–2 mg/kg q8h PO) and spironolactone (1–2 mg/kg q12h PO); if control is inadequate, hydrochlorothiazide (1–4 mg/kg q12h PO) can be added (*cautious*); must monitor serum potassium concentration to prevent potassium imbalances.
- Additionally for patients in CHF—pimobendan (0.3 mg/kg q12h PO) and an angiotensin-converting-enzyme inhibitor (e.g., enalapril 0.25–0.5 mg/kg q12h PO).
- Patients with hypoproteinemia, nephrotic syndrome, and associated ascitic fluid accumulation—can treat as above with the addition of hetastarch (6% hetastarch in 0.9% NaCl); administer an IV bolus (dogs, 20 mL/kg; cats, 10–15 mL/kg) slowly over ~1 hour; hetastarch increases plasma oncotic pressure and pulls fluid into the intravascular space for up to 24–48 hours.
- Systemic antibiotic therapy is dictated by bacterial identification and sensitivity testing in patients with septic exudate ascites.

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

- Varies with the underlying cause.
- Check sodium, potassium, BUN, creatinine, and weight fluctuations periodically if the patient is maintained on a diuretic.

POSSIBLE COMPLICATIONS

Aggressive diuretic administration may cause hypokalemia, which could predispose to metabolic alkalosis and exacerbation of hepatic encephalopathy in patients with underlying liver disease; alkalosis causes a shift from ammonium (NH₄⁺) to ammonia (NH₃).

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

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

Abdominal effusion.

SEE ALSO

- Cirrhosis and Fibrosis of the Liver.
- Congestive Heart Failure, Right-Sided.
- Hypoalbuminemia.
- Nephrotic Syndrome.

ABBREVIATIONS

- BUN = blood urea nitrogen.
- CHF = congestive heart failure.

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**Client Education Handout
available online**

ASPIRIN TOXICOSIS



BASICS

OVERVIEW

- Given for its antipyretic, analgesic, anti-inflammatory, and antiplatelet effects.
- Aspirin inhibits cyclooxygenase, reducing the synthesis of prostaglandins and thromboxanes.
- Gastric irritation and hemorrhage can occur.
- Repeated doses can produce gastrointestinal ulceration and perforation and hepatic injury; renal injury is uncommon.
- Toxic hepatitis, marked metabolic acidosis, and anemia can occur, especially in cats (long half-life).
- Hepatic damage may not be dose related.

SIGNALMENT

Cats and less commonly dogs.

SIGNS

- Depression, lethargy.
- Anorexia.
- Vomiting ± blood.
- Diarrhea ± blood; melena.
- Tachypnea.
- Hyperthermia.
- Pallor.
- Polyuria/polydipsia (rare).
- Muscular weakness and ataxia.
- Ataxia, coma, seizures, and death in 1 or more days.

CAUSES & RISK FACTORS

- Owners employing human dosage guidelines to medicate cats and dogs.
- Dogs—single 25 mg/kg dose has resulted in gastric bleeding.
- Cats have a decreased ability to conjugate salicylate with glycine and glucuronic acid due to a deficiency in glucuronyl transferase.
- Half-life increases with dosage—cats, 22–27 hours for 5–12 mg/kg and approximately 44 hours for 25 mg/kg; responsible for higher risk in cats. Dogs, half-life = 7.5 hours.
- Elimination is slower in neonatal and geriatric patients.
- Patients with hypoalbuminemia may be at higher risk of toxicity because aspirin is highly protein bound to plasma albumin.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Ethylene glycol or alcohol.
- Anticoagulant rodenticides.
- Other causes of liver failure, including acetaminophen, iron, metaldehyde, and blue-green algae.

CBC/BIOCHEMISTRY/URINALYSIS

- Cats—prone to Heinz body formation.
- Decreased packed cell volume (PCV); may be marked, especially in cats.

- Leukocytosis.
- Hypoproteinemia.
- Elevated liver enzymes.
- Elevated renal values (rare).

OTHER LABORATORY TESTS

- Initial respiratory alkalosis followed by marked metabolic acidosis.
- High ketones and pyruvic, lactic, and amino acid levels.
- Decreased sulfuric and phosphoric acid renal clearance.

IMAGING

- Abdominal imaging (perforation).

DIAGNOSTIC PROCEDURES

- Salicylic acid concentrations in serum.



TREATMENT

- Inpatient—following general principles of poisoning management.
- Induced gastric emptying—gastric lavage or induced emesis.
- Correction of acid-base balance—continuous IV fluids; assisted ventilation and supplemental oxygen for severely affected animals.
- Whole blood transfusions for severe cases of hemorrhage and hypotension.
- Peritoneal dialysis and hemodialysis are advanced procedures that will increase salicylate clearance in severe cases.



MEDICATIONS

DRUG(S) OF CHOICE

- No specific antidote available.
- Activated charcoal—1–2 g/kg PO with a cathartic (sorbitol); monitor sodium concentration.
- 5% dextrose IV to correct dehydration.
- Gastrointestinal protectants—sucralfate and an H2 blocker or proton pump inhibitor; misoprostol for patients at higher risk for gastrointestinal hemorrhage.
- Sodium bicarbonate 1 mEq/kg IV in severe ingestions—alkalinizes urine; must closely monitor acid-base status.
- Diazepam 0.5–1 mg/kg IV or rectal as needed for seizures.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Maintaining renal function and acid-base balance is vital.
- Severe acid-base disturbances, severe dehydration, toxic hepatitis, bone marrow

depression, and coma are poor prognostic indicators.



MISCELLANEOUS

- Be sure that history of “aspirin” medication does not refer to other available pain medications.
- Question owner about any preexisting painful condition that may have prompted the aspirin administration.

ABBREVIATIONS

- PCV = packed cell volume.

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BASICS

DEFINITION

- Chronic bronchitis—neutrophilic inflammation of the lower airways (bronchi and bronchioles) lacking a specific etiology; chronic daily cough of greater than 2 months in duration.
- Asthma—acute or chronic airway inflammation associated with increased airway responsiveness to various stimuli, airway narrowing due to smooth muscle hypertrophy or constriction, reversibility of airway constriction, and presence of eosinophils, lymphocytes, and mast cells within the airways.
- Bronchitis is thought to result in airflow obstruction due to airway remodeling, while asthma is associated with airway constriction; however, clinically the two disease processes can appear similar. No physical examination findings or biomarkers can distinguish between the two syndromes, although reversal of airflow obstruction following administration of a beta-agonist is suggestive of the asthmatic form of disease.

PATOPHYSIOLOGY

- Lower airway inflammation likely results from inhalation of irritant substances.
- Bronchiolar smooth muscle constriction—can resolve spontaneously or with treatment.
- Increase in mucosal goblet cells, mucus production, and edema of bronchial wall associated with inflammation.
- Excessive mucus can cause bronchiolar obstruction, atelectasis, or bronchiectasis.
- Smooth muscle hypertrophy implies chronicity—usually not reversible.
- Chronic inflammation leads to airway remodeling and irreversible airflow obstruction.

SYSTEMS AFFECTED

- Respiratory.
- Cardiac—pulmonary hypertension rarely.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Breed Predilections

Siamese overrepresented.

Mean Age and Range

Any age; more common between 2 and 8 years.

Predominant Sex

One study showed females overrepresented.

SIGNS

Historical Findings

- Coughing, tachypnea, labored breathing or wheezing.
- Signs are typically episodic and can be acute or chronic.

Physical Examination Findings

- Severely affected cats present with open-mouth breathing, tachypnea, and cyanosis.

- Increased tracheal sensitivity is common.
- Chest auscultation may reveal crackles and/or expiratory wheezes, but can be normal.
- Labored breathing with an abdominal push on expiration, increase in expiratory effort.

CAUSES

Triggers of airway inflammation unknown.

RISK FACTORS

- Cigarette smoke, poor environmental hygiene, dusty cat litter, hair sprays, and air fresheners can exacerbate disease.
- Use of potassium bromide—implicated in causing signs of bronchitis/asthma in some cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Rule out infectious pneumonia (*Mycoplasma*, *Toxoplasma*, bacterial or fungal pneumonia).
- Consider *Dirofilaria immitis* and primary lung parasites (*Aelurostrongylus abstrusus*, *Capillaria aerophilia*, *Paragonimus kellicotti*, *Troglotryongylus brevior*). More common in southern and midwest United States, and in outdoor and hunting cats in some geographic regions.
- Primary or metastatic neoplasia can have similar clinical and radiographic appearance.
- Clinical presentation of idiopathic pulmonary fibrosis may appear similar to feline bronchitis.

CBC/BIOCHEMISTRY/URINALYSIS

Frequently normal; ~40% of cats with bronchial disease have peripheral eosinophilia.

OTHER LABORATORY TESTS

- Fecal exams—flotation for *Capillaria*, sedimentation for *Paragonimus*, Baermann for *Aelurostrongylus*; false-negative results are common.
- Heartworm antigen and antibody testing, particularly if coughing occurs in conjunction with vomiting.
- Radioallergosorbent testing or intradermal skin testing—no correlation between skin allergies and respiratory disease currently documented.

IMAGING

Radiography

- Classically, diffuse bronchial wall thickening; interstitial or patchy alveolar patterns also possible.
- Severity of radiographic changes does not necessarily correlate with clinical severity or duration, and normal radiographs can be found.
- Hyperinflation of lung fields—flattened and caudally displaced diaphragm, increased distance between the heart and diaphragm, extension of lungs to the first lumbar vertebrae thought to reflect bronchoconstriction.
- Collapse of right middle lung lobe due to mucus plugging and atelectasis reported in 11% of cases.
- Pulmonary lobar arterial enlargement is suspicious for heartworm disease.

CT

Bronchial wall thickening, patchy alveolar patterns, and bronchiectasis.

Echocardiography

Useful to document heartworm disease or secondary pulmonary hypertension.

DIAGNOSTIC PROCEDURES

Transoral Tracheal Wash (TOTW)

Use a sterile endotracheal tube and polypropylene or red rubber catheter to collect airway fluids at the level of the carina.

Bronchoscopy

Allows visualization of trachea and bronchi. Excessive amounts of thick mucus are common with bronchitis. Mucosa of the airways is typically hyperemic and edematous.

Cytology of TOTW or Bronchoscopy/

Bronchoalveolar Lavage (BAL)

- Eosinophils and neutrophils are most prominent cell types.
- Up to 20% eosinophils on BAL cytology can be found in normal cats.
- A mixed inflammatory cell population occurs in about 21% of cats.

Bacterial Cultures

- Quantitated cultures recommended; positive cultures frequently encountered, but bacterial colony counts >100–300 cfu/mL uncommon with bronchitis.
- Specific *Mycoplasma* cultures and PCR for species detection.

Biopsy

Keyhole biopsy—can differentiate between idiopathic pulmonary fibrosis, neoplasia, and bronchitis if needed; rarely performed.

PATHOLOGIC FINDINGS

Hyperplasia/hypertrophy of goblet cells, hypertrophy of airway smooth muscle, epithelial erosion, and inflammatory infiltrates.



TREATMENT

APPROPRIATE HEALTH CARE

- Remove patient from environment that exacerbates disease.
- Hospitalize for acute respiratory distress.

NURSING CARE

- Oxygen therapy, bronchodilators, and sedatives in an acute crisis.
- Minimize manipulation in order to lessen stress and oxygen needs of the animal.

ACTIVITY

Usually self-limited by patient.

DIET

Calorie restriction for obese cats.

CLIENT EDUCATION

- Most causes are chronic and progressive.
- Do not discontinue medical therapy when clinical signs have resolved—subclinical inflammation is common and can lead to

ASTHMA, BRONCHITIS—CATS

(CONTINUED)

progression of disease; lifelong medication and environmental changes usually necessary.

- Some clients can be taught to give terbutaline subcutaneously and corticosteroid injections at home for a crisis situation.

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

- Oxygen and a parenteral bronchodilator—injectable terbutaline (0.01 mg/kg IV/SC); repeat if no clinical improvement (decrease in respiratory rate or effort) in 20–30 minutes.
- A sedative can aid in decreasing anxiety (butorphanol tartrate at 0.2–0.4 mg/kg IV/IM, buprenorphine at 0.01 mg/kg IV/IM, or acepromazine at 0.01–0.05 mg/kg SC).
- A short-acting parenteral corticosteroid may also be required—dexamethasone sodium phosphate (0.1–0.25 mg/kg IV/SC).

Long-Term Management**Corticosteroids**

- Decrease inflammation.
- Oral treatment is preferred over injectable for closer monitoring of dose and duration.
- Prednisolone—0.5–1 mg/kg PO q12h; begin to taper dose (50% each week) after 1–2 weeks if clinical signs have improved; maintenance therapy 0.5–1 mg/kg PO q24–48h.
- Longer-acting parenteral steroids (Vetalog® or Depo-Medrol®) should be reserved only for situations where owners are unable to administer oral or inhaled medication on a routine basis.

Inhaled Corticosteroids

- Requires a form-fitting facemask, spacer, and metered-dose inhaler (MDI); veterinary brand—Aerokat® (Trudell Medical).
- The most common corticosteroid used as an MDI is fluticasone propionate (Flovent)—110 µg Flovent MDI is recommended (1–2 actuations, 7–10 breaths q12h); in one study, use of 44 µg Flovent decreased BAL eosinophil counts in cats with experimentally induced lower airway disease.
- Flovent is used for long-term control of airway inflammation; takes 10–14 days to reach peak effect; use oral steroids concurrently during this time.
- Results in some suppression of the hypothalamic–pituitary axis, but systemic side effects appear to be limited.

Bronchodilators

- Methylxanthines—sustained-release theophylline formulations recommended, and pharmacokinetics can vary greatly; only compounded generic currently available; dose at 15–20 mg/kg PO once daily in the evening.
- Beta-2 agonists (terbutaline, albuterol)—reverse smooth muscle constriction; oral terbutaline dose is 1/4 of a 2.5 mg tablet; initial albuterol dose is 1–2 puffs; avoid giving beta-2 agonists daily as tachyphylaxis may develop.

Anthelmintics

- Empirical therapy is indicated for cats with clinical signs of bronchial disease and eosinophilic airway cytology in an appropriate geographic location.
- Consider fenbendazole, ivermectin, praziquantel, or milbemycin.

Antibiotics

Use based on a positive quantitative culture and susceptibility testing or *Mycoplasma* isolation.

CONTRAINDICATIONS

Beta-2 antagonists (e.g., propranolol) are contraindicated because of their ability to block sympathetically mediated bronchodilation.

PRECAUTIONS

- Long-term use of steroids increases risk of development of diabetes mellitus and predisposes to immunosuppression.
- Use of corticosteroids in cats may precipitate congestive heart failure.
- Beta agonists could cause tachycardia and exacerbate underlying cardiac disease.

ALTERNATIVE DRUG(S)

- Leukotriene receptor blockers and inhibitors of generation—no evidence to support use.
- Tyrosine kinase inhibitors—masitinib is no longer on the market; side effects were dose limiting.
- Antiserotonin and antihistamine drugs—no evidence to support use.
- Immunotherapy—allergen-specific rush immunotherapy (RIT) shows promise in treating asthma.
- Omega 3 fatty acids/neutraceuticals—diminished hyperresponsiveness of airway, but did not resolve airway eosinophilia.

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

- Owners should report any increase in coughing, sneezing, wheezing, or respiratory distress; medications should be increased appropriately, or additional therapy initiated if clinical signs worsen.
- Follow-up radiographs may be helpful to detect onset of new disease.
- Owner should watch for signs of polyuria/polydipsia (PU/PD) that could indicate diabetes mellitus or renal disease; monitor blood glucose and urine cultures.

PREVENTION/AVOIDANCE

Eliminate any environmental factors that can trigger a crisis situation (see Risk Factors); change furnace and air-conditioner filters on a regular basis; consider dust-free litters.

POSSIBLE COMPLICATIONS

- Acute episodes can be life-threatening.
- Right-sided heart disease develops rarely as a result of long-term bronchitis.

EXPECTED COURSE**AND PROGNOSIS**

- Long-term therapy should be expected.
- Most cats do well if recurrence of clinical signs is carefully monitored and medical therapy appropriately adjusted.
- A few cats will be refractory to treatment; these carry a much worse prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Cor pulmonale can be a sequela to chronic lower airway disease.

PREGNANCY/FERTILITY/BREEDING

Glucocorticoids are contraindicated in the pregnant animal; bronchodilators should be used with caution.

SYNONYMS

- Allergic bronchitis.
- Asthmatic bronchitis.
- Feline lower airway disease.
- Extrinsic asthma.
- Eosinophilic bronchitis.

SEE ALSO

- Heartworm Disease—Cats.
- Respiratory Parasites.

ABBREVIATIONS

- BAL = bronchoscopy/bronchoalveolar lavage.
- MDI = metered-dose inhaler.
- PU/PD = polyuria/polydipsia.
- RIT = rush immunotherapy.
- TOTW = transoral tracheal wash.

INTERNET RESOURCES

- www.aerokat.com
- www.fritzthebrave.com

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Acknowledgment The author and book editors acknowledge the prior contribution of Carrie J. Miller and Lynelle R. Johnson.



**Client Education Handout
available online**

ATOPIC DERMATITIS



BASICS

DEFINITION

• Genetically predisposed skin disease characterized by inflammation and pruritis. Clinical signs associated with immunoglobulin (Ig) E and most commonly directed against environmental allergens. • Differentiate from atopic-like dermatitis, in which clinical signs identical to atopic dermatitis but IgE response to environmental or other allergens cannot be demonstrated.

PATHOPHYSIOLOGY

• Allergen exposure in susceptible animals results in IgE production. Upon reexposure to allergen, mast cell degranulation and activation of T_H2 lymphocytes allow release of inflammatory cytokines, chemokines, histamine, proteolytic enzymes, and other chemical mediators. • Genetic defects—dogs: gene expression upregulated or downregulated; cats: not well documented. • Barrier function defects—dogs: impaired epidermal lipid barrier can lead to enhanced allergen penetration and increased transepidermal water loss (TEWL); filaggrin defect thought to be associated; cats: may not be as relevant as with dogs. • Immunologic defects—dogs: acute lesions characterized by increased T_H2 lymphocyte activity, while T_H1 cytokines predominate in chronic lesions; T_H2:T_H1 imbalance proposed; aberrant regulatory T-cell function reported; cats: T_H2-mediated dysfunction suspected, but cytokine pathways need further investigation. • Bacterial superantigens, auto-antigens released via keratinocyte damage, and *Malassezia* may play role in inflammation.

SYSTEMS AFFECTED

• Ophthalmic. • Respiratory. • Skin/exocrine.

GENETICS

• Dogs— inherited predisposition. • Cats— inherited predisposition less clear.

INCIDENCE/PREVALENCE

• Canine—3–27% of canine population estimated. • Feline—lower than for dogs.

GEOGRAPHIC DISTRIBUTION

Canine—worldwide; local factors influence seasonality, severity, and duration of signs.

SIGNALMENT

Species

Dogs and cats.

Breed Predilections

• United States—Boston terrier, boxer, Cairn terrier, Chinese Shar-Pei, cocker spaniel, Dalmatian, English bulldog, English and Irish setter, American Staffordshire terrier, Lhasa apso, miniature schnauzer, pug, Sealyham terrier, Scottish terrier, West

Highland white terrier, wirehaired fox terrier, Labrador retriever. • Feline—Abyssinian, Devon Rex, domestic shorthaired cats.

MEAN AGE AND RANGE

• Canine—6 months to 3 years. • Feline—6 months to 2 years, commonly under 3 years.

PREDOMINANT SEX

None reported.

SIGNS

General Comments

Cutaneous changes caused by self-induced trauma; primary lesions usually unrecognized.

Historical Findings

- Pruritus. • Early age of onset. • History in related individuals. • May be initially seasonal. • Recurring skin or ear infection.
- Temporary response to glucocorticosteroids.
- Signs worsen with time.

Physical Examination Findings

- Most common (dogs)—interdigital spaces, carpal/tarsal areas, muzzle, periocular, axillae, abdomen, pinnae; >40% can be generalized. • Most common (cats)—head and neck, mouth, abdomen, lateral thorax, hind limbs. • Lesions (dogs)—none to salivary staining, alopecia, erythema, papules, crusts, hyperpigmentation, lichenification, seborrhea sicca/oleosa, and/or hyperhidrosis.
- Lesions (cats)—miliary dermatitis (small crusted papules), alopecia, eosinophilic granuloma complex (indolent ulcers, eosinophilic granulomas, eosinophilic plaques). • Chronic relapsing bacterial and yeast skin/ear infections (common).
- Respiratory symptoms, conjunctivitis, and blepharitis possible.

CAUSES

- Pollens. • Mold spores. • *Malassezia*.
- House dust and storage mites. • Animal/human dander. • Insects.

RISK FACTORS

- Environments with long allergy seasons and high pollen and mold spore levels. • Concurrent hypersensitivities (summation effect). • Born during allergy season. • Breed predisposition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Adverse food reaction. • Flea bite hypersensitivity. • Sarcoptic mange. • Bacterial folliculitis. • Yeast dermatitis. • Contact dermatitis (allergic or irritant).

CBC/BIOCHEMISTRY/URINALYSIS

Eosinophilia—rare in dogs without concurrent flea infestations; common in cats.

DIAGNOSTIC PROCEDURES

- Diagnosis made by history, physical examination, and ruling out differential diagnoses.
- Serology/intradermal test (IDT) *not* meant for diagnosis. • Greatest treatment success noted when immunotherapy based on results of both serum and intradermal testing.

Serologic Allergy Tests

- Measures allergen-specific IgE in serum.
- Advantages—readily available; clipping/sedation not required; concurrent/recent medications and infections less likely to affect results; similar hyposensitization success to IDT. • Disadvantages—fewer allergens tested; quality control/reliability varies with laboratory.

IDT

- Test allergens injected intradermally causing wheal formation. • Advantages—tests affected organ, results available immediately, many allergens tested; preferred where available. • Disadvantages—requires experience to interpret results, clipping and sedation needed, difficult to interpret in cats; drug withdrawal periods recommended, concurrent infection may affect results.

PATHOLOGIC FINDINGS

Skin biopsy—rule out other differential diagnoses; results not pathognomonic; superficial perivascular dermatitis with lymphocytic exocytosis ± eosinophils, mast cells; often with secondary bacterial folliculitis.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient

ACTIVITY

Avoid offending allergens when possible.

DIET

Diets rich in essential fatty acids may be beneficial.

CLIENT EDUCATION

Explain inheritable, progressive, and incurable nature of condition.



MEDICATIONS

DRUG(S) OF CHOICE

Immunotherapy (Hyposensitization)

- Subcutaneous or sublingual administration of causative allergens. • Allergen selection based on allergy test results, patient history, and knowledge of local exposure.
- Immunotherapy protocols not standardized and vary widely between clinicians.
- Preferred treatment in most cases.
- Successfully reduces pruritus in 50–90% of dogs and cats. • 3 months to 1 year for full effect. • May continue lifelong if effective.

(CONTINUED)

ATOPIC DERMATITIS**A****Cyclosporine (Atopica® Preferred)**

- Cyclosporine, modified (dogs, 5 mg/kg/day; cats, 7 mg/kg/day). • 1–4 weeks for effect—frequency of dosing may be reduced to maintain control of symptoms.
- Monitoring recommended. • Cats—drug blood level monitoring recommended; keep indoors, do *not* feed raw meat.

Corticosteroids

- For short-term relief or taper to lowest dosage/frequency. • Dogs—e.g., prednisolone (1 mg/kg PO q24h). • Cats—e.g., prednisolone (2 mg/kg q24h).

Antihistamines

- Less effective than corticosteroids. • 2 weeks for effect. • Dogs—cetirizine (1 mg/kg PO q12–24h), chlorpheniramine (0.4 mg/kg PO q8–12h), diphenhydramine (2.2 mg/kg PO q8–12h), amitriptyline (1–2 mg/kg q12h).
- Cats—cetirizine (5 mg/cat q24h), chlorpheniramine (2 mg/cat PO q12h), amitriptyline (5–10 mg/cat q24h); diphenhydramine may cause paradoxical excitation in cats.

Oclacitinib (Apoquel®)

- Dogs—onset time/response similar to glucocorticoids (0.4–0.6 mg/kg q12h for 14 days, then q24h for maintenance). • Cats—not licensed; limited short-term studies report effectiveness, but higher doses may be needed.

Lokivetmab (Cytopoint®)

Dogs only—anti-IL-31 monoclonal antibody injectable; repeated as needed up to frequency of every 4–6 weeks.

PRECAUTIONS

- Immunotherapy—anaphylaxis rare (accompanied by diarrhea, weakness, collapse), hives, facial swelling; monitor for 1 hour post injection; increased pruritus after injection may indicate change in schedule needed; pain or swelling at injection site uncommon. • Cyclosporine—may affect glucose homeostasis; increased incidence of urinary tract infection; vomiting and diarrhea most common side effects; gingival hyperplasia, papillomavirus, and hirsutism possible; risk of fatal toxoplasmosis in naïve cats. • Corticosteroids—avoid iatrogenic hyperglucocorticism/hyperadrenocorticism; possible aggravation of pyoderma and induction of demodicosis.
- Antihistamines—can produce drowsiness, rarely anorexia, vomiting, diarrhea, increased pruritus; use with caution in patients with cardiac arrhythmias. • Oclacitinib—not for

use in dogs under 1 year of age; may cause existing parasitic skin infestations and/or prevent resolution of infections.

POSSIBLE INTERACTIONS

Concurrent use of cyclosporine and ketoconazole permits 50% dose reduction of each drug.

ALTERNATIVE DRUG(S)

- Frequent bathing (once to twice weekly) in cool water with antipruritic, antibacterial, antifungal, and/or moisturizing shampoos can be beneficial. • Fatty acids—diets rich in essential fatty acids typically provided higher amounts than with oral supplements.
- Pentoxifylline 25 mg/kg q12h. • Topical hydrocortisone or triamcinolone spray 0.015% (short-term use).

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

- Examination every 2–8 weeks initially; once acceptable level of control achieved, examine every 3–6 months. • Monitor pruritus, self-trauma, development of secondary infection, possible adverse drug reactions. • CBC/blood chemistry/urinalysis with culture—recommended every 3–12 months for patients on chronic corticosteroid, cyclosporine, or oclacitinib therapy.

PREVENTION/AVOIDANCE

- Avoidance of allergens seldom possible.
- Minimize other sources of pruritus.

POSSIBLE COMPLICATIONS

- Secondary bacterial folliculitis or *Malassezia* dermatitis. • Concurrent hypersensitivities.

EXPECTED COURSE AND PROGNOSIS

- Pruritus and duration of signs usually worsen over time without intervention.
- Some cases spontaneously resolve.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hypersensitivity (flea, food). • Bacterial folliculitis. • *Malassezia* dermatitis. • Otitis externa.

AGE-RELATED FACTORS

Severity worsens with age.

PREGNANCY/FERTILITY/BREEDING

- Corticosteroids—contraindicated during pregnancy. • Affected animals should not be used for breeding.

SYNOMYNS

- Atopy. • Canine atopic disease.

SEE ALSO

- Eosinophilic Granuloma Complex.
- Flea Bite Hypersensitivity and Flea Control.
- Food Reactions, Dermatologic.
- Otitis Externa and Media.
- Pyoderma.

ABBREVIATIONS

- IDT = intradermal test.
- Ig = immunoglobulin.
- TEWL = transepidermal water loss.

Suggested Reading

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Consulting Editor Alexander H. Werner Resnick

Acknowledgment The author acknowledges the prior contribution of Alexander H. Werner Resnick.



Client Education Handout
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ATRIAL FIBRILLATION AND ATRIAL FLUTTER



BASICS

DEFINITION

- Atrial fibrillation—rapid, irregularly irregular supraventricular rhythm. Two forms recognized: primary atrial fibrillation, an uncommon disease that occurs mostly in large dogs with no underlying cardiac disease; and secondary atrial fibrillation, which occurs in dogs and cats secondary to underlying cardiac disease.
- Atrial flutter is similar to atrial fibrillation, but the atrial rate is generally slower and is characterized by saw-toothed flutter waves in the baseline of the ECG. The ventricular response is generally rapid, but may be regular or irregular.

ECG Features

Atrial Flutter

- Atrial rhythm usually regular; rate approximately 300–400 bpm.
- P waves usually discerned as either discrete P waves or “saw-toothed” baseline.
- Ventricular rhythm and rate generally depend on atrial rate and atrioventricular (AV) nodal conduction, but are generally regular or regularly irregular and rapid.
- Conduction pattern to ventricles is variable—in some cases every other atrial depolarization produces a ventricular depolarization (2 : 1 conduction ratio), giving a regular ventricular rhythm (Figure 1); other times the conduction pattern appears random, giving an irregular ventricular rhythm that can mimic atrial fibrillation.

Secondary Atrial Fibrillation

- No P waves present—baseline may be flat or may have small irregular undulations (“f” waves); some undulations may look like P waves.
- Ventricular rate often elevated—usually 180–240 bpm in dogs and >220 bpm in cats.
- Interval between QRS complexes is irregularly irregular; QRS complexes usually appear normal (Figure 2).

Primary Atrial Fibrillation

Similar to secondary atrial fibrillation, except ventricular rate usually in normal range.

PATHOPHYSIOLOGY

- Atrial fibrillation—caused by numerous small reentrant pathways creating a rapid (>500 depolarizations/minute) and disorganized depolarization pattern in the atria that results in cessation of atrial contraction.
- Depolarizations continuously bombard the AV nodal tissue, which acts as a filter and does not allow all depolarizations to conduct to the ventricles. Many atrial depolarizations activate only a part of the atria, because the rapid rate renders portions of the atria refractory, and thus they cannot reach the AV junction. Other atrial impulses penetrate into the AV junctional tissue, but do not penetrate the entire length. Blocked impulses affect the conduction properties of the AV junctional tissue and alter

conduction of subsequent electrical impulses; electrical impulses are conducted through the AV junction irregularly, producing an irregular ventricular rhythm.

- Atrial flutter—probably originates from one site of reentry that moves continuously throughout the atrial myocardium and frequently and regularly stimulates the AV node. When the atrial rate becomes sufficiently fast, the refractory period of the AV node exceeds the cycle length (P to P interval) of the supraventricular tachycardia (SVT), and some atrial depolarizations are blocked from traversing the AV node (functional second-degree AV block).

SYSTEMS AFFECTED

Cardiovascular

Loss of atrial contraction may result in decreased stroke volume and cardiac output, depending on heart rate; high heart rate may result in deterioration in myocardial function (tachycardia-induced myocardial failure).

GENETICS

No breeding studies available.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Large- and giant-breed dogs more prone to primary atrial fibrillation.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

General Comments

- Generally relate to underlying disease process and/or congestive heart failure (CHF) rather than arrhythmia itself, but previously stable animals may decompensate.
- Patients with primary atrial fibrillation are generally asymptomatic, but may demonstrate mild exercise intolerance.

Historical Findings

- Coughing/dyspnea/tachypnea.
- Exercise intolerance.
- Rarely, syncope.
- Dogs with primary atrial fibrillation are typically asymptomatic.

Physical Examination Findings

- On auscultation, patients with atrial fibrillation have an erratic heart rhythm that sounds like “tennis shoes in a dryer.”
- First heart sound intensity in atrial fibrillation is variable; second heart sound only heard on beats with effective ejection, not on every beat.
- Third heart sounds (gallop sounds) may be present.
- Patients with atrial fibrillation have pulse deficits and variable pulse quality.
- Signs of CHF often present (e.g., cough, dyspnea, cyanosis).

CAUSES

- Myxomatous valve disease.
- Cardiomyopathy.
- Congenital heart disease.
- Digoxin toxicity.
- Idiopathic.
- Ventricular preexcitation (atrial flutter).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Frequent atrial (supraventricular) premature depolarizations.
- Supraventricular tachycardia with AV block.
- Multifocal atrial tachycardia (irregular).

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

• Echocardiography and radiography may characterize type and severity of underlying cardiac disease; moderate to severe heart enlargement common.

- Typically normal in patients with primary atrial fibrillation, although mild left atrial enlargement may accompany hemodynamic alterations imposed by arrhythmia.

DIAGNOSTIC PROCEDURES

A baseline 24-hour Holter is recommended to determine if arrhythmia is chronic or paroxysmal. If it is chronic, drug therapy may be indicated.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with fast (secondary) atrial fibrillation are treated medically to slow the ventricular rate. Converting the atrial fibrillation to sinus rhythm would be ideal, but such attempts in patients with severe underlying heart disease or left atrial enlargement are generally futile because of a low success rate and high rate of recurrence. Consider electrical cardioversion to sinus rhythm for a dog with primary atrial fibrillation and minimal structural heart disease.
- Patients with primary atrial fibrillation may be converted back to normal sinus rhythm. The success rate depends on chronicity. Patients that have been in atrial fibrillation for >4 months generally have a lower success rate and a higher rate of recurrence. In these patients, rate control, if necessary, is the recommended treatment.
- Electrical (DC) cardioversion—application of a transthoracic electrical shock at a specific time in the cardiac cycle; requires special equipment, trained personnel, and general anesthesia. Using a monophasic defibrillator: start with 4 J/kg; if no conversion occurs,

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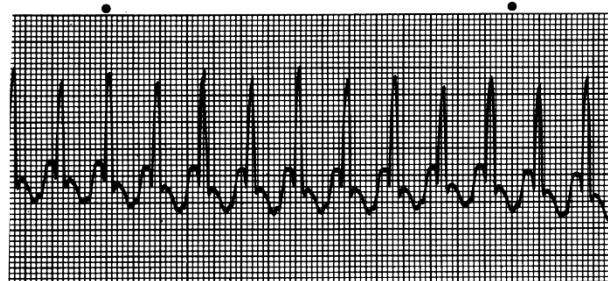
ATRIAL FIBRILLATION AND ATRIAL FLUTTER**A**

Figure 1.

Atrial flutter with 2 : 1 conduction at a ventricular rate of 330/minute in a dog with an atrial septal defect. This supraventricular tachycardia was associated with a Wolff-Parkinson-White pattern. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore, MD: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

increase dose by 50 J and repeat until a max of 360 J. Using a biphasic defibrillator: start with 1–2 J/kg; if no cardioversion occurs, increase dose by 50 J and repeat until max of 360 J.

- For atrial flutter, conversion to sinus rhythm can be accomplished by drug therapy, electrical cardioversion, or rapid atrial pacing (transvenous pacing electrode).

NURSING CARE

As indicated for CHF.

ACTIVITY

Restrict activity until tachycardia is controlled.

DIET

Mild to moderate sodium restriction if CHF.

CLIENT EDUCATION

- Secondary atrial fibrillation and atrial flutter are usually associated with severe underlying heart disease; goal of therapy is to lower heart rate and control clinical

signs. • Sustained conversion to sinus rhythm is unlikely with secondary atrial fibrillation.

SURGICAL CONSIDERATIONS

N/A

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

- Digoxin, β -adrenergic blockers, esmolol, and calcium channel blockers (diltiazem) are frequently used to slow conduction through the AV node; definition of an adequate heart rate response varies among clinicians, but in dogs is generally 130–150 bpm. • For atrial flutter, therapy is aimed at suppressing the atrial reentry circuit using sotalol, amiodarone, or procainamide. Conversion to normal sinus rhythm is usually unsuccessful.

Dogs

- Digoxin—maintenance oral dose 0.005–0.01 mg/kg PO q12h; to achieve therapeutic serum concentration more rapidly, maintenance dose can be doubled for the first day. If digoxin is administered alone and heart rate remains high, check digoxin level and adjust dose to bring level into therapeutic range. If heart rate remains high, consider adding calcium channel blocker or β -adrenergic blocker.
- Diltiazem—initially administered at dose of 0.5 mg/kg PO q8h, then titrated up to maximum of 1.5 mg/kg PO q8h or until adequate response is obtained. • Therapy for atrial flutter is aimed at suppressing atrial reentry circuit using sotalol, amiodarone, or procainamide. Conversion to normal sinus rhythm is usually unsuccessful.

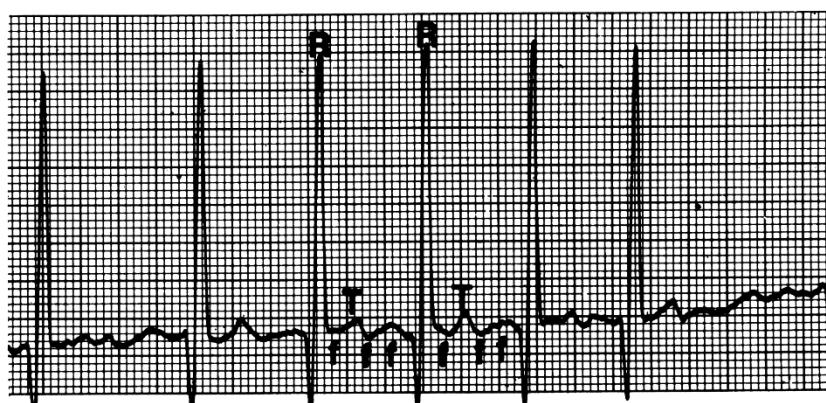


Figure 2.

“Coarse” atrial fibrillation in a dog with patent ductus arteriosus. The f waves are prominent. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore, MD: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

Cats

- Diltiazem (1–2.5 mg/kg PO q8h) or atenolol (6.25–12.5 mg/cat PO q12–24h) are drugs of choice in most cats. • If the heart rate is not sufficiently slowed with these drugs or myocardial failure is present, digoxin (5 µg/kg PO q24–48h) can be added.

CONTRAINDICATIONS

- Digoxin, diltiazem, propranolol, and atenolol should not be used in patients with preexisting AV block. • Use of calcium channel blockers in combination with beta blockers should be avoided because clinically significant bradyarrhythmias and/or AV block can develop.

PRECAUTIONS

- Calcium channel blockers and β-adrenergic blockers, both negative inotropes, should be used cautiously in animals with myocardial failure. • Using high-dose oral quinidine for conversion to sinus rhythm carries a risk of quinidine toxicity (e.g., hypotension, weakness, ataxia, and seizures)—administration of diazepam intravenously controls seizures; other signs abate within several hours of discontinuing quinidine administration.

POSSIBLE INTERACTIONS

Quinidine raises the digoxin level, generally necessitating a digoxin dose reduction.

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

- Monitor heart rate and ECG closely. • As heart rates in the hospital and those measured on the surface ECG may be inaccurate (due to patient anxiety and other environmental factors), Holter monitoring provides a more accurate means for assessing the need for heart rate control and/or the efficacy of medical therapy for heart rate control.

POSSIBLE COMPLICATIONS

Worsening of cardiac function with onset of arrhythmia.

EXPECTED COURSE AND PROGNOSIS

- Secondary atrial fibrillation—often associated with severe structural heart disease, so a guarded to poor prognosis. • Primary atrial fibrillation with normal ultrasound findings—generally a good prognosis.

**MISCELLANEOUS****ABBREVIATIONS**

- AV = atrioventricular.
- CHF = congestive heart failure.
- SVT = supraventricular tachycardia.

Suggested Reading

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Consulting Editor Michael Aherne



**Client Education Handout
available online**



BASICS

DEFINITION

Premature atrial complexes or beats (APC) that originate outside the sinoatrial node and disrupt the normal sinus rhythm for 1 or more beats.

ECG Features

- Heart rate usually normal; rhythm irregular due to the premature P wave (called a P' wave) that disrupts the normal P wave rhythm (Figure 1).
- Ectopic P' wave—premature; configuration differs from that of the sinus P waves and may be negative, positive, biphasic, or superimposed on the previous T wave.
- QRS complex—premature; configuration usually normal (same as that of the sinus complexes). If the P' wave occurs during the refractory period of the atrioventricular (AV) node, ventricular conduction does not occur (nonconducted APCs), so no QRS complex follows the P' wave. If there is partial recovery in the AV node or intraventricular conduction systems, the P' wave is conducted with a long P'-R interval or with an abnormal QRS configuration (aberrant conduction). The more premature the complex, the more marked the aberration.
- In the P–QRS relationship, the P'-R interval is usually as long as, or longer than, the sinus P'-R interval.
- An compensatory pause—when the R–R interval of the two normal sinus complexes enclosing an APC is less than the R–R intervals of three consecutive sinus complexes—usually follows an APC (Figure 2). The ectopic atrial impulse discharges the sinus node and resets the cycle.

PATHOPHYSIOLOGY

- Mechanisms—an increase in automaticity of atrial myocardial fibers or a single reentrant circuit.
- May be normal finding in aged

dogs; commonly seen in dogs with atrial enlargement secondary to chronic mitral valvular insufficiency; may also be observed in dogs or cats with any atrial disease.

- May not cause hemodynamic problems; the clinical significance relates to their frequency, timing relative to other complexes, and the underlying clinical problems.
- Can presage more serious rhythm disturbances (e.g., atrial fibrillation, atrial flutter, or atrial tachycardia).

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Not documented.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Small-breed dogs.

Mean Age and Range

Geriatric animals, except those with congenital heart disease.

SIGNS

Historical Findings

- No signs.
- Congestive heart failure (CHF).
- Coughing and dyspnea.
- Exercise intolerance.
- Syncope.

Physical Examination Findings

- Myxomatous valve disease.
- Cardiac murmur.
- Gallop sound.
- Signs of CHF.

CAUSES & RISK FACTORS

- Chronic valvular disease.
- Congenital heart disease.
- Cardiomyopathy.
- Atrial myocarditis.
- Electrolyte disorders.
- Neoplasia.
- Hyperthyroidism.
- Toxemias.
- Drug toxicity (e.g., digitalis).
- Normal variation in aged animals.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Marked sinus arrhythmia.
- Ventricular premature complexes when aberrant ventricular conduction follows an APC.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Echocardiography and Doppler ultrasound may reveal the type and severity of the underlying heart disease.

DIAGNOSTIC PROCEDURES

- ECG.
- Holter monitor to quantify APC frequency and event monitor/Holter ECG to correlate symptoms with rhythm.

PATHOLOGIC FINDINGS

Atrial enlargement; other features vary depending on underlying cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Treat animal as inpatient or outpatient.
- Treat the underlying CHF, cardiac disease, or other causes.

NURSING CARE

Usually not necessary; varies with underlying cause.

ACTIVITY

Restrict if symptomatic.

DIET

No modifications unless required for management of underlying condition (i.e., low-salt diet).

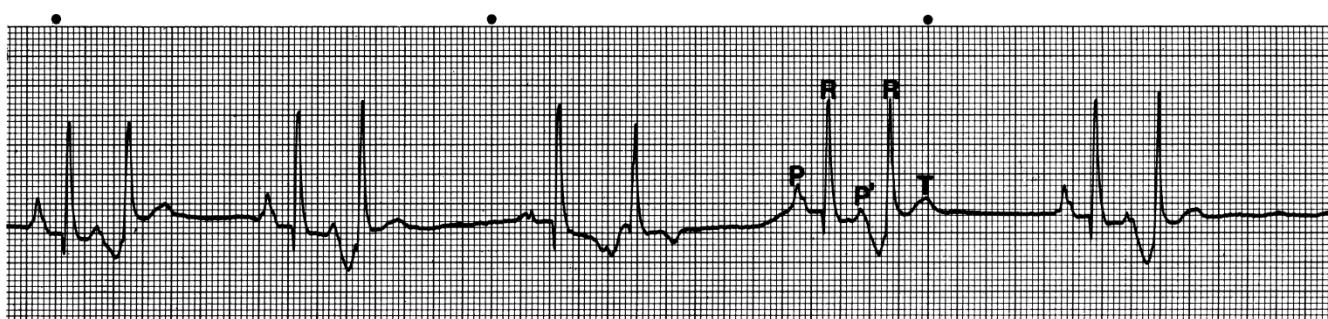


Figure 1.

APCs in a dog. P' represents the premature P wave. The premature QRS resembles the normal (sinus) QRS. The upright P' wave is superimposed on the T wave of the preceding complex. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Blackwell Publishing, 1992. Reprinted with permission of Wolters Kluwer.)

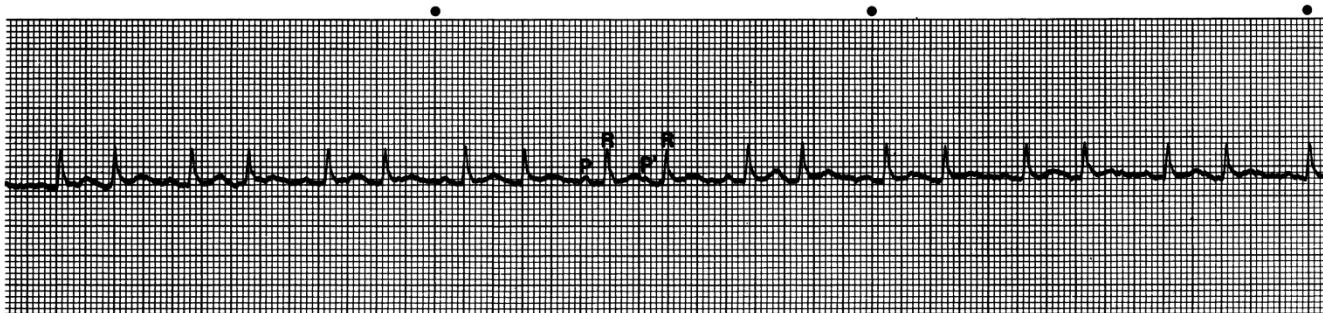


Figure 2.

APCs in bigeminy in a cat under general anesthesia. The second complex of each pair is an APC and the first is a sinus complex. The abnormality in rhythm disappeared after the anesthetic was stopped. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

CLIENT EDUCATION

APCs may not cause hemodynamic abnormalities; may be precursors of serious arrhythmias.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Treat CHF and correct any electrolyte or acid/base imbalances.

Dogs

- Digoxin (0.005–0.01 mg/kg PO q12h, maintenance dosage), diltiazem (0.5–1.5 mg/kg PO q8h), or atenolol (0.25–1 mg/kg PO q12h) are used to treat clinically significant arrhythmias.
- Digoxin—treatment of choice.
- CHF is treated with appropriate dosage of diuretic, angiotensin-converting enzyme inhibitor, and pimobendan; appropriate management of CHF may reduce APC frequency.

Cats

- Cats with hypertrophic cardiomyopathy—diltiazem (1–2.5 mg/kg PO q8h) or atenolol (6.25–12.5 mg PO q12–24h).
- Cats with dilated cardiomyopathy—digoxin (one-fourth of a 0.125 mg digoxin tablet q24h or q48h).

CONTRAINDICATIONS

Negative inotropic agents (e.g., propranolol) should be avoided in animals with CHF.

PRECAUTIONS

Use digoxin, diltiazem, atenolol, or propranolol cautiously in animals with underlying atrioventricular block or hypotension.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Monitor heart rate and rhythm with serial ECG.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Frequent APCs may further diminish cardiac output in patients with underlying heart disease and worsen clinical symptoms.

EXPECTED COURSE AND PROGNOSIS

Even with optimal antiarrhythmic drug therapy, some animals have an increased frequency of APCs or deteriorate to more severe arrhythmia as the underlying disease progresses.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

Typically occurs in geriatric dogs.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYNS

- Atrial extrasystoles.
- Atrial premature contractions.
- Atrial premature impulses.
- Premature atrial complexes/contractions.

SEE ALSO

Supraventricular Tachycardia.

ABBREVIATIONS

- APC = atrial premature complex.
- AV = atrioventricular.
- CHF = congestive heart failure.

Suggested Reading

Jackson BL, Lehmkohl LB, Adin DB. Heart rate and arrhythmia frequency of normal cats compared to cats with asymptomatic hypertrophic cardiomyopathy. J Vet Cardiol 2014; 16:215–225.

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Author Larry P. Tilley

Consulting Editor Michael Aherne



Client Education Handout
available online

ATRIOVENTRICULAR BLOCK, COMPLETE (THIRD DEGREE)



BASICS

DEFINITION

- All atrial impulses are blocked at the atrioventricular (AV) junction; atria and ventricles beat independently. A secondary “escape” pacemaker site (junctional or ventricular) stimulates the ventricles.
- Atrial rate normal.
- Idioventricular escape rhythm slow.

ECG Features

- Ventricular rate slower than atrial rate (more P waves than QRS complexes)—ventricular escape rhythm (idioventricular) usually <40 bpm; junctional escape rhythm (idiojunctional) 40–60 bpm in dogs and 60–100 bpm in cats.
- P waves—usually normal configuration (Figures 1 and 2).
- QRS complex—wide and bizarre when pacemaker located in the ventricle, or in the lower AV junction in a patient with bundle branch block; normal when escape pacemaker in the lower AV junction (above the bifurcation of the bundle of His) in a patient without bundle branch block.
- No conduction between the atria and the ventricles; P waves have no constant relationship with QRS complexes; P–P and R–R intervals relatively constant (except for a sinus arrhythmia).

PATHOPHYSIOLOGY

Slow ventricular escape rhythms (<40 bpm) result in low cardiac output and eventual heart failure, often when animal is excited or exercised, since demand for greater cardiac output is not satisfied. As the heart fails, signs increase with mild activity.

SYSTEMS AFFECTED

Cardiovascular

GENETICS

Can be an isolated congenital defect.

INCIDENCE/PREVALENCE

Not documented.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Cocker spaniel—can have idiopathic fibrosis.
- Pug and Doberman pinscher—can have associated sudden death, AV conduction defects, and bundle of His lesions.

Mean Age and Range

Geriatric animals, except congenital heart disease patients. Median age for cats—14 years.

Predominant Sex

Intact female dogs.

SIGNS

Historical Findings

- Exercise intolerance.
- Weakness or syncope.
- Occasionally, congestive heart failure (CHF).

Physical Examination Findings

- Bradycardia.
- Variable third and fourth heart sounds.
- Variation in intensity of first heart sounds.
- Signs of CHF possible.
- Intermittent “cannon” A waves in jugular venous pulses.
- Often bounding arterial pulses.

CAUSES & RISK FACTORS

- Isolated congenital defect.
- Idiopathic fibrosis.
- Infiltrative cardiomyopathy (amyloidosis or neoplasia).
- Hypertrophic cardiomyopathy in cats.
- Digitalis toxicity.
- Hyperthyroidism in cats.
- Myocarditis.
- Endocarditis.
- Electrolyte disorder.
- Myocardial infarction.
- Other congenital heart defects.
- Lyme disease.
- Chagas disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Advanced second-degree AV block.
- Atrial standstill.
- Accelerated idioventricular rhythm.

CBC/BIOCHEMISTRY/URINALYSIS

- Abnormal serum electrolytes (e.g., hyperkalemia, hypokalemia) possible.
- High white blood cell count with left shift in animals with bacterial endocarditis.

OTHER LABORATORY TESTS

- High serum digoxin concentration if AV block due to digoxin toxicity.
- Lyme titer and accompanying clinical signs if AV block due to Lyme disease.

IMAGING

Echocardiography and Doppler ultrasound to assess cardiac structure and function.

DIAGNOSTIC PROCEDURES

- Electrocardiography.
- His bundle electrogram to determine the site of the AV block is possible.
- Long-term (Holter) ambulatory recording if AV block is intermittent.

PATHOLOGIC FINDINGS

Degeneration or fibrosis of the AV node and its bundle branches, associated with endocardial and myocardial fibrosis and organized endomyocarditis.



TREATMENT

APPROPRIATE HEALTH CARE

- Temporary or permanent cardiac pacemaker—only effective treatment in symptomatic patients.
- Carefully monitor asymptomatic patients without a pacemaker for development of clinical signs.

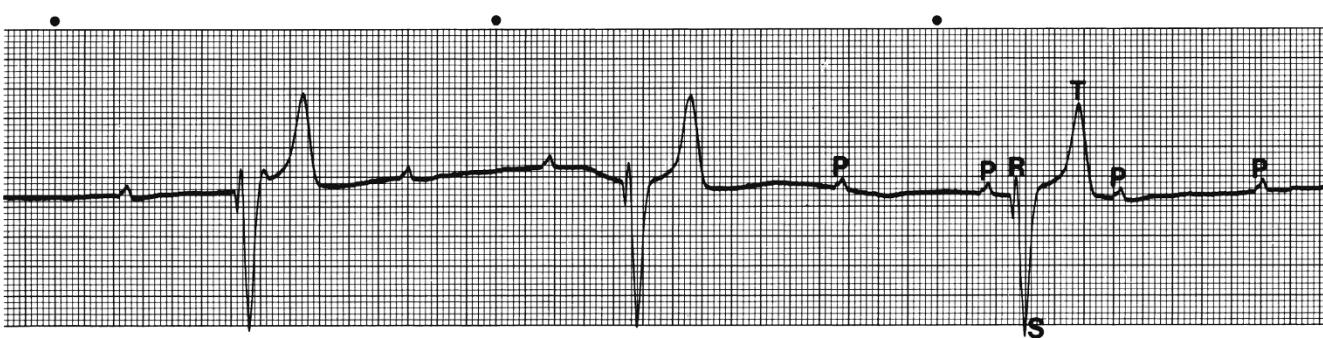


Figure 1.

Complete heart block in a dog. The P waves occur at a rate of 120, independent of the ventricular rate of 50. The QRS configuration is a right bundle branch block pattern. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

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ATRIOVENTRICULAR BLOCK, COMPLETE (THIRD DEGREE)

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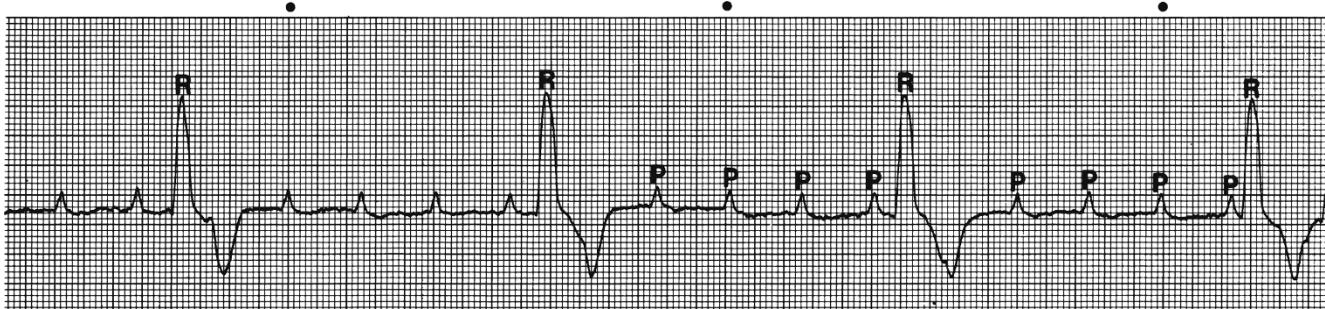


Figure 2.

Complete heart block in a cat. The P wave rate is 240/minute, independent of the ventricular rate of 48/minute. QRS configuration is a left bundle branch block pattern. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

NURSING CARE

Cage rest prior to pacemaker implantation; when the pulse generator is implanted into a subcutaneous pocket, a nonconstricting bandage is placed around the ventral neck or abdomen for 3–5 days to prevent seroma formation or pacemaker movement.

ACTIVITY

Restrict if symptomatic.

DIET

No modifications unless required to manage underlying condition (e.g., low-salt diet).

CLIENT EDUCATION

- Temporary or permanent cardiac pacemaker—only effective treatment in symptomatic patients.
- Asymptomatic patients without a pacemaker—must be carefully monitored for development of clinical signs.

SURGICAL CONSIDERATIONS

- Most patients—at high anesthetic cardiopulmonary risk; usually paced preoperatively with a temporary external pacemaker system.
- The small size of cats makes pacemaker implantation more difficult than in dogs.

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

- Treatment with drugs—usually of no value. Traditionally used to treat complete AV block: atropine, isoproterenol, corticosteroids, and dobutamine.
- Intravenous isoproterenol infusion may help increase the rate of the ventricular escape rhythm to

stabilize hemodynamics. • If CHF—diuretic and vasodilator therapy may be needed before pacemaker implantation.

CONTRAINDICATIONS

Avoid digoxin, xylazine, acepromazine, beta blockers (e.g., propranolol and atenolol), and calcium channel blockers (e.g., verapamil and diltiazem); ventricular antiarrhythmic agents are dangerous because they suppress lower escape foci.

PRECAUTIONS

Vasodilators—may cause hypotension in animals with complete AV block; monitor closely if used, especially prior to pacemaker implantation.

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

- Monitor—pacemaker function with serial electrocardiograms.
- Radiographs—following pacemaker implantation, to confirm the position of the lead and generator.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Pulse generators—pacemaker replacement necessary if battery becomes depleted, pulse generator malfunction occurs, or exit block develops; pacemaker leads can become dislodged and infected.

EXPECTED COURSE AND PROGNOSIS

Poor long-term prognosis if no cardiac pacemaker implanted, especially when the animal has clinical signs. Cats can sometimes survive >1 year without a permanent pacemaker.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

ABBREVIATIONS

- AV = atrioventricular.
- CHF = congestive heart failure.

Suggested Reading

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Author Larry P. Tilley

Consulting Editor Michael Aherne



Client Education Handout
available online

ATRIOVENTRICULAR BLOCK, FIRST DEGREE



BASICS

DEFINITION

Refers to a delay in conduction that occurs between atrial and ventricular activation.

ECG Features

- Rate and rhythm—usually normal.
- Usually there are regularly occurring normal P waves and QRS complexes (Figures 1 and 2).
- Prolonged, consistent PR intervals—dogs, >0.13 sec; cats, >0.09 sec (Figures 1 and 2).

PATHOPHYSIOLOGY

- Virtually never causes clinical signs.
- May become a more severe atrioventricular (AV) conduction disturbance in some animals.
- Normally the PR interval tends to shorten with rapid heart rates.
- May be the result of intra-atrial conduction delay (prolongation of the PA interval on surface ECG and simultaneous His bundle electrogram) or delay of conduction within the AV node itself (prolongation of the AH interval on His bundle electrogram).

SYSTEMS AFFECTED

Cardiovascular

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat.

Breed Predilections

American cocker spaniel, dachshund, brachycephalic dogs, Persian cats.

Mean Age and Range

- May occur in young, otherwise healthy dogs as a manifestation of high vagal tone.
- Intra-atrial conduction delay involving the right atrium may be seen with congenital heart disease, especially AV septal defects.
- May be noted in aged patients with degenerative conduction system disease, particularly cocker spaniels and dachshunds.
- Persian cats of any age with high vagal tone and in cats of any age with hypertrophic cardiomyopathy.

SIGNS

Historical Findings

- Most animals are asymptomatic.
- If drug induced, may have a history of clinical signs related to drug toxicity—anorexia, vomiting, and diarrhea with digoxin; weakness with calcium channel blockers or β -adrenergic antagonists.

Physical Examination Findings

Normal—unless also signs of more generalized myocardial disease, drug toxicity, or noncardiac disease.

CAUSES

- May occur in normal animals.
- Enhanced vagal stimulation resulting from noncardiac diseases—usually accompanied by sinus arrhythmia, sinus arrest, and/or Mobitz type I second-degree AV block.
- Pharmacologic agents—e.g., digoxin, β -adrenergic antagonists, calcium channel blocking agents, propafenone, amiodarone, α_2 -adrenergic agonists, parasympathomimetic

agents (bethanechol, physostigmine, pilocarpine), and severe procainamide or quinidine toxicity.

- Degenerative disease of the conduction system.
- Hypertrophic cardiomyopathy.
- Myocarditis (especially *Trypanosoma cruzi*, *Borrelia burgdorferi*, *Rickettsia rickettsii*).
- Infiltrative diseases (tumors, amyloid).
- Atropine administered intravenously may briefly prolong the PR interval.

RISK FACTORS

Any condition or intervention that raises vagal tone.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

P waves superimposed upon preceding T waves because of first-degree AV block should be differentiated from bifid T waves.

CBC/BIOCHEMISTRY/URINALYSIS

- Serum electrolytes—hypokalemia and hyperkalemia may predispose to AV conduction disturbances.
- Leukocytosis—may be noted with bacterial endocarditis or myocarditis.

OTHER LABORATORY TESTS

- Serum digoxin concentration—may be high.
- *T. cruzi*, *B. burgdorferi*, *R. rickettsii* titers—may be high.
- Thyroxine (T_4)—may be high in cats if associated with thyrotoxic myocardial disease.

IMAGING

Echocardiographic examination—may reveal hypertrophic or infiltrative myocardial disorder.

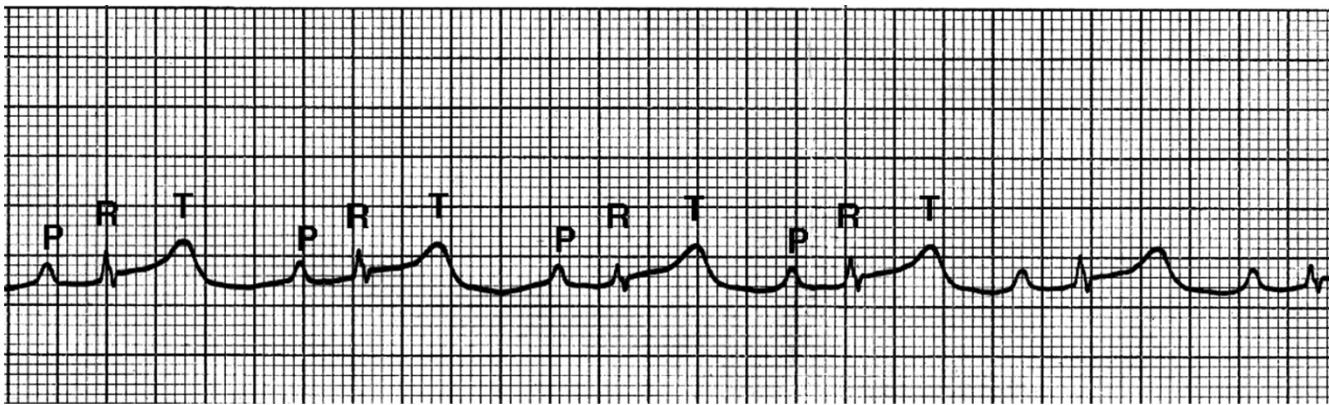


Figure 1.

Lead II ECG rhythm strip recorded from a cat with hypertrophic cardiomyopathy. There is sinus bradycardia (120 bpm) and first-degree AV conduction block. The PR interval is 0.12 second (paper speed = 50 mm/s).

(CONTINUED)

ATRIOVENTRICULAR BLOCK, FIRST DEGREE

A

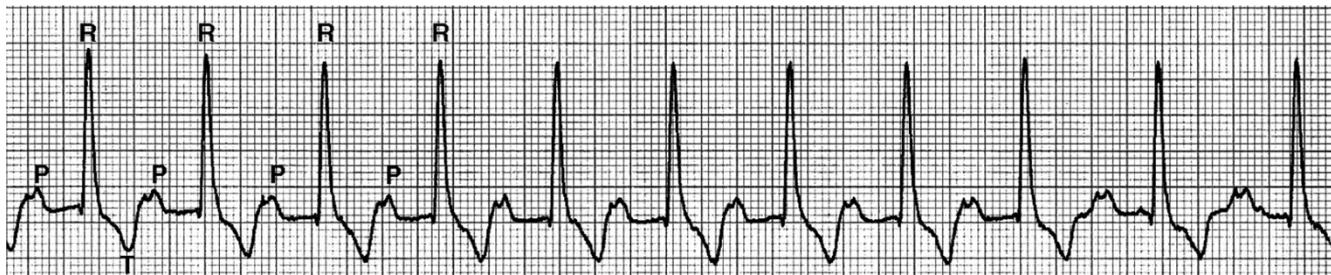


Figure 2.

Lead II ECG rhythm strip recorded from a dog showing sinus tachycardia (175 bpm) and first-degree AV conduction block. Because the heart rate is rapid, P waves are superimposed on the downslope of the preceding T waves. The PR interval exceeds 0.16 second (paper speed = 50 mm/s).

DIAGNOSTIC PROCEDURES

May be needed to identify causes of high vagal tone—upper airway disease, cervical and thoracic masses, gastrointestinal disorders, and high intraocular pressure.

PATHOLOGIC FINDINGS

Variable—depend on underlying cause.

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

- Remove or treat underlying cause(s).
- Hospitalization may be necessary to manage the underlying cause (e.g., cardiomyopathy, gastrointestinal disease, airway disease).

NURSING CARE

N/A

ACTIVITY

Unrestricted; unless restriction required for an underlying condition.

DIET

No modifications or restrictions, unless required to manage an underlying condition.

CLIENT EDUCATION

Generally unnecessary.

SURGICAL CONSIDERATIONS

None, unless required to manage an underlying condition.

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

Medications used only if needed to manage an underlying condition.

CONTRAINdications

- Avoid hypokalemia—increases sensitivity to vagal tone; may potentiate AV conduction delay.

- Avoid drugs likely to impair impulse conduction further (calcium channel blocking agents, β -adrenergic antagonists, α_2 -adrenergic agonists, amiodarone, propafenone).

PRECAUTIONS

Drugs with vagomimetic action (e.g., digoxin, bethanechol, physostigmine, pilocarpine) may potentiate first-degree block.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

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

Except in healthy young animals, monitor ECG to detect any progression in conduction disturbance.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Depends on underlying cause.
- Prognosis usually excellent if no significant underlying disease is present.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

PR interval—tends to lengthen with advancing age.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Atrioventricular Block, Complete (Third Degree).
- Atrioventricular Block, Second Degree—Mobitz Type I.
- Atrioventricular Block, Second Degree—Mobitz Type II.

ABBREVIATIONS

- AV = atrioventricular
- T_4 = thyroxine

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**Client Education Handout
available online**



BASICS

DEFINITION

- Azotemia is an excess of urea, creatinine, or other nonprotein nitrogenous substances in blood, plasma, or serum.
- Uremia is the polysystemic toxic syndrome resulting from marked loss in kidney functions. Uremia occurs simultaneously in animals with increased quantities of urine constituents in blood (azotemia), but azotemia may occur in the absence of uremia.

PATHOPHYSIOLOGY

- Azotemia can be caused by (1) increased production of nonprotein nitrogenous substances, (2) decreased glomerular filtration rate (GFR), or (3) reabsorption of urine that has escaped from the urinary tract into the bloodstream. High production of nonprotein nitrogenous waste substances may result from high intake of protein (diet or gastrointestinal bleeding) or accelerated catabolism of endogenous proteins. GFR may decline because of reduced renal perfusion (prerenal azotemia), acute or chronic kidney disease (renal azotemia), or urinary obstruction (postrenal azotemia). Reabsorption of urine into the systemic circulation may also result from leakage of urine from the excretory pathways (also a form of postrenal azotemia).
- Pathophysiology of uremia—incompletely understood; may be related to (1) metabolic and toxic systemic effects of waste products retained because of renal excretory failure, (2) deranged renal regulation of fluid, electrolytes, and acid-base balance, and (3) impaired renal production and degradation of hormones and other substances (e.g., erythropoietin and 1,25-dihydroxycholecalciferol).

SYSTEMS AFFECTED

- Uremia affects all body systems.
- Cardiovascular—arterial hypertension, left ventricular hypertrophy, heart murmur, cardiomegaly, cardiac rhythm disturbances.
- Endocrine/metabolic—renal secondary hyperparathyroidism, inadequate production of calcitriol and erythropoietin, hyperglycemia, weight loss.
- Gastrointestinal—anorexia, nausea, vomiting, diarrhea, uremic stomatitis, xerostomia, uremic breath, constipation.
- Hemolymph/immune—anemia and immunodeficiency.
- Neuromuscular—dullness, lethargy, fatigue, irritability, tremors, gait imbalance, flaccid muscle weakness, myoclonus, behavioral changes, dementia, isolated cranial nerve deficits, seizures, stupor, coma, impaired thermoregulation (hypothermia).
- Ophthalmic—scleral and conjunctival injection, retinopathy, acute-onset blindness.
- Respiratory—dyspnea.
- Skin/exocrine—pallor, bruising, increased shedding, unkempt appearance, loss of normal sheen to coat.

SIGNALMENT

Dog and cat.

SIGNS

General Comments

Azotemia may not be associated with historical or physical abnormalities. Unless patient has uremia, clinical findings are limited to disease responsible for azotemia.

Historical Findings

- Weight loss.
- Declining appetite or anorexia.
- Depression.
- Fatigue.
- Weakness.
- Vomiting.
- Diarrhea.
- Halitosis.
- Constipation.
- Polyuria.
- Changes in urine volume.
- Poor haircoat or unkempt appearance.

Physical Examination Findings

- Muscle wasting/sarcopenia/cachexia.
- Mental depression.
- Dehydration.
- Weakness.
- Pallor.
- Petechiae and ecchymoses.
- Dull and unkempt haircoat.
- Uremic breath.
- Uremic stomatitis (including oral ulcers, infarctions of the tongue).
- Scleral and conjunctival injection.
- Relative hypothermia.

CAUSES

Prerenal Azotemia

- Reduced renal perfusion due to low blood volume or low blood pressure.
- Accelerated production of nitrogenous waste products because of enhanced catabolism of tissues in association with infection, fever, trauma, corticosteroid excess, or burns.
- Increased gastrointestinal digestion and absorption of protein sources (diet or gastrointestinal hemorrhage).

Renal Azotemia

Acute or chronic kidney diseases (primary kidney disease affecting glomeruli, renal tubules, renal interstitium, and/or renal vasculature) that impair at least 75% of kidney function (GFR).

Postrenal Azotemia

Urinary obstruction; rupture of excretory pathway.

RISK FACTORS

- Medical conditions—kidney disease, hypoadrenocorticism, low cardiac output, hypotension, fever, sepsis, liver disease, pyometra, hypoalbuminemia, dehydration, acidosis, exposure to nephrotoxic chemicals, gastrointestinal hemorrhage, urolithiasis, urethral plugs in cats, urethral trauma, and neoplasia.
- Advanced age may be a risk factor.
- Drugs—potentially nephrotoxic drugs,

nonsteroidal anti-inflammatory drugs, diuretics, antihypertensive medications; failure to adjust dosage of drugs primarily eliminated by the kidneys to correspond with decline in renal function.

- Toxins—ethylene glycol, grapes (dogs), lilies (cats).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dehydration, poor peripheral perfusion, low cardiac output, history of recent fluid loss, high-protein diet—rule out prerenal azotemia.
- Recent onset of altered urine output (high or low), clinical signs consistent with uremia, exposure to possible nephrotoxicants or ischemic renal injury, or kidney size normal or enlarged—rule out acute kidney injury (AKI).
- Progressive weight loss, polyuria, polydipsia, small kidneys, disparate kidney size (cats—big kidney and little kidney), pallor, and signs of uremia that have developed over several weeks to months—rule out chronic kidney disease (CKD).
- Abrupt decline in urine output and onset of signs of uremia; disparate kidney size, dysuria, stranguria, and hematuria; large urinary bladder or fluid-filled abdomen—rule out postrenal azotemia.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Nonregenerative anemia (normocytic, normochromic)—often present with CKD.
- Hemoconcentration—often present with prerenal azotemia; can also be seen with AKI and postrenal azotemia.

Biochemistry

- Serial determinations of serum urea nitrogen and creatinine concentrations may help differentiate the cause of azotemia. Appropriate therapy to restore renal perfusion typically yields a dramatic reduction in azotemia in patients with prerenal azotemia (typically within 24–48 hours). Correcting obstruction to urine flow or a rent in the excretory pathway typically is followed by a rapid reduction in the magnitude of azotemia.
- Hyperkalemia may be consistent with postrenal azotemia, primary renal azotemia due to oliguric renal failure, or prerenal azotemia associated with hypoadrenocorticism.
- Increased serum albumin and globulin concentration suggest prerenal component.

Urinalysis

- Urine specific gravity (USG) ≥ 1.030 (dog) and ≥ 1.035 (cat) supports a diagnosis of prerenal azotemia. Administration of fluid therapy before urine collection may interfere with interpretation of USG.
- Azotemic patients that have not been treated with fluids and have USG <1.030 (dog) and <1.035 (cat) typically have primary renal azotemia. A notable exception is glomerular

disease, which is sometimes characterized by glomerulotubular imbalance, where adequate urine-concentrating ability may persist despite sufficient renal glomerular damage to cause primary renal azotemia; these patients are recognized by moderate to marked proteinuria in the absence of hematuria and pyuria.

- USG is not useful in identifying postrenal azotemia.

OTHER LABORATORY TESTS

Endogenous or exogenous creatinine, iohexol, or inulin clearance tests or other specific tests of GFR may be used to confirm that azotemia is caused by reduced GFR.

IMAGING

- Abdominal radiographs—used to determine kidney size (small kidneys consistent with CKD; mild-to-moderate enlargement of kidneys may be consistent with AKI or urinary obstruction) and to rule out urinary obstruction (marked dilation of urinary bladder or mineral densities within excretory pathway).
- Ultrasonography—may detect changes in echogenicity of renal parenchyma and size and shape of kidneys; useful to rule out postrenal azotemia characterized by distension of excretory pathway and uroliths or masses within or impinging on excretory pathway and intra-abdominal fluid accumulation (with rupture of excretory pathway).
- Excretory urography, pyelography, or cystourethrography—may help establish diagnosis of postrenal azotemia due to urinary obstruction or rupture of excretory pathway.

DIAGNOSTIC PROCEDURES

Renal biopsy can confirm the diagnosis of primary kidney disease, to differentiate acute from chronic kidney disease, and to attempt to establish the underlying disease process responsible for kidney disease.



TREATMENT

- Prerenal azotemia caused by impaired renal perfusion—correct the underlying cause of renal hypoperfusion; aggressiveness of treatment depends on severity of underlying condition.
- Primary renal azotemia and associated uremia—(1) specific therapy directed at halting or reversing primary disease process affecting the kidneys, and (2) symptomatic, supportive, and palliative therapies that ameliorate clinical signs of uremia; minimize clinical impact of deficits and excesses in fluid, electrolyte, acid-base balances; minimize effects of inadequate renal biosynthesis of hormones and other substances; and maintain adequate nutrition.
- Postrenal azotemia—eliminate urinary obstruction or repair rents in excretory pathway; supplemental fluid administration often required to prevent dehydration

that may develop during solute diuresis that follows correction of postrenal azotemia.

- Fluid therapy—indicated for most azotemic patients; isotonic balanced crystalloid is preferred replacement fluid, followed by hypotonic maintenance fluid administration. Determine fluid volume to administer on basis of severity of dehydration or volume depletion. If no clinical dehydration is evident, cautiously assume that patient is <5% dehydrated and administer corresponding volume of fluid. Provide 25% of calculated fluid deficit in first hour. Thereafter, serially monitor perfusion (capillary refill time, pulse pressure, heart rate, and temperature of feet), blood pressure, and urine output to assess adequacy of fluid therapy. If perfusion has not improved, additional fluid should be administered. Provide the remaining fluid deficit over the next 12–24 hours. Fluid therapy should be cautiously administered to patients with overt or suspected cardiac failure and patients that are oliguric or anuric.
- Consider feeding diets formulated for kidney disease to reduce magnitude of azotemia, hyperphosphatemia, and acidosis.



MEDICATIONS

DRUG(S) OF CHOICE

- Symptomatic therapy for myriad manifestations of uremia.
- Omeprazole (1 mg/kg q12h) may be used to reduce gastric hyperacidity.
- Antiemetics such as maropitant (1 mg/kg q24h) are indicated for vomiting.

CONTRAINDICATIONS

Administration of nephrotoxic drugs.

PRECAUTIONS

- Use caution when administering drugs requiring renal excretion. Consult appropriate references concerning dose-reduction schedules or adjustments of maintenance intervals.
- Cautiously administer fluids to oligoanuric patients. Monitor urine production rates and body weight during fluid therapy to minimize likelihood of inducing overhydration.
- Stop fluid therapy in overhydrated oliguric/anuric patients. Use caution in administering drugs that may promote hypovolemia or hypotension (e.g., diuretics); carefully monitor response to such drugs by assessing hydration status, peripheral perfusion, and blood pressure, with serial evaluation of renal function tests.
- Corticosteroids may worsen azotemia by increasing catabolism of endogenous proteins.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Serum urea nitrogen and creatinine concentrations 24 hours after initiating fluid administration; also urine production, blood pressure, body weight, and hydration status.

POSSIBLE COMPLICATIONS

- Failure to correct prerenal azotemia caused by renal hypoperfusion rapidly could result in ischemic primary kidney disease.
- Primary renal azotemia can progress to uremia.
- Failure to restore normal urine flow in patients with postrenal azotemia can result in progressive renal damage or death due to hyperkalemia and uremia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

An association may exist between hypokalemia and azotemia in cats.

AGE-RELATED FACTORS

Primary renal failure may occur in animals of any age, but geriatric dogs and cats appear to be at substantially higher risk for both acute and chronic kidney disease; these patients are also at higher risk for prerenal and postrenal causes of azotemia.

ZOONOTIC POTENTIAL

Leptospirosis

PREGNANCY/FERTILITY/BREEDING

- Data on azotemia and pregnancy are very limited.
- Pregnant azotemic animals—pharmacologic agents excreted by nonrenal pathways are preferred.

SEE ALSO

- Acute Kidney Injury.
- Chronic Kidney Disease.
- Urinary Tract Obstruction.

ABBREVIATIONS

- AKI = acute kidney injury.
- CKD = chronic kidney disease.
- GFR = glomerular filtration rate.
- USG = urine specific gravity.

INTERNET RESOURCES

International Renal Interest Society (IRIS): www.iris-kidney.com.

Suggested Reading

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BILE PERITONITIS



BASICS

OVERVIEW

- Chemical peritonitis due to release of free bile into the abdominal cavity.
- Can involve focal or diffuse peritoneal inflammation, depending on chronicity and causal factors, and omental adhesions.

SIGNALMENT

- More common in dog than in cat.
- No age, breed, or sex predilection.

SIGNS

Historical Findings

- Acute presentation if septic peritonitis.
- May have chronic illness if nonseptic.
- Rare asymptomatic biliary rupture associated with omental encapsulation of leakage.
- Abdominal discomfort—vague.
- Lethargy.
- Gastrointestinal signs—anorexia, vomiting, diarrhea.
- Weight loss.
- ± Abdominal distention.
- Variable jaundice.
- Collapse, if septic.

Physical Examination Findings

- Lethargy.
- Variable (cranial) abdominal pain.
- Jaundice.
- Abdominal effusion.
- ± Fever.
- ± Endotoxic shock, if septic.

CAUSES & RISK FACTORS

- Limited arterial perfusion (cystic artery) to gallbladder (GB) fundus predisposes to ischemic necrosis and GB rupture.
- Trauma to biliary structures—automobile injuries, surgical, animal bites, gunshot wounds, cystic artery laceration during cholecystocentesis.
- Common bile duct (CBD)—frequent site of rupture with blunt trauma.
- Cholecystitis/choledochitis—may derive from GB mucocele (GBM); sepsis more common with necrotizing cholecystitis.
- Extrahepatic bile duct obstruction (EHBD)—may derive from neoplasia, cholelithiasis, pancreatitis, duct stricture.
- Focal, small-volume, bile peritonitis—associated with cholecystitis; may reflect omental entrapment of bile or transmural bile leakage without rupture.
- Chemical peritonitis due to bile—predisposes to septic peritonitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Conditions promoting inflammation/devitalization of biliary structures—e.g.,

cholecystitis, choledochitis, neoplasia, GBM, neoplasia, blunt trauma.

- Conditions causing EHBD—e.g., neoplasia, choleliths, pancreatitis, duct stricture/fibrosis.
- Sepsis or endotoxemia.
- Ascites—in jaundiced cirrhotic patient.
- Nonhepatic conditions causing abdominal effusion and jaundice.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

Inflammatory leukogram—left shift and toxic neutrophils if necrotizing cholecystitis or sepsis; nonregenerative anemia if chronic inflammation.

Biochemistry

- High liver enzymes, especially alkaline phosphatase (ALP); hyperbilirubinemia; ± hypoalbuminemia; ± prerenal azotemia.
- Electrolyte, fluid, and acid-base disturbances; hyponatremia common.

Urinalysis

Bilirubinuria

OTHER LABORATORY TESTS

Coagulation tests—abnormal if sepsis syndrome, disseminated intravascular coagulation (DIC), or chronic EHBD.

IMAGING

- Abdominal radiography—reduced abdominal detail, generalized or focal in GB area; cranial abdominal mass effect; rare mineralized cholelith or biliary gas (emphysematous cholecystitis).
- Thoracic radiography—rare bicavity effusion (pleural effusion), signs of trauma (e.g., fractured rib, hernia).
- Abdominal ultrasonography—effusion; EHBD—distended GB or CBD; cholecystitis/choledochitis—thick GB or duct wall; necrotizing cholecystitis—segmental GB wall hyperechogenicity, laminated wall (represents necrosis); pericholecystic fluid; hepatic/pancreatic mass effect; common with bile peritonitis; choleliths or GBM (“kiwifruit sign”); gas in GB or bile ducts (emphysematous inflammation, implicates gas-forming organisms) casting acoustic shadow; ruptured GB may be difficult to image; liver size usually normal; variable parenchymal echogenicity reflects hepatic pathology (e.g., ascending cholangitis/cholangiohepatitis [CCHS]).

DIAGNOSTIC PROCEDURES

- Abdominocentesis—physicochemical, cytologic, and culture evaluations; ultrasound guidance optimizes sampling; sample close to biliary structures but avoid structure penetration.
- Cytology—impression smears of GB, liver, and bile (with particulate material) used for immediate detection of infection and neoplasia; modified transudate or exudate, phagocytized/free bile, and bilirubin.

- Acellular mucinous material reflects biliary mucin production; GBM material may be free within abdominal cavity.

- Ratio of bilirubin in effusion : serum usually $\geq 2-3 : 1$.
- Bacterial aerobic/anaerobic culture and sensitivity—effusion, GB wall, liver, GB contents; Gram-negative enteric opportunists and anaerobes most common; polymicrobial infection possible.
- Exploratory laparotomy—appropriate for definitive diagnosis and treatment; permits cholecystectomy, cholecysto-enterostomy, duct or GB repair.
- Liver biopsy—important, evaluates for antecedent or coexistent disease, sample distant to the GB to avoid artifacts.

PATHOLOGIC FINDINGS

Depend on cause and site of rupture.



TREATMENT

- Inpatient—expediency of surgery depends on patient condition: achieve euhydration, correct electrolyte and acid-base status, provide preoperative antimicrobial treatment for best survival.

- Abdominal lavage to reduce peritoneal contamination if surgery delayed; use warm polyionic fluids and aseptic technique.
- Surgical experience important for best outcome—complicated resections and anastomoses may be required.
- Need for cholecystectomy decided at surgery; discolored GB wall indicates ischemic devitalized wall.



MEDICATIONS

DRUG(S) OF CHOICE

- Antimicrobials—in all patients, initiate broad-spectrum antimicrobials *before* surgical intervention; enteric Gram-negative and anaerobic organisms most common opportunists (good initial choices: ticarcillin, piperacillin, or third-generation cephalosporins, with enrofloxacin and metronidazole); customized antimicrobial treatment, thereafter based on cultures; continue antimicrobials $\geq 4-8$ weeks if signs of infection confirmed by culture or on cytology.
- Vitamin K₁ (0.5–1.5 mg/kg IM/SC q12h for up to 3 doses)—all jaundiced patients *before* surgery.
- Prepare for blood component ± synthetic colloid therapy.
- Antiemetics if patient is vomiting—metoclopramide (0.2–0.5 mg/kg PO/SC q6–8h or 1–2 mg/kg/24h IV by CRI); ondansetron (0.5–1.0 mg/kg q12h IV/PO

BILE PERITONITIS

(CONTINUED)

30 min before feeding); maropitant (1.0 mg/kg/day IV/SC/PO max 5 days).

- Proton pump inhibitor if gastric bleeding—pantoprazole (0.7–1.0 mg/kg IV q12–24h); omeprazole (0.5–1.0 mg/kg PO q12–24h); H₂-receptor antagonists if proton pump inhibitor is not available: famotidine (0.5–2.0 mg/kg PO/IV/SC q12–24h); sucralfate (0.25–1.0 g PO q8–12h).
- Ursodeoxycholic acid as choleretic and hepatoprotectant if GBM, choleliths, CCHS, or chronic hepatitis—may administer chronically if GBM or cholelithiasis: 10–15 mg/kg PO daily, divided, with food for best bioavailability.
- Antioxidants—vitamin E (10 IU/kg/24h); *S*-adenosylmethionine (SAMe, with proven bioavailability and efficacy) 20 mg/kg PO daily 2h before feeding until enzymes normalize, indefinitely if chronic hepatitis or CCHS, GBM, inspissated bile syndrome; choleretic influence requires higher dose (40 mg/kg/day).



FOLLOW-UP

PATIENT MONITORING

- Sequential hematologic, biochemical, and imaging tests.

- Repeat abdominocentesis to assess continued infection and/or bile leakage as indicated.

POSSIBLE COMPLICATIONS

- Cholangitis/cholangiohepatitis.
- Pancreatitis.
- Recurrent bacterial cholangitis if biliary-enteric anastomosis required.

EXPECTED COURSE AND PROGNOSIS

- High survival rate for dogs with sterile bile peritonitis, if successful surgery, depending on underlying cause.
- Higher mortality in septic bile peritonitis (up to 73%).
- Anticipate slow clinical recovery and normalization of liver enzymes, but rapid resolution of hyperbilirubinemia with successful surgery.



MISCELLANEOUS

SEE ALSO

- Cholecystitis and Choledochitis.
- Cholelithiasis.
- Gallbladder Mucocele.
- Hepatitis, Chronic.

ABBREVIATIONS

- ALP = alkaline phosphatase.

- CBD = common bile duct.
- CCHS = cholangitis/cholangiohepatitis.
- DIC = disseminated intravascular coagulation.
- EHBDO = extrahepatic bile duct obstruction.
- GB = gallbladder.
- GBM = GB mucocele.
- SAMe = *S*-adenosylmethionine.

Suggested Reading

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BLEPHARITIS



BASICS

DEFINITION

Inflammation of outer (skin) and middle (muscle, connective tissue, and glands) portions of eyelid, usually with secondary inflammation of palpebral conjunctiva.

PATHOPHYSIOLOGY

- Inflammation—immune mediated, infectious, endocrine mediated, self- and external trauma, parasitic, radiation, nutritional. Inflammatory response often exaggerated because conjunctiva is rich in mast cells and densely vascularized.
- Meibomian gland dysfunction—bacterial lipases alter meibomian lipids and plug gland; produce irritating fatty acids, enhance bacterial growth, and destabilize tear film.

SYSTEMS AFFECTED

Ophthalmic

SIGNALMENT

See Causes.

SIGNS

- Serous, mucoid, or mucopurulent ocular discharge.
- Blepharospasm.
- Eyelid hyperemia, edema, and thickening.
- Pruritus.
- Excoriation.
- Depigmentation—skin, hair (in Siamese-type cats with color points, lightening of hair on affected lids due to increased skin temperature).
- Alopecia.
- Swollen, cream-colored meibomian glands.
- Elevated, pinpoint meibomian gland orifices.
- Abscesses.
- Scales, crusts, papules, or pustules.
- Single or multiple nodular hyperemic swellings.
- Concurrent conjunctivitis and/or keratitis.

CAUSES

Congenital

- Eyelid abnormalities—may promote self-trauma or moist dermatitis.
- Prominent nasal folds, medial trichiasis, and lower lid entropion—shih tzu, Pekingese, English bulldog, Lhasa apso, pug; Persian and Himalayan cat.
- Distichia—shih tzu, pug, golden retriever, Labrador retriever, poodle, English bulldog.
- Ectopic cilia.
- Lateral lid entropion—Chinese Shar-Pei, chow chow, Labrador retriever, Rottweiler.
- Lagophthalmos—brachycephalic dogs; Persian, Himalayan, and Burmese cats.
- Deep medial canthal pocket—dolichocephalic dogs.
- Dermoids—Rottweiler, dachshund, and others; Burmese cat.

Allergic

- Type I (immediate)—atopy, food, insect bite, inhalant, *Staphylococcus* hypersensitivity (SH).
- Type II (cytotoxic)—pemphigus, pemphigoid, drug eruption.
- Type III (immune complex)—systemic lupus erythematosus (SLE), SH, drug eruption.
- Type IV (cell mediated)—contact and flea bite hypersensitivity; drug eruption.

erythematosus (SLE), SH, drug eruption.

- Type IV (cell mediated)—contact and flea bite hypersensitivity; drug eruption.

Bacterial

- Hordeolum—localized abscess of eyelid glands, usually staphylococcal; may be external (sty in young dogs, glands of Zeis) or internal (in old dogs, meibomian glands).
- Generalized bacterial blepharitis and meibomianitis—usually *Staphylococcus* or *Streptococcus*.
- Bartonella henselae*—chronic blepharoconjunctivitis in cats.
- Pyogranulomas.
- SH—young and old dogs.

Neoplastic

- Sebaceous adenomas and adenocarcinomas—from meibomian gland.
- Squamous cell carcinoma—white cats.
- Mast cell—may appear as swollen, hyperemic lesion.

Other

- External trauma—eyelid lacerations, thermal or chemical burns.
- Mycotic—dermatophytosis; systemic fungal granulomas.
- Parasitic—demodicosis; sarcoptic mange; *Cuterebra* and *Notoedres cati*. Note: *Demodex injai* has a propensity for sebaceous glands and can be associated with meibomian gland dysfunction in dogs, including chalazia and granulomatous blepharitis.
- Chalazia—sterile, yellow-white, painless meibomian gland swellings caused by granulomatous inflammatory response to meibum in surrounding eyelid tissue.
- Nutritional—zinc-responsive dermatosis (Siberian husky, Alaskan Malamute, puppies), fatty acid deficiency.
- Endocrine—hypothyroidism (dogs); hyperadrenocorticism (dogs); diabetic dermatosis.
- Viral—chronic blepharitis in cats (feline herpesvirus type 1 [FHV-1]).
- Irritant—drug reaction (e.g., neomycin); smoke in environment; post-parotid duct transposition.
- Familial canine dermatomyositis—collie and Shetland sheepdog.
- Nodular granulomatous episclerokeratitis—fibrous histiocytoma and collie granuloma; may affect eyelids, cornea, or conjunctiva.
- Eosinophilic granuloma—cats; may affect eyelids, cornea, or conjunctiva.
- Eyelid contact with tear overflow and purulent exudate (tear burn).
- Keratitis, conjunctivitis, dacryocystitis.
- Dry eye.
- Orbital disease.
- Radiotherapy.
- Idiopathic—especially Persians and Himalayans.

RISK FACTORS

- Breed predisposition to eyelid abnormalities (e.g., entropion, ectropion).
- Hypothyroidism—may promote chronic bacterial disease in dogs.
- Canine seborrhea—may promote chronic generalized meibomianitis, with predisposition for *Demodex injai* infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Clinical signs are diagnostic.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal unless metabolic cause (e.g., diabetic dermatosis).

OTHER LABORATORY TESTS

Indicated for systemic disorders, including hypothyroidism.

DIAGNOSTIC PROCEDURES

- Eye examination—inciting cause, corneal ulcer, foreign body, distichia, ectopic cilia, keratoconjunctivitis sicca (KCS).
- Ancillary ocular tests—fluorescein, Schirmer tear test.
- Thorough history and dermatologic exam:
- Cytology—deep skin scrape, conjunctival scrape, or exudate from glands and pustules.
- Wood's light evaluation, dermatophyte culture.
- KOH preparation.
- Intradermal skin testing, other testing for hypersensitivity-induced disease.
- Consider referral to a dermatologist for refractory cases.
- Aerobic bacterial culture and sensitivity—of exudate from skin, conjunctiva, expressed meibomian glands, or pustules; often will not recover *Staphylococcus* from patients with chronic meibomianitis and suspected SH.
- Immuno-fluorescent antibody assay or PCR for FHV-1 and *Chlamydia*—in conjunctival scrapings from cats with primary conjunctivitis or keratitis.
- Full-thickness wedge biopsy of eyelid.

PATHOLOGIC FINDINGS

Routine histopathology often nondiagnostic in chronic disease.



TREATMENT

APPROPRIATE HEALTH CARE

See Nursing Care.

NURSING CARE

- Prevent self-trauma—Elizabethan collar.
- Cleanse eyelids—to remove crusts; warm compresses applied for 5–15 minutes 3–4 times daily, avoiding ocular surfaces. Use saline, lactated Ringer's solution, or a commercial ocular cleansing agent (e.g., I-Lid 'n Lash[®]); clip periocular hair short.
- Common underlying cause in cats is FHV-1 infection; minimize stress.

DIET

Only if food allergy.

CLIENT EDUCATION

In cats with FHV-1-related blepharitis, inform client that there is no cure and that clinical signs often recur when animal is stressed.

(CONTINUED)

BLEPHARITIS**B****SURGICAL CONSIDERATIONS**

- Temporary everting eyelid sutures—spastic entropion; or in puppies before permanent surgical correction.
- Repair eyelid lacerations.
- Lancing—large abscesses only; lance and curette hordeola that resist medical treatment and chalazia that have hardened and cause keratitis; manually express infected meibomian secretions.

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

- Systemic—for bacterial eyelid infections (e.g., cephalexin 20 mg/kg IV q8h). For *Bartonella henselae* infection in cats, therapy may include doxycycline (10 mg/kg PO q12h for 3 weeks), pradofloxacin (5–10 mg/kg PO q12–24h for 28–42 days), or azithromycin (10 mg/kg PO q24h for 3 weeks).
- Topical—neomycin, polymyxin B, and bacitracin combination or chloramphenicol.

Congenital

- Topical antibiotic ointment—q6–12h to prevent frictional rubbing of eyelid hairs or cilia on ocular surface.
- Regularly flush debris from deep medial canthal pocket using saline, lactated Ringer's solution, or ocular irrigant.

External Trauma

- Topical antibiotic ointment—q6–12h; in patients with spastic entropion and blepharospasm until surgical correction.
- Systemic antibiotics.

Allergic

- SH blepharitis—systemic broad-spectrum antibiotics and systemic corticosteroids (prednisolone 0.5 mg/kg PO q12h for 3–5 days, then taper); many patients respond to systemic corticosteroids alone; systemic cyclosporine (5 mg/kg PO q24h until remission, then q48–72h) if refractory to corticosteroids; failure of treatment—consider injections of *Staphylococcus aureus* bacterin (*Staphage Lysate*). • Infected meibomian glands—oral tetracycline (15–20 mg/kg PO q8h), doxycycline (3–5 mg/kg PO q12h), or cephalexin (22 mg/kg PO q8h) for 3 weeks (the former two are lipophilic and cause decreased production of bacterial lipases and irritating fatty acids); topical polymyxin B and neomycin with 0.1% dexamethasone (q6–8h) or topical 0.02% tacrolimus compounded ointment (q8–12h). Some

affected dogs might also require treatment for demodectosis. • Eyelid lesions associated with puppy strangles—treat generalized condition.

- Atopy—see Atopic Dermatitis.

Bacterial

- Based on culture and sensitivity or serologic testing.
- Pending results—topical polymyxin B and neomycin with 0.1% dexamethasone ointment (q4–6h) and systemic broad-spectrum antibiotic.

Mycotic

Microsporum canis infection—see Dermatophytosis.

Parasitic

Demodicosis, *Notoedres* infection, sarcoptic mange—see relevant chapters.

Idiopathic

Clinical signs often controlled with topical polymyxin B and neomycin with 0.1% dexamethasone (q8–24h or as needed); occasionally may need prednisolone (0.5 mg/kg PO q12h for 3–5 days, then taper) and/or systemic antibiotic.

CONTRAINDICATIONS

- Topical corticosteroids—do not use with corneal ulceration.
- Many cats with presumed idiopathic blepharoconjunctivitis have FHV-1 infection; topical and systemic corticosteroids may exacerbate infection.
- Oral tetracycline and doxycycline—do not use in puppies and kittens.
- Neomycin—avoid topical use if possible cause of blepharitis.
- Neomycin, bacitracin, and polymyxin—avoid topical ophthalmic use in cats due to rare but potentially fatal anaphylactic reaction.

PRECAUTIONS

- Ectoparasitism—wear gloves; do not contact ocular surfaces with a drug topically applied to skin; apply artificial tear ointment to eyes for protection.
- Topical gentamicin, neomycin, terramycin, and most ointments—may cause irritant blepharoconjunctivitis (rare); withdrawal may resolve condition.

POSSIBLE INTERACTIONS

Staphylococcal bacterin may cause anaphylactic reaction (rare).

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

- Depends on cause, therapy.
- Bacterial—systemic and topical treatment for at least 3

weeks; should notice improvement within 10 days.

- Most common causes of treatment failure—use of subinhibitory antibiotic dosages, failure to correct one or more predisposing factors, early discontinuation of medications.

PREVENTION/AVOIDANCE

Depends on cause.

POSSIBLE COMPLICATIONS

- Cicatricial lid contracture—results in trichiasis, ectropion, or lagophthalmos.
- Spastic entropion—because of blepharospasm and pain.
- Qualitative tear film deficiency—loss of proper meibum secretion.
- Recurrence of bacterial infection or FHV-1 blepharoconjunctivitis.

EXPECTED COURSE AND PROGNOSIS

Depend on cause.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Dermatophytosis.
- Sarcoptic mange.

SEE ALSO

- Atopic Dermatitis.
- Conjunctivitis—Cats.
- Conjunctivitis—Dogs.
- Dermatophytosis.
- Epiphora.
- Keratitis—Nonulcerative.
- Keratitis—Ulcerative.
- Red Eye.

ABBREVIATIONS

- FHV-1 = feline herpesvirus type 1.
- KCS = keratoconjunctivitis sicca.
- SH = *Staphylococcus* hypersensitivity.
- SLE = systemic lupus erythematosus.

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Client Education Handout available online

BOTULISM



BASICS

OVERVIEW

- Paralytic illness caused by preformed neurotoxin produced by bacterium *Clostridium botulinum* (Gram +, anaerobe) contained in uncooked food, carrion, and contaminated or improperly stored silage.
- Most cases in dogs caused by *Clostridium botulinum* neurotoxin serotype C; neurotoxin interferes with release of acetylcholine at neuromuscular junction, resulting in diffuse lower motor neuron signs. • Heavy molecular weight of the toxin seems to preclude its transfer to placenta.

SIGNALMENT

Dogs (naturally infected) and cats (experimentally infected except for one case report of natural *Clostridium botulinum* type C toxicosis).

SIGNS

Historical Findings

- Signs appear a few hours to 6 days after toxin ingestion. • Other dogs living in the same environment may be affected. • Acute, symmetric, progressive weakness develops, starting in the pelvic limbs and ascending to the trunk, thoracic limbs, neck, and muscles innervated by the cranial nerves; severe tetraparesis or tetraplegia ensues.

Physical Examination

- Possible increased or decreased heart rate.
- In severe cases—diaphragmatic respiration.

Neurologic Examination Findings

- Mental status—normal. • Cranial nerves—may reveal sluggish pupillary light reflexes (PLR), diminished palpebral reflexes, decreased jaw tone, decreased gag reflex, salivation, and dysphonia. • Gait and posture—a stiff, short-stride gait (no ataxia) is initially observed until recumbence develops (usually within 12–24 hours). • Spinal reflexes—decreased to absent with decreased muscle tone (to atonia) and muscle atrophy.
- Autonomic signs—mydriasis with decreased PLR, decreased lacrimation, ileus, and urine retention or frequent voiding of small volumes. • No hyperesthesia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute canine polyradiculoneuritis (coonhound paralysis). • Myasthenia gravis.
- Tick bite paralysis. • Coral snake venom toxicity. • Dumb form of rabies. • Lasalocid (growth promoter in ruminants) toxicosis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

- Definitive diagnosis is based on detection of botulinum toxin in serum, feces, vomitus, or ingested food sample; by neutralization test in small rodents; or by in vitro test that measures toxin antigenicity rather than toxicity. • Detection of anti-C botulinum neurotoxin antibodies may help support clinical diagnosis.

IMAGING

Thoracic radiographs—possible megaesophagus and/or signs of aspiration pneumonia.

DIAGNOSTIC PROCEDURES

- Electromyography may reveal fibrillation potentials and positive sharp waves in affected muscles. • Motor nerve conduction velocity may be normal or decreased, with reduced amplitude of evoked muscle action potentials; compound muscle action potentials can be decreased after low-frequency repetitive nerve stimulations.



TREATMENT

- If recent ingestion—gastric lavage, cathartics (avoid agents containing magnesium), or enemas may be useful.
- Mildly affected dogs recover over a period of several days with supportive treatment including physical therapy, frequent turning, good bedding (to prevent decubital sores), bladder care (catheterization), artificial tears (to prevent corneal ulceration), and feeding from an elevated position (when megaesophagus present). • Dogs with respiratory difficulties require intensive care monitoring with arterial blood gas, intermittent esophageal suction, alimentation by nasogastric or gastrostomy tube, and eventually ventilatory support.



MEDICATIONS

DRUG(S) OF CHOICE

- Type C antitoxin may cause anaphylaxis; not effective when the toxin is already fixed at the nerve ending. • Antibiotics are not recommended since they might increase the release of toxins through bacterial lysis or by promoting intestinal infection; to be used only if secondary infections occur.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Aminoglycosides, procaine penicillin, tetracyclines, phenothiazines, antiarrhythmic agents, and magnesium should be avoided (neuromuscular transmission blockade).



FOLLOW-UP

PATIENT MONITORING

Monitor patients for respiratory failure, aspiration pneumonia, progressive lower motor neuron signs, urinary tract infection, and ocular complications.

PREVENTION/AVOIDANCE

- Prevent access to carrion and feed dogs cooked food. • Avoid contact with spoiled raw meat. • Samples should be refrigerated (not frozen) and manipulated with caution, since humans are also sensitive to the toxin.

POSSIBLE COMPLICATIONS

- Respiratory failure and death in severe cases.
- Aspiration pneumonia from megaesophagus and regurgitations. • Keratoconjunctivitis sicca and corneal ulceration. • Prolonged recumbence—pulmonary atelectasis and infection; decubital sores; urine scalding.

EXPECTED COURSE AND PROGNOSIS

- Maximum severity of signs usually reached within 12–24 hours. • Neurologic signs disappear in reverse order of appearance; complete recovery usually occurs within 1–3 weeks, and requires the formation of new nerve terminals and functional neuromuscular junctions.



MISCELLANEOUS

SEE ALSO

- Coonhound Paralysis (Acute Polyradiculoneuritis). • Myasthenia Gravis.
- Snake Venom Toxicosis—Coral Snakes.
- Tick Bite Paralysis.

ABBREVIATIONS

- PLR = pupillary light reflex.

Suggested Reading

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Author Hélène L.M. Ruel
Acknowledgment The author and book editors acknowledge the prior contribution of Roberto Poma (deceased).

BRAIN INJURY



BASICS

DEFINITION

- Traumatic—external forces.
- Nontraumatic—hypoxia, metabolic disorders, vascular disruption, infection, toxicity, neoplasia.
- Primary—direct initial insult when tissue and vessels are stretched, compressed, or torn.
- Secondary—alterations of brain vasculature and tissue following primary injury.

PATHOPHYSIOLOGY

- Acceleration, deceleration, and rotational forces traumatize brain tissue.
- The brain has high oxygen and glucose requirements; reduced blood flow puts it at great risk for hypoxia.
- Oxygen delivery dependent on cerebral blood flow (CBF) and cerebral perfusion pressure (CPP) (= mean arterial pressure [MAP] – intracranial pressure [ICP]).
- Intracranial bleeding, edema (vasogenic and cytotoxic), vasodilation, and/or vasospasms increase ICP, causing low CBF, ischemia, brain swelling, and herniation; slow, progressive increase in ICP better tolerated than small, acute rise.
- Hypotension, hypoxia—major contributors to secondary injury.

SYSTEMS AFFECTED

- Nervous—altered mentation, cranial nerve deficit, seizures, twitching, postural changes.
- Cardiovascular—arrhythmia.
- Endocrine/metabolic—alteration in antidiuretic hormone (ADH) release and sodium concentration; central temperature dysregulation; insulin resistance; depletion of cortisol.
- Ophthalmic—changes in eye position, eye movements, pupillary light reflex, papilledema.
- Respiratory—hyper- or hypocapnea; abnormal breathing patterns; neurogenic pulmonary edema.

INCIDENCE/PREVALENCE

- Head and neck injuries found in up to 34% of dogs and cats suffering blunt force trauma.
- Head trauma reported in up to 25% of dogs with severe blunt force trauma and in 50% of dogs and cats injured by motor vehicles and crush injuries.
- Additional causes—penetrating injuries, fall from heights, human-inflicted trauma.
- Parenchymal and extradural hematomas found in 10% of dogs and cats with signs of mild head injury and in up to 80% with severe head injury.

SIGNALMENT

Species

Dog and cat.

SIGNS

Historical Findings

- Determine cause—trauma, cardiac arrest, heart failure, hypertension, toxins, vascular event, coagulopathy, severe respiratory compromise, prolonged seizures, hypoglycemia, jaundice.
- Decline in neurologic condition—

implies progression from intracranial bleeding, cerebral edema, ischemia.

- Seizure activity—cerebral or diencephalon involvement.

Physical Examination Findings

- Evidence of head trauma—open wounds, epistaxis, blood in ear canal.
- Cardiac or respiratory insufficiency—hypoxia, cyanosis, hypoventilation.
- Poor perfusion—weak pulse, pale mucous membranes.
- Skull palpation—fracture, open fontanelle.
- Sustained bradycardia—midbrain, pontine, or medullary lesion.
- Cushing reflex—bradycardia and hypertension.
- Ecchymosis, petechiae, retinal hemorrhages, or distended vessels—hypertension, coagulopathy.
- Papilledema—cerebral edema.
- Retinal detachment—infectious, neoplastic, or hypertensive cause.

Neurologic Examination Findings

Mental Status

- Level of consciousness and cranial nerve deficits—cerebral cortex (better prognosis), midbrain/brainstem, or multifocal.
- Postural changes—decerebrate rigidity with midbrain lesion; decerebellate rigidity with cerebellar lesion.
- Peracute focal deficits—vascular or neoplastic causes.

Pupillary Light Reflexes

- Miotic responsive pupils—cerebral or diencephalic lesion (rule out traumatic uveitis, Horner's syndrome).
- Pinpointed unresponsive pupils—diencephalic, pontine, or medullary lesion.
- Dilated unresponsive pupil(s) or midpoint fixed unresponsive pupils—midbrain lesion.

Cranial Nerves

- Normal with altered mentation—cerebrum/diencephalic lesion.
- CN II—loss of menace and dazzle response with dilated unresponsive pupils; cranial forebrain.
- Loss of physiologic nystagmus—brainstem lesion.
- CN III—midbrain lesion.
- CN V–XII—pontine or medullary lesion.

Respiratory Patterns

- Cheyne-Stokes—severe diffuse cerebral or diencephalon lesion.
- Hyperventilation—midbrain lesion.
- Ataxic or apneustic—pontine or medullary lesion.

CAUSES

- Trauma.
- Prolonged hypoxia or ischemia.
- Prolonged shock.
- Severe hypoglycemia.
- Prolonged seizures.
- Severe hyper- or hypothermia.
- Alterations in serum osmolality.
- Toxins.
- Neoplasia.
- Hypertension.
- Hemorrhage.
- Inflammatory, infectious, immune-mediated diseases.
- Thiamin deficiency.
- Hydrocephalus.
- Parasitic migration.

RISK FACTORS

- Free-roaming—trauma, toxins.
- Coexisting cardiac, respiratory, hematologic, hepatic disease.
- Diabetes mellitus—insulin therapy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Systemic causes of altered states of consciousness or central vestibular signs—metabolic disease; toxins; drugs; infection.

CBC/BIOCHEMISTRY/URINALYSIS

- Reflect systemic effects of neurologic signs.
- Alterations in serum sodium suggest central ADH abnormalities.

OTHER LABORATORY TESTS

- Arterial blood gas.
- Coagulation profile.
- Infectious disease titers.

IMAGING

- Skull radiographs—detect fractures, lytic lesion.
- CT—detect acute hemorrhage, infarcts, fractures, lytic lesion, penetrating foreign bodies, hydrocephalus, herniation.
- MRI—detect cerebral edema, hemorrhage, mass, hydrocephalus, infiltrative diseases, inflammation, herniation, fractures.
- Ultrasound optic disk—more than 3 mm diameter may be associated with brain edema.

DIAGNOSTIC PROCEDURES

- ECG—detects arrhythmias.
- BP—assess perfusion.
- Cerebrospinal fluid (CSF) analysis—if cause unknown and no contraindications.

PATHOLOGIC FINDINGS

- Brain edema, inflammation.
- Herniation.
- Hemorrhage.
- Hydrocephalus.
- Infarct.
- Laceration, contusion.
- Hematoma.
- Skull fracture, lytic lesion.
- Necrosis.
- Apoptosis.



TREATMENT

APPROPRIATE HEALTH CARE

- Goals of therapy—support oxygenation and ventilation; maintain BP and CPP; decrease ICP; decrease cerebral metabolic rate.
- Maintain systolic BP >90 mmHg and partial pressure of carbon dioxide (PCO_2) at 35–40 mmHg; with suspected elevated ICP, hyperventilation to 32–35 mmHg.
- Maintain partial pressure of oxygen (PaO_2) >60 mmHg, arterial oxygen saturation (SaO_2) >90%, peripheral oxygen saturation (SpO_2) >94%.
- Avoid cough or sneeze reflex during intubation or nasal oxygen supplementation; lidocaine (dogs: topical and 1–2 mg/kg IV) before.
- Do not compress jugular veins.
- Orotracheal intubation if gag reflex lost.

NURSING CARE

- Aggressive therapy for midbrain/brainstem lesion or declining neurologic signs.
- Overzealous fluid resuscitation can contribute to brain edema.
- Small-volume fluid resuscitation techniques to maintain systolic BP >90 mmHg with normal heart rate.
- Combination of

(CONTINUED)

BRAIN INJURY**B**

isotonic crystalloids (10–20 mL/kg increments) with hydroxyethyl starch (5 mL/kg increments) over 5–8 minutes. • Avoid hypertension.

- Level head with body or elevate head and neck to 20° angle. • Keep airway unobstructed; use suction and humidify if intubated; hyperoxygenate, consider IV lidocaine prior to suctioning. • Lubricate eyes. • Reposition every 2–4 hours to avoid hypostatic pulmonary congestion, pressure sores. • Prevent fecal/urine soiling. • Maintain normal body temperature.
- Maintain hydration with balanced crystalloid solution. • Rehabilitation exercises.

ACTIVITY

- Restricted. • Consult rehabilitation specialist for appropriate exercises to maintain muscle tone.

CLIENT EDUCATION

- Neurologic signs may worsen before improving.
- Neurologic recovery may not be evident for several days; possibly >6 months for residual neurologic deficits. • Serious systemic abnormalities contribute to CNS instability.

SURGICAL CONSIDERATIONS

Depressed skull fracture, penetrating foreign body, uncontrollable ICP elevation (insufficient CSF drainage, hematoma/mass evacuation, herniation).

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

- Ensure systolic BP >90 mmHg; lower ICP by hyperventilation, drug therapy, drainage of CSF from ventricles, or surgical decompression.
- 7% hypertonic saline—2–4 mL/kg IV.
- Furosemide—0.75 mg/kg IV; may decrease CSF production. • Mannitol—0.5–1 g/kg IV bolus repeated at 2h intervals 3–4 times in dogs, and 2–3 three times in cats; repeated doses must be given on time; improves CBF and lowers ICP; may exacerbate hemorrhage.
- Glucocorticosteroids—no benefit in acute management and long-term outcome in human traumatic brain injury (TBI); anti-inflammatory doses (prednisone 1 mg/kg/day) may be of benefit with brain edema related to intracranial neoplasia and infectious meningoencephalomyelitis (MEM); immunosuppressive doses (2 mg/kg/day) in combination with additional immunosuppressive drugs in immune-mediated MEM. • Provide analgesia/sedatives (e.g., fentanyl 3–5 µg/kg IV, then 3–5 µg/kg/h CRI ± lidocaine 3–5 mg/kg/h) as indicated; avoid agents that can reduce CPP. Avoid ketamine with obstructive intracranial lesions. • Thrashing, seizures, or uncontrolled motor activity—diazepam CRI (0.5–1 mg/kg/h), midazolam CRI (0.2–0.4 mg/kg IV), or propofol (3–6 mg/kg IV titrated to effect; 0.1–0.6 mg/kg/min CRI); monitor for hypotension; intubate if unable to protect airway.

- Levetiracetam—20–30 mg/kg IV/IM/PO/rectal q8h if seizure activity.

Other

- Reducing cerebral metabolic rate with heavy sedation using dexmedetomidine (3 µg/kg slow bolus followed by 3–7 µg/kg/h CRI IV) with ketamine (1 µg/kg slow bolus followed by 1 µg/kg/h CRI IV) with uncontrolled seizures or propofol (2–4 mg/kg IV then 0.1–0.4 mg/kg/min); must intubate and support blood pressure, oxygenation, and ventilation. • Cooling patient to 32–33 °C (89–91 °F) for 48h may provide cerebral protection when administered within 6 hours of global ischemia or severe brain injury.
- Glucose regulation. • Careful nasogastric tube feeding for early trickle flow feeding; cisapride (0.5 mg/kg PO q8–12h) and metoclopramide (1–2 mg/kg/day) may promote gastrointestinal motility. • Desmopressin for refractory hypernatremia; emergency dosage not established for animals (dogs: 4 µg topical conjunctival q12h; cats: 5 µg SC q12h).

CONTRAINdications

Drugs that cause hypertension, hypotension, hyperexcitability, or increase in metabolic rate.

PRECAUTIONS

- Avoid hypotension, hypoxemia, hypertension, hyperglycemia, hypoglycemia, hypernatremia, hypo- or hypervolemia.
- Keep head and neck above plane of body.
- Do not compress jugular veins.
- Furosemide, mannitol, and hypertonic saline—can cause hypovolemia and hypotension. • Maintain PCO₂ >32 mmHg; avoid hyperventilation in the first 24–8h and do not perform therapeutic hyperventilation (32–35 mmHg) for extended periods (>48h).

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

- Repeated neurologic examinations—deterioration warrants aggressive therapeutic intervention. • BP—maintain systolic BP >90 mmHg. • Blood gases, pulse oximetry, end-tidal CO₂—to assess need for oxygen supplementation or ventilation. • Blood glucose—avoid severe persistent hyperglycemia and hypoglycemia. • ECG—arrhythmias may affect perfusion, oxygenation, and CBF.
- ICP—to detect elevations and monitor response to therapy.

PREVENTION/AVOIDANCE

Keep pets in a confined area or leashed.

POSSIBLE COMPLICATIONS

- Seizures. • Brain herniation. • Intracranial hemorrhage. • Progression from cerebral cortical to midbrain signs. • Malnutrition. • Aspiration pneumonia. • Hypostatic pulmonary congestion. • Corneal desiccation. • Urine scalding. • Airway obstruction from mucus.

- Arrhythmias. • Hypotension. • Hypernatremia. • Hypokalemia. • Respiratory failure. • Residual neurologic deficits. • Death.

EXPECTED COURSE AND PROGNOSIS

- Young animals, minimal primary brain injury, secondary injury consisting of cerebral edema—best prognosis. • No deterioration for 48 hours—better prognosis. • Rapid resuscitation of systolic BP to >90 mmHg and avoiding hypoxemia—better neurologic outcome. • Modified Glasgow Coma Score may offer prognostic insight.

**MISCELLANEOUS****SYNOMYMS**

- Head trauma. • TBI.

SEE ALSO

Stupor and Coma.

ABBREVIATIONS

- ADH = antidiuretic hormone. • CBF = cerebral blood flow. • CPP = cerebral perfusion pressure. • CRI = continuous rate infusion
- CSF = cerebrospinal fluid. • ICP = intracranial pressure. • MAP = mean arterial pressure.
- MEM = meningoencephalomyelitis. • PaO₂ = partial pressure of oxygen. • PCO₂ = partial pressure of carbon dioxide. • SaO₂ = arterial oxygen saturation. • SpO₂ = peripheral oxygen saturation. • TBI = traumatic brain injury.

INTERNET RESOURCES

<http://www.traumaticbraininjury.com>

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Acknowledgment The author and book editors acknowledge the prior contribution of Rebecca Kirby.



Client Education Handout
available online

(CONTINUED)

- behavior, topographic pattern, and secondary changes present within and surrounding the tumor. • Meningioma is most common intracranial neoplasm of dogs and cats. • Classification of glial subset of neuroepithelial tumors is based on predominant cell type (e.g., astrocyte or oligodendrocyte).

Dogs

- Embryonal tumors have been consolidated under single term “primitive neuroectodermal tumors” (or PNETs) to accommodate their anaplastic nature.
- Brain tumors arising from lymphoreticular cells traditionally have been grouped under a heading of reticulosis or histiocytic lymphoma.
- Skull tumors that affect the brain by local extension include osteosarcoma, chondrosarcoma, and multilobular osteochondrosarcoma.
- The most frequently seen secondary tumors of dogs include local extension of nasal adenocarcinoma; metastases from mammary, prostatic, or pulmonary adenocarcinoma; metastases from hemangiosarcoma; and extension of pituitary adenoma or carcinoma.
- Nerve sheath tumors arising from cranial nerves (particularly oculomotor nerve and trigeminal nerve) may occur in dogs.

Cats

- Meningiomas involving multiple intracranial sites (including third ventricle) relatively common in cats.
- Primary brain tumors other than meningiomas occur infrequently in cats.
- Tumors that have been reported include astrocytoma, ependymoma, oligodendrogloma, choroid plexus papilloma, medulloblastoma, lymphoma, olfactory neuroblastoma, and gangliocytoma.
- Lymphoma of the brain may be primary or secondary, or may be an aspect of multicentric lymphoma of cats.
- Secondary tumors that have been reported to occur in the brain of cats include pituitary macroadenomas and macrocarcinomas, and metastatic carcinoma.
- Local extension may occur either from tumors of middle ear cavity (e.g., squamous cell carcinoma), nasal cavity (e.g., nasal adenocarcinoma), or skull (e.g., osteosarcoma).

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

- Beyond general efforts to maintain homeostasis, major goals of therapy for brain tumor are to control secondary effects, such as increased ICP or cerebral edema, and to eradicate the tumor or reduce its size.
- Beyond palliative care, three methods of therapy for a brain tumor currently are

available for use in dogs and cats: surgery, irradiation, and chemotherapy.

Surgery

- Neurosurgical intervention is an essential consideration in management of brain tumors in cats or dogs, whether for complete excision, partial removal, or biopsy.
- Meningiomas, particularly those located over cerebral convexities or in frontal lobes of cerebrum, may be completely (or almost completely) removed by surgery, especially in cats.
- Primary calvarial tumors also may be removed surgically prior to other types of therapy.

Radiation Therapy

- Irradiation may be used either alone or in combination with other treatments for either primary or secondary brain tumors.
- Careful treatment planning by qualified and experienced radiation therapist is essential to success of radiation therapy.
- A major development in radiation therapy is emergence of more precise protocols that spare tissues surrounding the brain tumor (e.g., stereotactic radiotherapy).

Chemotherapy

Alkylating agents (e.g., carmustine [BCNU], lomustine [CCNU], and temozolamide), antimetabolic agents (e.g., cytosine arabinoside), and ribonucleotide reductase inhibitors (e.g., hydroxyurea) may result in reduction of tumor size and improvement of clinical signs in dogs with glial cell tumors; however, evidence of efficacy in animals is lacking.

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

- Glucocorticoids may be used for edema reduction and, in some cases (e.g., lymphoma), for retardation of tumor growth.
- Some animals with brain tumor demonstrate dramatic improvement in clinical signs for weeks or months with sustained glucocorticoid therapy.
- Antiepileptic drugs (e.g., phenobarbital, bromide, levetiracetam) may be utilized for control of generalized seizures.
- Mannitol and hypertonic saline are agents best suited for effective reduction of increased ICP.

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

- Serial neurologic examinations.
- Serial CT or MRI examinations.

BRAIN TUMORS

B

POSSIBLE COMPLICATIONS

- Aspiration pneumonia due to depressed swallowing reflexes associated with increased ICP.
- Seizures.

EXPECTED COURSE AND PROGNOSIS

- Little information available concerning survival times of dogs or cats with brain tumor that have received only palliative therapy (i.e., therapy to control secondary effects of a tumor without an attempt to eradicate the tumor).
- Results of one study indicate mean and median survival of 81 days and 56 days, respectively, following CT diagnosis of primary brain tumor in each of 8 dogs.
- Results from several studies confirm that prognosis for a dog or cat with a primary brain tumor may be significantly improved by surgical removal and irradiation, either alone or in combination.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Dogs that have been treated for a brain tumor may develop a second type of tumor elsewhere in the body.

ABBREVIATIONS

- CSF = cerebrospinal fluid.
- ICP = intracranial pressure.
- PNET = primitive neuroectodermal tumor.

Suggested Reading

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Author Richard A. LeCouteur



**Client Education Handout
available online**

BREEDING, TIMING



BASICS

DEFINITION

Timing of insemination(s) to maximize pregnancy risk and litter size.

PATHOPHYSIOLOGY

Dogs

- Must determine ovulation day so that breeding(s) occur(s) at proper time.
- Fresh, chilled, or frozen semen—usually limited to one or two inseminations; insemination must be timed relative to ovulation for maximum fertility.
- Ovulation may vary relative to onset of heat (proestrus), standing heat (estrus), vaginal cytology.
- Luteinizing hormone (LH)—controls ovulation; peaks on same day or after full cornification is observed; ovulation occurs approximately 2 days after peak; 2–3 days (54–72 hours) more required for oocyte maturation; mature oocytes viable for minimum 2–3 days; thus fertile period is 4–8 days after LH peak, and maximum fertility is 5–6 days after LH peak.
- Serum progesterone concentration—increase closely associated with LH peak.

Cats

- Ovulation—usually induced; timing of breeding is not as critical as with dogs; depends on adequate gonadotropin-releasing hormone (GnRH) and then LH release triggered by vaginal stimulation.
- Adequate stimulation—characterized by copulatory cry and postcoital reaction; frequency of coital stimuli important in determining adequacy of coital contact.
- LH—peak concentration and duration of elevation determine number of follicles ovulating; higher concentration with multiple copulations; response to copulation depends on day of estrus (greater release on estrus day 3 than on estrus day 1); release partially depends on duration of exposure to estrogen.

SYSTEMS AFFECTED

Reproductive

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Dog and cat.

SIGNS

General Comments

Dogs

- Onset of estrus—usually associated with a change in the vaginal discharge from sanguineous to barely red and decreased vulvar edema; sanguineous discharge may

continue during estrus and cease only at the onset of diestrus.

- Physical signs alone—unreliable for precise determination of fertile period.
- Receptivity—may be detected by touching the perineum near the vulva; if receptive, female will “flag” by elevating the tail to one side and lifting the vulva dorsally.

Cats

LH response to a single mating—may vary substantially.

Historical Findings

Dogs

Sanguineous vulvar discharge during estrus.

Cats

Return to estrus in <30 days may indicate failure to ovulate; interestrus usually 8–10 days, but highly variable even within queen; some queens will breed while pregnant.

Physical Examination Findings

Dogs

- Interest shown by male.
- Vulva less turgid.
- Vaginal discharge—less color and amount.
- Flagging.
- Females show mounting behavior.
- Fully cornified and crenulated pale vaginal epithelium.
- Digital palpation of vagina may be resisted by bitch in proestrus, improving throughout proestrus until estrus. May feel edematous mass on floor of caudal vagina, just cranial to urethral os, that should shrink as optimal breeding period approaches.

Cats

- Fully cornified vaginal epithelium.
- Interest shown by male.
- No changes in external genitalia.
- Vocalizes, rubs objects.
- Lordosis.

CAUSES

Dogs

- Limited number of breedings.
- Female unreceptive to male.
- Artificial insemination (fresh, chilled, or frozen semen).

Cats

- Coitus—too early or too late in estrus; too few times.
- Artificial insemination.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vaginal discharge—proestrus or estrus; vaginitis; neoplasia, pyometra, urinary tract infection.
- Refusal to allow intromission—anatomic abnormalities of Mullerian duct development, vulvovestibular or vestibulo-vaginal junction, acquired abnormality from dystocia or breeding trauma, vaginal hyperplasia, behavioral.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

Dogs

- Semi-quantitative progesterone ELISA—adjunct to vaginal cytologic examination.
- Quantitative serum progesterone testing—preferred when breeding with frozen semen; especially useful in animals with reduced fertility. Commercial labs or in-house machines available.
 - Progesterone concentration <1 ng/mL (3.18 nmol/L) before LH peak, 1.5–4 ng/mL (4.8–12.7 nmol/L) at LH peak, 4–10 ng/mL (12.7–31.8 nmol/L) at ovulation; continues to rise during diestrus/pregnancy.
 - Commercial laboratories use various methods of progesterone concentration measurement, so values indicative of LH and ovulation vary among labs.
 - Documenting rapid rise in progesterone concentration subsequent to initial rise is more reliable indicator of ovulation than single measurement of LH peak or initial rise in progesterone.
 - LH testing—must sample daily to observe LH peak; can use serum progesterone to signal when to start testing or use the initial rise in progesterone concentration as surrogate for LH peak.

Cats

Serum progesterone testing to verify ovulation.

IMAGING

Ultrasonographic imaging of ovaries—may help determine ovulation; perform daily, best if using color flow Doppler.

DIAGNOSTIC PROCEDURES

Dogs

- Vaginal cytologic examination—imprecise indicator of fertile period; cornification of vaginal epithelium with clear background usually coincides with sexual receptivity.
- Proestrus (in breeder terms, “day 1,” first sign of hemorrhagic vaginal discharge)—most epithelial cells are noncornified.
- Percentage of cornified cells (cells with angular cytoplasm and pyknotic nuclei or nuclei that fail to take up stain) increases during proestrus.
- Estrus—90% or more cornified cells, background of slide free of debris.
- Breeders refer to estrus by day, usually occurs day 10–18 in breeder terms.
- Diestrus—abrupt decline in percentage of cornified cells (20–50%) in a single day; day 1 of diestrus (D1); normal to see neutrophils on days 1–4 of diestrus.
- Vaginoscopy—edematous vaginal folds until LH peak, then vagina pale with slight wrinkling (crenulation) as edema decreases with estradiol decline; by optimum breeding period crenulation is obvious, until diestrus when folds are flat and edema disappears.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Dogs

- Fresh semen, multiple breedings— inseminate q48h, starting 48–96h after initial rise in serum progesterone concentration is observed until D1. • Fresh semen, two breedings— inseminate either on days 3 and 5 or on days 4 and 6 after LH peak or initial rise in serum progesterone concentration; use standard artificial insemination (AI) pipettes or modified Foley catheters (several sizes available); vaginal insemination on or after day 5 may be associated with reduced pregnancy rates and litter sizes due to beginning of cervical closure. • Frozen or chilled semen— frozen semen is less viable than chilled, thus timing is more critical; one or two intrauterine inseminations most common: inseminate on day 5 or 6 after LH peak or initial rise in serum progesterone concentration (day 0) or 3 days after serum progesterone concentration ≥ 5 ng/mL (16 nmol/L); for intrauterine insemination via transcervical endoscopy (TCI) or surgical insemination, serum progesterone concentration on day of insemination should be ≥ 12 ng/mL (38 nmol/L; value is laboratory dependent). • Timing insemination based on serum progesterone concentration improves chance of conception and increased litter size.
- Blood collection and vaginal examination q48h are adequate in most cases.

Cats

- Increase likelihood of ovulation and litter size by maximizing number of matings; breed on successive days. • Breed at least 4 times daily at least 2–3 hours apart on days 2 and 3 of estrus to maximize LH release. • May induce ovulation by administration of exogenous hormones—GnRH or human chorionic gonadotropin (hCG) after mating.

ACTIVITY

- No alteration in activity necessary except confinement—bitch will search for male.
- Keep strictly away from unintended sexually intact males.

CLIENT EDUCATION

Client education on physical, behavioral, and endocrinologic changes that occur during estrous cycle, and how variable timing of these changes can be from animal to animal, can improve owner compliance and satisfaction.

SURGICAL CONSIDERATIONS

Surgical AI requires standard postoperative care.



MEDICATIONS

DRUG(S) OF CHOICE

Cats—hCG (100–500 IU/cat IM); GnRH (25–50 µg/cat IM).



FOLLOW-UP

PATIENT MONITORING

- Dogs—serial vaginal cytology to determine D1; ovulation is ~6 days before D1. • Dogs— whelping is 65 ± 1 days from LH peak, 63 ± 1 days from ovulation, or 57 ± 1 days from D1; for fresh, chilled, or frozen semen: repeat quantitative serum progesterone measurement after initial progesterone rise or LH peak to verify >10 ng/mL (32 nmol/L). • Cats—use serum progesterone assay 1 week post insemination to verify ovulation. • Cats—queening is $62\text{--}71$ days from first breeding.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Dogs

- Vaginal cytologic examinations—compare D1 with prospective estimation based on progesterone; if estimates differ, pregnancy rates are reduced. • Semi-quantitative progesterone kits—must come to room temperature before use; concentrations falsely elevated when using a cold kit. • Serum progesterone concentration—allow blood to clot at room temperature; separate cells from serum 20 minutes after collection; falsely low concentrations occur when using serum mixed with red blood cells (progesterone binds to erythrocytes). • Hemolyzed or lipemic specimen—may give falsely low progesterone concentration. • Quantitative

(chemiluminescence assay, fluorescence, ELISA) progesterone assay—more accurate than semi-quantitative kits; several in-house analyzers available; turnaround times should be less than 24 hours. • Serum separator tubes cause false elevations in chemiluminescence progesterone assay; anticoagulant may affect reported concentration (serum > heparin plasma > EDTA plasma).



MISCELLANEOUS

AGE-RELATED FACTORS

Split heats in young bitches—period of proestrus (may be prolonged to 6 weeks or more), followed by cessation of signs, and subsequent resumption of estrus cycle (1–3 weeks later); no initial rise in progesterone or LH concentration occurs with first proestrus/estrus; subsequent estrus usually normal.

PREGNANCY/FERTILITY/BREEDING

Ultrasound—conceptuses can first be detected 18–20 days after LH peak (requires high-resolution, high-frequency probe, easier in toy breeds) or 2–3 days earlier in cats; commonly done 4 weeks post breeding; recommend earlier exam in bitches with history of pregnancy loss or infertility.

SEE ALSO

- Infertility, Female—Dogs.
- Ovulatory Failure.
- Vaginal Discharge.
- Vaginal Malformations and Acquired Lesions.

ABBREVIATIONS

- AI = artificial insemination.
- D1 = first day of diestrus.
- GnRH = gonadotropin-releasing hormone.
- hCG = human chorionic gonadotropin.
- LH = luteinizing hormone.
- TCI = endoscopic transcervical insemination.

Suggested Reading

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BRONCHITIS, CHRONIC



BASICS

DEFINITION

- Chronic coughing for longer than 2 months that is not attributable to another cause (e.g., neoplasia, congestive heart failure, eosinophilic pneumonia, or infectious bronchitis).
- Partly nonreversible and often slowly progressive condition owing to accompanying pathologic airway changes.

PATHOPHYSIOLOGY

- Recurrent airway inflammation suspected, but a specific cause is rarely determined.
- Persistent tracheobronchial irritation—causes chronic coughing; leads to changes in tracheobronchial epithelium and submucosa.
- Airway inflammation, epithelial edema, and thickening—prominent.
- Excess production of thickened mucus is a hallmark.
- In severe, very chronic cases—probable increased lung resistance; decreased expiratory airflow, especially in cats; in dogs, possible sequelae such as broncholamacia and bronchiectasis.

SYSTEMS AFFECTED

- Respiratory
- Cardiovascular—pulmonary hypertension, cor pulmonale.
- Nervous—syncope (infrequent).

INCIDENCE/PREVALENCE

Common in dogs and cats.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dogs and cats.

Breed Predilections

- Dogs—small and toy breeds common; also observed in large breeds.
- Siamese cats and domestic shorthairs affected.

Mean Age and Range

Most often affects middle-aged and old animals.

Predominant Sex

N/A, although spayed females are often overrepresented (might be due to weight gain).

SIGNS

Historical Findings

- Coughing—hallmark of tracheobronchial irritation; usually harsh and dry; post-tussive gagging common (owners often misinterpret this as vomiting, especially in dogs).
- Exercise intolerance, difficult breathing, wheezing (in cats).
- Cyanosis and even syncope may be noted in severe cases.

Physical Examination Findings

- Patients usually bright, alert, and afebrile.
- Tracheal palpation—typically results in

coughing because of increased tracheal sensitivity.

- Small airway disease—assumed when expiratory abdominal push (during quiet breathing) or end-expiratory wheezing is detected.
- Bronchovesicular lung sounds, end-inspiratory crackles, and wheezing (result of airflow into obstructed airways) may be heard.
- Loud end-expiratory snap is suggestive of concurrent airway collapse.
- Cardiac auscultation—murmurs secondary to valvular insufficiency common in dogs, but not always associated with congestive heart failure; chronic bronchitis usually results in normal or slower than normal resting heart rate and pronounced sinus arrhythmia; in cats, tachycardia is possible.
- Obesity—common; important complicating factor.
- Severe dental disease may predispose to lower airway colonization and possible infection (dogs).

CAUSES

Chronic airway inflammation initiated by multiple causes, although specific cause rarely identified.

RISK FACTORS

- Long-term exposure to inhaled irritants.
- Obesity.
- Recurrent bacterial infection.
- Dental disease and laryngeal disease—result in bacterial showering of lower airways.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bronchiectasis.
- Eosinophilic bronchopneumopathy.
- Foreign bodies.
- Heartworm disease.
- Bacterial, pneumonia.
- Neoplasia—metastatic more than primary.
- Pulmonary parasites or parasitic larval migration.
- Pulmonary fibrosis—cats and dogs.
- Pulmonary granulomatosis.
- Congestive heart failure—typically associated with high resting heart rate and left atrial enlargement, which may lead to collapse of left principal bronchus.

CBC/BIOCHEMISTRY/URINALYSIS

- Rarely diagnostic.
- Neutrophilic leukocytosis common.
- Absolute eosinophilia—suggests but not diagnostic for allergic bronchitis.
- Polycythemia secondary to chronic hypoxia—may be seen.
- Liver enzymes and bile acids may be elevated due to passive congestion.

OTHER LABORATORY TESTS

- Fecal and heartworm tests—rule out pulmonary parasites.
- Pulse oximetry—useful for detecting hemoglobin desaturation.
- Arterial blood gas analysis—collect, ice, and have analyzed at a local hospital; mild to moderately low partial pressure of oxygen (PaO_2) seen with severe condition; aids in prognosis and monitoring treatment.
- As

hyperadrenocorticism could be responsible for obesity and/or enlarged liver/abdomen, testing should be considered if clinically indicated.

IMAGING

Thoracic Radiography (High Resolution Computed Tomography)

Common features (in descending order of frequency)—bronchial thickening; interstitial pattern; middle lung lobe consolidation (cats); atelectasis; hyperinflation and diaphragmatic flattening (primarily cats).

Echocardiography

- May reveal right heart enlargement with pulmonary hypertension.
- Helps rule out cardiac disease as a cause of coughing.
- Check for pulmonary hypertension via Doppler echocardiography.

DIAGNOSTIC PROCEDURES

Bronchoscopy

Preferred test for assessing the lower airways.

- Allows direct visualization of structural as well as functional (dynamic) changes; allows selected airway sampling (e.g., biopsy and lavage).
- Gross changes—excess mucoid to mucopurulent secretions; epithelial edema or thickening with blunting of bronchial bifurcations; irregular or granular mucosa; mucosal polypoid proliferations can indicate chronic bronchitis or chronic eosinophilic pneumonia.
- Large airway caliber changes (e.g., static or dynamic airway collapse and bronchiectasis)—may be detected as complicating problems.

Evaluation of Airway Secretions

- Must collect from lower airways—helps to establish underlying cause if present or to determine the severity of inflammation.
- Throat swab cultures are not representative of lower airway flora.
- Tracheal aspiration or bronchoalveolar lavage—collect specimens for cytologic examination and bacterial/mycoplasmal culture or qPRC assessment.
- Quantitated aerobic bronchoalveolar lavage (BAL) cultures help differentiate infection versus airway colonization; reported cutoff is $>1.7 \times 10^3$ colony-forming units (CFU) for infection in dogs. Anaerobic and *Mycoplasma* cultures recommended as well.
- Cytology—Inflammation primary finding; most cells are neutrophils, eosinophils, or macrophages; evaluate for bacteria, parasites, neoplastic cells, and contamination with foreign material.
- Recurrent infections—implicated in pathogenesis of bronchitis; however, positive cultures are not frequently reported; *Mycoplasma* infection discussed but rarely confirmed as a cause.

PATHOLOGIC FINDINGS

See Bronchoscopy under Diagnostic Procedures.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient—oxygen can be given at home in chronic cases.
- Inpatient—if requires oxygen therapy, parenteral medication, or aerosol therapy; patients that owners cannot keep calm at home during initial stages of therapy.

NURSING CARE

Consider saline nebulization followed by coughing and/or gentle exercise to encourage removal of airway secretions.

ACTIVITY

- Exercise—moderate (not forced) useful in clearing secretions; assists with weight loss.
- Limit if exertion causes excessive coughing.
- Use a harness instead of a collar.

DIET

Weight loss critical—improves PaO_2 , attitude, and exercise tolerance in obese patients; reduces cough frequency.

CLIENT EDUCATION

- Warn client that chronic bronchitis is an incurable disease and complete suppression of all coughing is an unattainable goal.
- Stress that aggressive treatment (including weight control, avoiding risk factors, and medical treatment) minimizes the severity of the coughing and slows disease progression in most patients.

SURGICAL CONSIDERATIONS

Treat severe dental disease to minimize secondary bacterial complications.



MEDICATIONS

DRUG(S) OF CHOICE

Corticosteroids

- Diminish airway inflammation and coughing regardless of the underlying cause.
- Indicated for noninfectious conditions.
- With allergic or hypersensitivity reactions—require long-term administration; attempt to wean off steroids or determine lowest effective dosage.
- Prednisolone preferred in cats.
- Prednisone or prednisolone usually initiated at 0.5–1 mg/kg PO q12h for a variable time, with tapering of the dosage based on clinical signs.
- Inhaled agents (e.g., budenoside or fluticasone 1–3 puffs using metered dose inhalers [variable concentrations exist] a day) are often effective and can be used to reduce systemic side effects of corticosteroids; they are delivered via a spacer chamber and face

mask (e.g., AeroDawg); however, the most adequate dose is not clearly established.

Bronchodilators

Commonly prescribed, although limited evidence of efficacy.

Antibiotics

- Select on basis of quantitated culture and sensitivity test results.

Antitussives

- Indicated for nonproductive, paroxysmal, continuous, or debilitating cough.
- Dogs—butorphanol (0.55 mg/kg PO q6–12h; 0.055–0.11 mg/kg SC); hydrocodone (0.1–0.3 mg/kg q6–8h PO). Over-the-counter cough suppressants are rarely effective; gabapentin 2–5 mg/kg by mouth every eight hours (but unestablished efficacy).

CONTRAINdications

Lasix and atropine—do not use because of drying effects on tracheobronchial secretions.

PRECAUTIONS

- Beta agonists (e.g., terbutaline and albuterol)—may cause tachycardia, nervousness, and muscle tremors; typically transient.
- Theophylline—may cause tachycardia, restlessness, excitability, vomiting, and diarrhea; evaluate ethylene diamine tetra-acetate (EDTA) plasma sample for peak plasma concentration (ideally 5–20 µg/mL); toxicity may be more common with generic formulations.

POSSIBLE INTERACTIONS

Fluoroquinolones decrease theophylline clearance in dogs and can result in theophylline toxicity.

ALTERNATIVE DRUG(S)

Maropitant (some antitussive properties suggested, but not advised yet).



FOLLOW-UP

PATIENT MONITORING

- Follow abnormalities revealed by physical examination and selected diagnostic tests—determine response to treatment.
- Monitor weight; arterial blood gases usually improve after significant weight loss.

PREVENTION/AVOIDANCE

Avoid and address risk factors (see Risk Factors).

POSSIBLE COMPLICATIONS

- Syncope—possible complication of chronic coughing, particularly in toy-breed dogs.
- Pulmonary hypertension and cor pulmonale—most serious

BRONCHITIS, CHRONIC

B

complications.

- Bronchiectasis and airway remodeling.

EXPECTED COURSE AND PROGNOSIS

- Progressive airway changes—syncope episodes, chronic hypoxia, right ventricular hypertrophy, and pulmonary hypertension.
- Acute exacerbations—common with seasonal changes, air quality changes, worsened inflammation, and potentially development of secondary infection.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Syncope—secondary to chronic coughing or development of pulmonary hypertension.
- Increased susceptibility to airway infection, chronic hypoxia, pulmonary hypertension, and cor pulmonale.

PREGNANCY/FERTILITY/BREEDING

Safety in pregnant animals not established for most of the recommended drugs.

SYNOMYS

Chronic bronchitis.

SEE ALSO

- Asthma, Bronchitis—Cats.
- Bronchiectasis.
- Cough.
- Hypoxemia.
- Tracheal Collapse.

ABBREVIATIONS

- BAL = bronchoalveolar lavage.
- CFU = colony-forming unit.
- EDTA = ethylene diamine tetra-acetate.
- PaO_2 = partial pressure of oxygen.

Suggested Reading

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Author Cécile Clercx

Consulting Editor Elizabeth Rozanski



Client Education Handout
available online

CAMPYLOBACTERIOSIS



BASICS

OVERVIEW

- Campylobacter jejuni*—fastidious, microaerophilic, Gram-negative curved bacteria; often isolated from healthy dogs and cats; may cause superficial erosive enterocolitis.
- Infection—fecal–oral route from contaminated food, water, raw meat (especially chicken), environment; localized in crypts of intestine; motile; produces multiple enterotoxins.
- Invasion of gut mucosa—hematochezia, inflammation, ulceration, edema; bacteria shed in feces for weeks to months.
- Up to 49% of dogs without diarrhea and 45% of normal cats carry *C. jejuni* and shed it in feces.

SIGNALMENT

- Dogs; less commonly cats.
- Prevalence—higher in puppies and kittens up to 6 months.
- Can cause chronic disease.

SIGNS

- Diarrhea—varies; mucoid and watery, hemorrhagic; may be chronic.
- Tenesmus.
- Fever, anorexia, intermittent vomiting possible.
- Adults—may be asymptomatic carriers.
- Abortion and perinatal death.

CAUSES & RISK FACTORS

- C. jejuni*, *C. coli*, *C. upsaliensis*, *C. helveticus*, *C. lari*, and more uncommon species.
- Kennels/intensive housing, poor sanitation/hygiene, fecal contamination in environment.
- Young animals—debilitated, immunosuppressed, parasitized.
- Nosocomial infection in hospitalized patients.
- Adults—concurrent intestinal infections (e.g., *Salmonella*, parvovirus, hookworms).
- Feeding homemade or commercially available raw meat-based diets.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial enterocolitis—*Salmonella*, *Yersinia enterocolitica*, *Clostridium difficile*, *Clostridium perfringens*.
- Parasitic—helminths (whipworms); protozoa (*Giardia*, *Isospora*).
- Viral—parvovirus; signs often more severe.
- Dietary indiscretion, intolerance.
- Drugs, toxins.
- Pancreatitis.
- Intussusception, other causes of abdominal pain.
- Distinguish from other causes of chronic diarrhea.
- Primary intestinal disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis—possible.
- Biochemistry abnormalities—effects of diarrhea, dehydration (e.g., azotemia, electrolyte disturbances).

DIAGNOSTIC PROCEDURES

- Fecal leukocytes—in gastrointestinal tract and stool.
- Fecal culture—submit feces in Amies transport medium with charcoal or Cary-Blair medium kept refrigerated at 4 °C in transit.
- Species-specific quantitative PCR—current methodology may be biased to detect *C. jejuni* and *C. coli*.

Direct Examination of Feces

- Gram stain—make smear; leave Gram safranin on for longer period.
- Wet mount—large numbers of highly motile bacteria (characteristic darting motility).

PATHOLOGIC FINDINGS

- Gross—diffuse colon thickening, congestion/edema; hyperemia of small intestine; enlarged mesenteric lymph nodes.
- Thickening of intestinal smooth muscle in cats.



TREATMENT

Mild Enterocolitis

- Outpatient.
- Usually self-limiting.

Severe Enterocolitis

- Inpatient, especially if very young, fever, hematochezia, melena.
- Severe neonatal disease—isolate; aggressive therapy.
- NPO for 24 hours; then bland diet.
- Mild dehydration—oral fluid therapy with enteric fluid replacement solution.
- Severe dehydration—intravenous fluid therapy with balanced isotonic replacement solution.
- Plasma transfusion may be required.
- Locally acting intestinal adsorbents/protectionants.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics—for systemic illness (e.g., high fever, dehydration), when diarrhea or abnormal clinical signs persist >7 days, in immune-suppressed patients.
- Erythromycin 10–20 mg/kg PO q8h for 5 days; drug of choice.
- Enrofloxacin—dog, 10 mg/kg PO/IV/IM q24h; cat, 5 mg/kg PO/IM/IV q24h.
- Tylosin 11 mg/kg PO q8h for 7 days.
- Septicemia—parenteral broad-spectrum antibiotics indicated.
- Multidrug resistance (vs. macrolides, quinolones) becoming more common.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Antidiarrheal drugs that reduce intestinal motility are contraindicated.
- Enrofloxacin—may induce arthropathy in dogs <28 weeks of age; caution with use in cats.



FOLLOW-UP

PATIENT MONITORING

Repeat fecal culture after treatment.

PREVENTION/AVOIDANCE

- Good hygiene (hand washing).
- Routinely clean and disinfect runs, food and water bowls.
- Do not feed raw-meat diets to companion animals.

EXPECTED COURSE AND PROGNOSIS

- Adults—usually self-limiting.
- Juveniles with severe or persistent enterocolitis—prognosis good with appropriate intervention.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Concurrent infection with other pathogenic bacteria, enteric parasites, viruses.

ZOONOTIC POTENTIAL

High (*C. jejuni*, *C. coli*, *C. upsaliensis*).

PREGNANCY/FERTILITY/BREEDING

Erythromycin—safe in early pregnancy.

INTERNET RESOURCES

<http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=campylobacteriosis&lang=en>

Suggested Reading

Acke E. Campylobacteriosis in dogs and cats: a review. N Z Vet J 2018; 66:221–228.

Marks SL, Rankin SC, Byrne BA, et al.

Enteropathogenic bacteria in dogs and cats: diagnosis, epidemiology, treatment, and control. J Vet Intern Med 2011; 25:1195–1208.

Montgomery MP, Robertson S, Koski L, et al. MDR Campylobacter jejuni outbreak linked to puppy exposure. MMWR Morb Mortal Wkly Rep. 2018; 67:1032–1035.

Author Patrick L. McDonough

Consulting Editor Amie Koenig



BASICS

OVERVIEW

- *Candida*—dimorphic fungus with the yeast phase (*Candida* spp.) being part of the normal flora of the mouth, nose, ears, and gastrointestinal (GI) and urogenital tracts of dogs and cats.
- *C. albicans* and *C. parapsilosis* most commonly cultured from clinically healthy dogs.
- Recovery from mucosal surfaces does not imply disease; organisms may cause opportunistic infection, colonize damaged tissues, or invade normal tissues of immunosuppressed animals.
- Pathogenic role determined by infiltration of organisms into tissues, or detection of organisms in presumed sterile sites (e.g., urinary bladder, peritoneal cavity).
- Organ systems most affected include GI, renal/urologic, skin, and respiratory.
- Conditions that suppress the immune system (e.g., feline immunodeficiency virus [FIV] infection) increase the likelihood of isolation in asymptomatic animals.

SIGNALMENT

Cats and dogs—any age and breed.

SIGNS

- Nonhealing ulcers in the oral, upper respiratory, GI, or urogenital mucosa—signs reflect location/extent of disease:
 - Cystitis—hematuria, stranguria, and pollakiuria.
 - Otitis—head shaking, scratching.
 - Oral cavity—drooling.
- Inflammation around IV catheters or gastrostomy tubes.
- Ulcerative, red skin lesions.
- Systemic disease with fever, cardiac and/or neurologic abnormalities can be seen.

CAUSES & RISK FACTORS

- Infection—rare; associated with neutropenia, parvovirus or FIV infection, endocrinopathies, glucocorticoid therapy, gastrostomy tubes, indwelling urinary catheters/urethrostomy, IV catheters, and incomplete bladder emptying.
- Lower urinary tract disease may predispose to candiduria.
- Administration of antibiotics in prior 30 days.
- Occasionally local or systemic infection is seen in animals without predisposing conditions.
- Skin damaged by burns, trauma, or necrotizing dermatitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Considered whenever the primary condition does not respond as expected.

CBC/BIOCHEMISTRY/URINALYSIS

- Reflect underlying inflammation and organ involvement (unless neutropenic).
- Urinalysis—may show yeast or clumps of mycelial elements (pseudohyphae) with inflammatory cells; concurrent bacterial urinary tract infection common.

OTHER LABORATORY TESTS

- Cytology—spherical to oval yeast cells 5–7 µm in diameter; pseudohyphae and septate hyphae 3–5 µm wide.
- Culture—grows well on blood agar and often is isolated from specimens submitted for bacterial culture; more easily isolated from urine than blood.
- PCR and antigen tests available.

DIAGNOSTIC PROCEDURES

- Lesions—to determine if *Candida* is truly a pathogen, requires demonstration of organisms penetrating the tissues.
- Urine sample—cystocentesis; culture of multiple colonies of *Candida* supports diagnosis.
- Otitis (dogs)—culture of *Candida* spp. or identification of yeast or mycelial elements on ear cytology suggests diagnosis.
- In febrile patients, culture catheter tips.

PATHOLOGIC FINDINGS

- White caseous foci in the infected tissue.
- Large numbers of both yeast and pseudo-hyphae in tissues surrounded by necrosis and suppurative inflammatory reaction.
- May be pyogranulomatous in more chronic infections.



TREATMENT

- Treat underlying causes of immunosuppression.
- Remove indwelling catheters, if possible.



MEDICATIONS

DRUG(S) OF CHOICE

- Topical therapy (mucosal lesions)—nystatin or amphotericin B.

- Fluconazole—5 mg/kg PO q12h; very effective and excreted unchanged in urine (high concentration in commonly infected sites).

- Itraconazole—5–10 mg/kg PO q12h; effective, can use if organism resistant to fluconazole; not recommended for urinary tract infection (poor urinary excretion).
- In lower urinary tract *Candida* infections resistant to fluconazole—infuse 10–30 mL of 1% clotrimazole into the bladder every other day for three treatments.
- *Candida* may develop drug resistance—consider drug sensitivity testing if suspected.
- Caspofungin—may be option for resistant isolates.



FOLLOW-UP

PATIENT MONITORING

- Fluconazole and itraconazole—hepatotoxicity; monitor serum alanine aminotransferase (ALT) activity monthly initially and check if patient becomes anorexic.
- After signs have resolved—reculture sites of infection; continue treatment for 2 weeks beyond negative culture; repeat cultures 2 weeks after completion of treatment and again if signs recur.

EXPECTED COURSE AND PROGNOSIS

- Should resolve within 2–4 weeks of treatment with correction of immunosuppression.
- Control of the underlying disease is necessary to prevent recurrence.
- May resolve spontaneously if the underlying condition is corrected.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Genetic similarities between human and animal isolates suggest a potential for transfer of *C. albicans* between species.

ABBREVIATIONS

- ALT = alanine aminotransferase.
- FIV = feline immunodeficiency virus.
- GI = gastrointestinal.

Suggested Reading

Reagan KL, Dear JD, Kass PH, et al. Risk factors for *Candida* urinary tract infections in dogs and cats. J Vet Intern Med 2019, 33:648–653.

Author Daniel S. Foy

Consulting Editor Amie Koenig

C CANINE CORONAVIRUS INFECTIONS



BASICS

OVERVIEW

- Canine enteric coronavirus (CCoV)—sporadic outbreaks of enteritis in dogs; worldwide distribution.
- Canine pantropic coronavirus (CPCoV)—variant of CCoV, fatal disease in dogs <6 months, described principally in Europe.
- CCoV, CPCoV—closely related to feline infectious peritonitis (FIP) virus, feline enteric coronavirus.
- Canine respiratory coronavirus (CRCoV)—associated with canine infectious respiratory disease complex (kennel cough); worldwide distribution; genetically and serologically distinct from CCoV.
- Incubation period 1–3 days.
- CCoV infection—usually inapparent; mild to severe enteritis possible; death reported in young pups; infects upper two-thirds of small intestine and associated lymph nodes; crypt cells spared.
- Simultaneous infection with canine parvovirus (CPV)-2 possible; severe, often fatal.
- CPCoV—infests intestinal tract, after short viremia distributes to organs like spleen, lungs, brain.
- Coronaviruses undergo rapid evolution, are highly variable; differences in virulence likely between isolates.

SIGNALMENT

- Dogs of all ages, breeds; disease more severe in young.
- CRCoV infections more common in winter, in shelters.

SIGNS

- Vary greatly—CPCoV virulent isolates cause systemic disease.
- Adults—most infections inapparent.
- Puppies—mild to severe, occasionally fatal, enteritis.
- Diarrhea—may be explosive; yellow-green or orange; loose or liquid; typically malodorous (characteristic); may persist for days to >3 weeks; may recur; young dogs may suffer severe, protracted diarrhea, dehydration.
- Vomiting.
- Coughing, dyspnea—CRCoV associated with kennel cough complex.
- Anorexia, lethargy.
- For CPCoV—pyrexia, anorexia, depression, vomiting, hemorrhagic enteritis, respiratory distress, and leukopenia that persists >1 week; ataxia, seizures, and death also possible.

CAUSES & RISK FACTORS

- Stress—greatest risk; sporadic outbreaks have occurred in dogs attending shows, in kennels where new dogs frequently introduced; crowding and unsanitary conditions promote illness.
- For CCoV, CPCoV—feces primary source of infection; virus shed for 2 weeks.

- For CRCoV—respiratory secretions, fomites likely sources of infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infections caused by enteric bacteria, protozoa, other viruses; canine kennel cough complex pathogens.
- Other mild to moderate upper respiratory disease.
- Food intoxication or intolerance.

CBC/BIOCHEMISTRY/URINALYSIS

Normal; lymphopenia with more virulent CCoV isolates.

OTHER LABORATORY TESTS

Serologic tests—available; not standardized, difficult to interpret due to frequent asymptomatic infection.

DIAGNOSTIC PROCEDURES

- Viral isolation for CCoV, CRCoV—possible but not recommended.
- Specific reverse transcriptase polymerase chain reaction (RT-PCR)—using feces for CCoV, respiratory swabs for CRCoV; CPCoV defined by presence of virus in extraintestinal organs.
- Immunofluorescence of small intestine—fatal cases; may show viral antigen in cells lining villous epithelium.

PATHOLOGIC FINDINGS

- Gross—dilated small intestine filled with gas, watery green-yellow material.
- Bowel loops congested, hemorrhagic; mesenteric lymph nodes enlarged, edematous.
- Histopathology—atrophy and fusion of intestinal villi, deepening of crypts, increased cellularity of lamina propria, epithelial cell flattening, increased goblet cells.
- CPCoV—hemorrhagic lesions in various organs (lungs, small intestines, spleen, lymph nodes).



TREATMENT

- Most dogs recover without treatment.
- CCoV—fluid, electrolyte treatment if dehydration severe.
- CRCoV—as for canine kennel cough complex.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics—not usually indicated, except with enteritis, sepsis, severe respiratory illness.



FOLLOW-UP

PREVENTION/AVOIDANCE

- CCoV vaccines—controversial; inactivated and live viral vaccines; appear safe; moderate efficacy may be due to variability of CCoV strains; not recommended; do not cross-protect against CPCoV, CRCoV.
- Strict quarantine, sanitation essential in kennels: susceptible to common disinfectants.
- CCoV, CRCoV—highly contagious; spread rapidly.

POSSIBLE COMPLICATIONS

Diarrhea with CCoV—may persist 10–12 days, may recur.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—good, except severe infections of young pups.
- Majority recover after short illness.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Concurrent infection with CPV or other agent.
- Infections with other respiratory pathogens with CRCoV.

ABBREVIATIONS

- CCoV = canine enteric coronavirus.
- CPCoV = canine pantropic coronavirus.
- CPV = canine parvovirus.
- CRCoV = canine respiratory coronavirus.
- FIP = feline infectious peritonitis.
- RT-PCR = reverse transcriptase polymerase chain reaction.

Suggested Reading

Decaro N, Cordonnier N, Demeter Z, et al. European surveillance for pantropic canine coronavirus. J Clin Microbiol 2013, 51:83–88.

Mitchell JA, Cardwell JM, Leach H. European surveillance of emerging pathogens associated with canine infectious respiratory disease. Vet Microbiol 2017, 212:31–38.

Author Sophie Le Poder

Consulting Editor Amie Koenig

Acknowledgment The author and book editors acknowledge the prior contribution of John S. Parker.

CANINE DISTEMPER

C



BASICS

DEFINITION

- Acute to subacute, contagious, febrile, often fatal disease with respiratory, urogenital, gastrointestinal, ocular, and CNS manifestations.
- Caused by canine distemper virus (CDV), a *Morbillivirus* in the *Paramyxoviridae* family.
- Affects many Carnivora species; mortality rate varies greatly.

PATHOPHYSIOLOGY

- Natural route of infection—airborne and droplet exposure; from nasal cavity, pharynx, and lungs, virus replication occurs in local lymph nodes; within 1 week, viral shedding occurs (mainly in respiratory exudates but also urine) and virtually all lymphatic tissues become infected; spreads via viremia to surface epithelium of respiratory, gastrointestinal, and urogenital tracts and to CNS.
- Disease progression depends on virus strain and host immune response:
 - Strong cellular and humoral immune response—subclinical infection.
 - Weak immune response—subacute infection; longer survival.
 - Failed immune response—death within 2–4 weeks after infection; frequently due to CNS manifestations.
- Viral excretion can occur for up to 2–3 months.

SYSTEMS AFFECTED

- Multisystemic—all lymphatic tissues, surface epithelium in respiratory, alimentary, and urogenital tracts, skin, endocrine and exocrine glands.
- CNS—brain and/or spinal cord.

INCIDENCE/PREVALENCE

- Dogs—sporadic outbreaks.
- Wildlife (raccoons, skunks, fox, tigers)—fairly common.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Most species of the order Carnivora; has been reported in large exotic cats.

Mean Age and Range

Young, especially unvaccinated animals are most susceptible.

SIGNS

- Fever—intermittent peaks starting 3–6 days after infection.
- Gastrointestinal and/or respiratory signs—nasal and ocular discharge, depression, anorexia, vomiting, diarrhea; often exacerbated by secondary bacterial infection.
- CNS—common; generally after systemic disease (depends on virus strain).

◦ Gray matter disease—affects cerebral cortex, brainstem, and spinal cord and may cause a nonsuppurative meningitis, seizures, mentation change, and ataxia; dogs may die in 2–3 weeks; some dogs recover (associated with prompt humoral and cell-mediated immunity), others develop white matter disease.

◦ White matter disease—multifocal disease, commonly cerebellovestibular signs, paresis, ataxia, occasionally myoclonus; some dogs die 4–5 weeks after initial infection with noninflammatory, demyelinating disease; some dogs may recover with minimal CNS injury.

• Optic neuritis and retinal lesions may occur; anterior uveitis, keratoconjunctivitis sicca possible.

• Hardening of footpads (hyperkeratosis) and nose—some virus strains; uncommon.

• Enamel hypoplasia of teeth after neonatal infection.

CAUSES

- CDV exposure.
- Incompletely attenuated vaccines (rare).

RISK FACTORS

Contact of nonimmunized animals with CDV-infected animals (dogs, wild carnivores).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Diagnosis based on clinical suspicion; combination of respiratory and gastrointestinal, ± CNS disease, in unvaccinated dog.
- Respiratory signs—can mimic kennel cough.
- Enteric signs—differentiate from canine parvovirus, coronavirus, parasitism (giardiasis), bacterial infections, gastroenteritis from toxin ingestion, inflammatory bowel disease.
- CNS form—differentiate from autoimmune meningoencephalitis (granulomatous meningoencephalomyelitis, necrotizing encephalitis, meningoencephalitis of unknown etiology), protozoal (e.g., toxoplasmosis, neosporosis), fungal (e.g., cryptococcosis), and rickettsial (e.g., ehrlichiosis, Rocky Mountain spotted fever) meningoencephalitis, rabies.

CBC/BIOCHEMISTRY/URINALYSIS

Lymphopenia in early infection; rare thrombocytopenia; intracytoplasmic inclusions in white and red blood cells.

OTHER LABORATORY TESTS

- Serology—positive antibody tests do *not* differentiate between vaccination and exposure to virulent virus; patient may die from acute disease before neutralizing antibody is produced. Immunoglobulin (Ig) M responses may occur up to 3 months after exposure to virulent virus, up to 3 weeks after vaccination; rising IgG titers in unvaccinated

dog are suggestive of infection; may be useful for risk assessment of clinically healthy dogs in shelter environment.

- CDV antibody in cerebrospinal fluid (CSF)—indicative of distemper encephalitis, false negatives possible.

IMAGING

- Radiographs—evaluate pulmonary disease.
- CT and MRI—may or may not show lesions; MRI sensitive for demyelination.

DIAGNOSTIC PROCEDURES

- Immunohistochemical detection in haired skin, nasal mucosa, and footpad epithelium.
- Viral antigen or viral inclusions—in buffy coat cells, urine sediment, conjunctival or vaginal imprints, trans-tracheal wash (negative results do not rule out CDV).
- Reverse transcriptase polymerase chain reaction (RT-PCR)—on buffy coat, urine sediment cells, respiratory secretions, conjunctival swabs, CSF; false negatives possible, false positives with recent vaccination (uncommon).
- CSF—moderate mononuclear pleocytosis, elevated concentrations of CDV-specific antibody, interferon, and viral antigen early in disease course.

PATHOLOGIC FINDINGS

Gross

- Thymus—greatly reduced in size (young animals); sometimes gelatinous.
- Lungs—patchy consolidation.
- Footpads, nose—hyperkeratosis.
- Mucopurulent discharges—from eyes and nose, bronchopneumonia, catarrhal enteritis, skin pustules (secondary bacterial infection).

Histologic

- Intracytoplasmic eosinophilic inclusion bodies—in epithelium of bronchi, stomach, urinary bladder; also in reticulum cells and leukocytes in lymphatic tissues.
- Inclusion bodies in glial cells and neurons—frequently intranuclear; also in cytoplasm.
- Immunofluorescence and/or immunocytochemistry, virus isolation, and/or RT-PCR performed on tissues from lungs, stomach, urinary bladder, lymph nodes, brain.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient medical management to intensive care as indicated; isolate patient to prevent spread to other dogs.

NURSING CARE

- Symptomatic.
- IV fluids—for hypovolemia, support.
- Oxygen therapy, nebulization, and coupage—for pneumonia.
- Clean ocular, nasal discharges.

C CANINE DISTEMPER

C

ACTIVITY

Limited, to reduce spread.

DIET

Depends on extent of gastrointestinal involvement.

CLIENT EDUCATION

- Inform client that mortality rate is about 50%.
- Inform client that dogs appearing to recover from early catarrhal signs may develop fatal CNS disease.
- Presenting neurologic abnormalities usually not reversible.



MEDICATIONS

DRUG(S) OF CHOICE

- Antiviral drugs—none known to be effective.
- Broad-spectrum antibiotics—for secondary bacterial infection (CDV is immunosuppressive), beta-lactams or cephalosporins are good initial choices.
- Anticonvulsant therapy—phenobarbital, potassium bromide, levetiracetam.
- Myoclonus—no proven treatment; single case report describes use of botulinum toxin type A.

CONTRAINDICATIONS

Corticosteroids—use anti-inflammatory dosages with caution; may provide short-term control. Immunosuppressive dosages may enhance viral dissemination.

PRECAUTIONS

Tetracycline, fluoroquinolones—avoid in growing animals.



FOLLOW-UP

PATIENT MONITORING

- Monitor for CNS abnormalities, particularly seizures.
- Monitor for respiratory distress or dehydration in acute phase.

PREVENTION/AVOIDANCE

- Vaccination.
- Isolate puppies to prevent infection from wildlife (e.g., raccoons, foxes, skunks), CDV-infected dogs, ferrets.
- Recovered dogs may shed virus for up to 4 months; isolate for this time period or until multiple negative RT-PCR tests.

Vaccines

- Duration of immunity from most vaccines is >3 years.

- Modified live vaccine for CDV (MLV-CD)—prevents infection and disease; two types available:

- Canine tissue culture-adapted vaccines (e.g., Rockborn strain)—induce complete immunity in virtually 100% of susceptible dogs; rarely, a postvaccinal fatal encephalitis develops 7–14 days after vaccination, especially in immunosuppressed animals.
 - Chick embryo-adapted vaccines (e.g., Lederle strain)—safer; postvaccinal encephalitis does not occur; only about 80% of susceptible dogs seroconvert.
 - Other species—chick embryo can safely be used in variety of wildlife species (e.g., gray fox); Rockborn type fatal in these animals.
- Killed vaccines—useful for species in which either type of MLV-CD is fatal (e.g., red panda, blackfooted ferret).
 - Canarypox recombinant CDV vaccine.

Maternal Antibody

- Important.
- Most puppies lose protection from maternal antibody at 6–12 weeks of age; 2–3 vaccinations should be given during this period.
- Heterotypic (measles virus) vaccination—recommended for puppies that have maternal antibody; induces protection from disease but not from infection.

POSSIBLE COMPLICATIONS

Possibility of CNS signs developing for 2–3 months after catarrhal signs have subsided.

EXPECTED COURSE

AND PROGNOSIS

- Depends on strain and individual host response—subclinical, acute, subacute, fatal, or nonfatal infection.
- Mild CNS signs—patient may recover; myoclonus may continue for several months or indefinitely.
- Death—2 weeks to 3 months after infection; mortality rate ~50%.
- Euthanasia—owner may elect if or when neurologic signs develop; indicated if uncontrollable seizures occur.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Persistent or latent *Toxoplasma gondii* infections—may be reactivated due to immunosuppressive state.
- Respiratory infections with *Bordetella bronchiseptica* (kennel cough).

AGE-RELATED FACTORS

- Young puppies—more susceptible; mortality rate is higher.
- Nonimmunized old dogs—highly susceptible to infection and disease.

ZOONOTIC POTENTIAL

Possible that humans may become subclinically infected with CDV; immunization against measles virus also protects against CDV infection.

PREGNANCY/FERTILITY/BREEDING

In utero infection—occurs in antibody-negative bitches; rare; may lead to abortion or to persistent infection; infected neonates may develop fatal disease by 4–6 weeks of age.

SYNONYMS

- Canine distemper.
- Hard pad disease.

SEE ALSO

Myoclonus

ABBREVIATIONS

- CDV = canine distemper virus.
- CSF = cerebrospinal fluid.
- Ig = immunoglobulin.
- MLV-CD = modified live virus of canine distemper.
- RT-PCR = reverse transcriptase polymerase chain reaction.

INTERNET RESOURCES

<https://www.uwsheltermedicine.com/library/resources/canine-distemper-cdv>

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Loots AK, Mitchell E, Dalton DL, et al. Advances in canine distemper virus pathogenesis research: a wildlife perspective. *J Gen Virol* 2017, 98:311–321.

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Acknowledgment The author and book editors acknowledge the prior contribution of Stephen C. Barr.



Client Education Handout
available online

CANINE INFECTIOUS DIARRHEA

C



BASICS

DEFINITION

- Viral, enteropathogenic bacterial, protozoal, or parasitic etiologies; small, large, or mixed-bowel diarrhea.
- Secondary systemic signs with canine parvovirus (CPV)-2 and salmonellosis.
- Presence of organisms on diagnostic screening does not indicate causation; patient factors (clinical signs, age, environmental exposure) should be considered before treatment.
- Some dogs will have self-resolution; diagnostic testing appropriate for more severely affected animals or if clinical signs are persistent having ruled out other causes of acute or chronic diarrhea.
- Puppies with acute diarrhea should be screened for CPV-2.

PATHOPHYSIOLOGY

- Typically, fecal-oral route of infection.
- Diarrhea from enterotoxins, osmotic diarrhea, or invasion of epithelium resulting in inflammation.
- Up to 50% of dogs may have coinfections.

SYSTEMS AFFECTED

- Gastrointestinal (GI)—vomiting, diarrhea.
- Cardiovascular—fluid balance.

INCIDENCE/PREVALENCE

- Prevalence of most pathogens similar in dogs with or without diarrhea.
 - Coronaviruses more common in dogs with diarrhea.
 - Dogs with diarrhea more likely to have >1 enteropathogen.
- Specific prevalence in dogs in United States:
 - 0–6%—CPV-2, *Salmonella* spp., *Cystoisospora* spp., *Dipylidium caninum*, *Campylobacter* spp., *C. difficile* toxin A and B, ascarids.
 - 7–20%—whipworms, *Giardia* spp., *Cryptosporidium*, circovirus.
 - 35–60%—*C. perfringens* enterotoxin A or alpha toxin gene, hookworm.

GEOGRAPHIC DISTRIBUTION

- Widespread.
- Prevalence of etiologies varies by location.

SIGNALMENT

- Species—dog.
- Breed predilections—none.
- Mean age and range—largely pediatric and young adult dogs; older animals if in high-risk environments.

SIGNS

- General comments—range from mild to severely affected.
- Historical findings—acute or chronic, small or large bowel diarrhea; possibly vomiting, weight

loss, hyporexia; no history of dietary indiscretion.

- Physical examination findings—depends on etiology and severity; may include dehydration, poor body condition, borborygmus, flatulence, hematochezia, melena, visualization of worms on rectal exam or peri-anal, signs of sepsis or systemic inflammatory response syndrome (SIRS).

CAUSES

- Viral—coronavirus, CPV-2, circovirus.
- Bacterial—*Campylobacter* spp., *Clostridium perfringens* enterotoxin, *Clostridium difficile* toxins, *Salmonella* spp.
- Parasitic—*Toxocara* spp., *Ancylostoma* spp., *Toxascaris leonine*, *Dipylidium caninum*, *Trichuris vulpis*.
- Protozoal—*Giardia* spp.
- Coccidian—*Cryptosporidium* spp., *Cystoisospora* spp.

RISK FACTORS

- Pediatric and young adult dogs more commonly affected, particularly for viral enteritis, *Cryptosporidium* spp., roundworm (*Toxocara* and *Toxascaris*), *Cystoisospora* spp., and *Campylobacter* spp.
- Administration of antimicrobials and immunosuppressive drugs increase risk for hospital-associated colonization of *C. difficile*.
- Crowding and poor sanitation.
- Lack of regular parasiticide administration.
- Dogs with environmental exposure to livestock or wildlife for *Cryptosporidium* spp., *Campylobacter* spp., *Giardia* spp.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute diarrhea—dietary indiscretion, foreign body, pancreatitis, GI neoplasia; non-GI diseases: hepatotoxicity, renal disease, other systemic diseases (commonly other clinical signs such as hyporexia, vomiting, icterus).
- Chronic diarrhea—chronic enteropathy (dietary responsive, antibiotic responsive, or inflammatory bowel disease), chronic pancreatitis, primary GI neoplasia, and non-GI diseases of other organs.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia—possible with intestinal parasitism.
- Anemia and/or microcytosis—GI hemorrhage or iron deficiency, particularly with high worm burden (e.g., *T. vulpis*) or GI mucosal shedding (e.g., CPV).
- Leukopenia—parvoviral enteritis (bacterial translocation or bone marrow suppression) or systemic salmonellosis.
- Hyponatremia and hyperkalemia with large bowel diarrhea—*T. vulpis*.
- Azotemia and electrolyte derangements with dehydration.

- Hypoglycemia—parvoviral enteritis and systemic salmonellosis.
- Panhypoproteinemia and hypocholesterolemia if secondary protein-losing enteropathy or GI blood loss.

IMAGING

- Abdominal radiographs if no response to symptomatic care to rule out other causes of diarrhea.
- Abdominal ultrasound recommended in nonpediatric patients with diarrhea that is nonresponsive to symptomatic care.

DIAGNOSTIC PROCEDURES

- Fecal flotation—for intestinal parasitism; false negatives possible (ova are intermittently shed); dogs suspected to have intestinal parasitism should have multiple fecal flotations performed or be treated with anthelmintics.
- Fecal cytology—bacterial morphology (frequent spirochetes, spores) or presence of fungal or protozoal organisms.
- *Giardia* ELISA.
- Infectious diarrhea PCR panels detect a range of possible causes of diarrhea; however, caution should be used in interpretation of these assays, as a positive result does not necessarily indicate causation and false-negative results are possible.

PATHOLOGIC FINDINGS

- Gross examination of intestinal mucosa may demonstrate parasites attached to intestinal mucosa with multifocal hemorrhagic ulcerations, submucosal congestion or hemorrhage, intestinal wall thickening.
- Histopathology of intestine may show eosinophilic, neutrophilic, or lymphoplasmacytic enteritis with varying degrees of hemorrhage and necrosis, depending on etiology.



TREATMENT

APPROPRIATE HEALTH CARE

- Mildly affected dogs—outpatient basis.
- Moderate to severely affected dogs may require IV administration of isotonic balanced electrolyte solution for dehydration.
- Electrolyte and acid-base imbalances should be corrected with fluid therapy and monitored closely.
- Dextrose should be supplemented parenterally in dogs with hypoglycemia.
- Packed red blood cell or plasma transfusions should be given as needed for severe anemia or coagulopathies from sepsis (rare).

DIET

- Easily digestible diets until clinical signs have resolved, followed by slow transition (3–4 days) to maintenance diet.
- In anorexic pediatric patients, nasogastric tube feeding of liquid diet recommended if anorexia persists ≥48 hours.

C CANINE INFECTIOUS DIARRHEA

(CONTINUED)

C

CLIENT EDUCATION

- For most infectious organisms, environmental decontamination prevents transmission to other pets/people and reinfection; isolation during hospitalization may be warranted depending on underlying cause.
- Appropriate vaccination and deworming schedules should be followed.
- Dogs with identified infectious causes of diarrhea should be isolated from other dogs if possible until clinical signs resolve.

SURGICAL CONSIDERATIONS

Viral and parasitic enterocolitis can result in intussusceptions, especially in puppies.



MEDICATIONS

DRUG(S) OF CHOICE

- Many cases will self-resolve with supportive care and time.
- Empiric therapy pending diagnostics, if clinical signs persist—probiotics, or metronidazole (10 mg/kg PO q12h) and fenbendazole (50 mg/kg PO q24h for 5 days).
- Anthelmintics—fenbendazole (50 mg/kg PO q24h for 5 days), pyrantel pamoate (5–10 mg/kg PO for 3 days).
- Coccidiostatic—sulfadimethoxine (50–60 mg/kg PO q24h for 5–10 days), ponazuril (50 mg/kg PO once).
- Antiprotozoal drugs—fenbendazole (50 mg/kg PO q24h for 5 days).
- Campylobacteriosis with persistent clinical signs—erythromycin (10–15 mg/kg PO q8h) or azithromycin (5–10 mg/kg PO q24h).
- Probiotics may be of benefit for dogs with bacterial enteritis with acute or chronic signs; probiotics should be selected with evidence of efficacy (e.g., Visbiome®).
- Patients with systemic illness, leukopenia, or suspected GI mucosal barrier breakdown (evidenced by blood in the feces) should be treated with broad-spectrum antimicrobial agents and as indicated by specific etiology.
- Dogs with confirmed salmonella should *not* be treated with antibiotics unless systemically ill.

PRECAUTIONS

Metronidazole dose should be reduced in animals with hepatic insufficiency.

POSSIBLE INTERACTIONS

- Metronidazole given at higher doses for giardiasis or long-term use can lead to vestibular signs.
- Some dogs may be sensitive to sulf-containing medications used for treatment of coccidiosis.



FOLLOW-UP

PATIENT MONITORING

- Case-based, may include reassessment of anemia, leukopenia, or electrolyte derangements as appropriate.
- Persistent clinical signs after appropriate treatment is suggestive for alternative cause of diarrhea.
- Patients with recurrent clinical signs should be retested, particularly if environmental reinfection is possible (e.g., giardiasis, campylobacteriosis).

PREVENTION/AVOIDANCE

- Routine vaccination.
- Monthly flea/tick or heartworm preventative with combination anthelmintic therapy.
- Avoid subjecting poorly vaccinated or immunocompromised animals to high-traffic areas, including but not limited to pet supply stores, dog parks, or newly introduced poorly vaccinated pets.

POSSIBLE COMPLICATIONS

- Sepsis.
- Anemia.
- Electrolyte disturbances.
- Aspiration pneumonia if concurrent vomiting (uncommon).

EXPECTED COURSE AND PROGNOSIS

- Usually good to excellent; underlying immunosuppressive conditions may increase susceptibility to infection and worsen prognosis.
- Parvoviral enteritis carries guarded to poor prognosis without treatment; appropriate supportive care provides full recovery rates of 90% or more.



MISCELLANEOUS

AGE-RELATED FACTORS

Puppies and young dogs affected.

ZOONOTIC POTENTIAL

- Giardiasis—low risk of transmission.
- Cryptosporidiosis.
- Salmonellosis.
- Campylobacter jejuni*.
- Toxocara* spp. (ascarids)—visceral larval migrans in humans, most common in children.
- Ancylostoma* (hookworms)—cutaneous larval migrans in humans, most common in children.

PREGNANCY/FERTILITY/BREEDING

If heavy endoparasite load, fenbendazole can be administered to pregnant bitches from 14th day of gestation through to 14th day of lactation. If risk of infection is high, all puppies (and mothers) should be treated with appropriate anthelmintics at 2, 4, 6, and 8 weeks of age.

SEE ALSO

- Acute Diarrhea.
- Campylobacteriosis.
- Canine Coronavirus Infections.
- Canine Parvovirus.
- Clostridial Enterotoxicosis.
- Coccidiosis.
- Diarrhea, Chronic—Dogs.
- Giardiasis.
- Hookworms (Ancylostomiasis).
- Roundworms (Ascariasis).
- Salmonellosis.
- Whipworms (Trichuriasis).

ABBREVIATIONS

- CPV-2 = canine parvovirus.
- GI = gastrointestinal.
- SIRS = systemic inflammatory response syndrome.

Suggested Reading

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CANINE INFECTIOUS RESPIRATORY DISEASE



BASICS

DEFINITION

A multifaceted disease whereby infectious disease and environment contribute to the genesis of cough and other respiratory signs in dogs.

PATHOPHYSIOLOGY

Initiated by injury to the respiratory epithelium by viral infection followed by invasion of damaged tissue by bacterial, mycoplasmal, or other virulent organisms, resulting in further damage and clinical signs.

SYSTEMS AFFECTED

Respiratory—upper and lower airways can be involved. Multisystemic—cases that develop sepsis.

GENETICS

None

INCIDENCE/PREVALENCE

Most common in areas of high density with immunologically naïve or immunosuppressed patients (i.e., training kennels, shelters, veterinary hospitals).

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predilections

None

Mean Age and Range

- Most severe in puppies 6 weeks–6 months old.
- Can develop in dogs of all ages, particularly with preexisting airway disease.

Predominant Sex

None

SIGNS

General Comments

- Related to the degree of respiratory tract damage and age of the affected dog and virulence of infectious organism.
- Can be subclinical, mild, or severe with pneumonia.
- Most viral, bacterial, and mycoplasmal agents spread rapidly from seemingly healthy dogs to others in the same environment; signs usually begin about 3–7 days after exposure to the infecting agent(s).

Historical Findings

- Uncomplicated—acute-onset cough in an otherwise healthy animal; dry and hacking, soft and dry, moist and hacking, or paroxysmal, followed by gagging, retching, and expectoration of mucus; excitement, exercise, and pressure on the trachea induce coughing spells.
- Complicated (severe)—inappetence to anorexia; cough is moist and productive; lethargy, difficulty breathing, hemoptysis, and exercise intolerance can occur.

Physical Examination Findings

- Uncomplicated—cough readily induced with minimal tracheal pressure; lung sounds often normal; systemically healthy.
- Complicated—low-grade or intermittent fever (39.4–40.0 °C; 103–104 °F); increased intensity of normal lung sounds, crackles or wheezes possible.

CAUSES

- Viral—canine distemper virus (CDV); canine adenovirus (CAV-2); canine parainfluenza (CPIV); canine respiratory coronavirus (CRCoV), canine reovirus; canine herpesvirus-1 (CHV-1); canine influenza virus (CIV; H3N8 or H3N2); canine bocavirus, canine hepacivirus; canine pneumovirus (CnPV). • Most viral pathogens (except CHV and CDV) primarily infect epithelial and lymphoid tissue of the upper and lower respiratory tract; in severe cases, causing desquamation of the epithelium and aggregation of inflammatory cells in the lungs, leading to secondary bacterial colonization and infection; CRCoV infection leads to loss of cilia associated with the respiratory epithelium, increasing the severity and duration of secondary infections.
- Bacterial—*Bordetella bronchiseptica*, with no other respiratory pathogens, produces clinical signs indistinguishable from those of other bacterial causes; *Streptococcus equi* subsp. *zooepidemicus* is associated with a particularly virulent course that can progress to death; *Pseudomonas*, *Escherichia coli*, *Klebsiella*, *Pasteurella*, *Streptococcus*, *Mycoplasma*, and other species equally likely.

RISK FACTORS

- Substandard hygienic conditions and overcrowding—encountered in some pet shops, shelters, research facilities, and boarding and training kennels.
- Coexisting subclinical airway disease—congenital anomalies; chronic bronchitis; bronchiectasis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- In systemically well dogs—parasitic bronchitis, irritant tracheobronchitis, airway foreign body, airway collapse.
- In a dog with systemic signs—fungal or bacterial (aspiration) pneumonia, primary or metastatic neoplasia, congestive heart failure, migrating foreign body.
- Provisional diagnosis of infectious tracheobronchitis is made in a dog with compelling clinical signs and a history of exposure to the implicated organisms.
- See Cough.

CBC/BIOCHEMISTRY/URINALYSIS

- Early, mild leukopenia (5,000–6,000 cells/dL)—can be detected; suggests viral cause.
- Neutrophilic leukocytosis with a toxic left shift—frequently found with severe pneumonia.

OTHER LABORATORY TESTS

Pulse oximetry and arterial blood gas analysis—can reveal hypoxemia in pneumonia.

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IMAGING

- Uncomplicated disease—radiographs: unremarkable; most useful for ruling out other differential diagnoses.
- Complicated disease—radiographs: interstitial and alveolar lung pattern with a cranoventral distribution typical of bacterial pneumonia; can see diffuse interstitial lung pattern typical of viral pneumonia; mixed lung pattern can be present.

DIAGNOSTIC PROCEDURES

- In cases with severe disease—ideally perform bronchoalveolar lavage via bronchoscopy for cytology and microbial culture; tracheal wash sample acceptable, but increased likelihood for upper airway contamination.
- Antimicrobial sensitivity pattern of cultured bacteria—identification aids markedly in providing an effective treatment plan.
- PCR from bronchoalveolar lavage, nasal, ocular, or pharyngeal secretions can be used to detect virus, though there is difficulty in interpreting results as many healthy animals shed virus in the absence of clinical signs.

PATHOLOGIC FINDINGS

- CPIV—causes few to no clinical signs; lungs of infected dogs 6–10 days after exposure may contain petechial hemorrhages that are evenly distributed over the surfaces; detected by immunofluorescence in columnar epithelial cells of the bronchi and bronchioles 6–10 days after aerosol exposure.
- CAV-2—lesions confined to the respiratory system; large intranuclear inclusion bodies found in bronchial epithelial cells and alveolar septal cells; clinical signs tend to be mild and short-lasting; lesions persist for at least a month after infection.
- CIV (H3N8, H3N2)—fulminant disease characterized by secondary *Mycoplasma* or bacterial infection and pulmonary hemorrhage.
- CRCoV—characterized by marked inflammation of the trachea and nares with cilia loss in the former; detected by immunohistochemistry of the trachea or bronchioles.
- *Streptococcus equi* subsp. *zooepidemicus* infection—acute, fibrinosuppurative pneumonia with large numbers of cocci found within the pulmonary parenchyma and, often, septic thromboemboli.
- Bordetellosis and severe bacterial infection—evidence of purulent bronchitis, tracheitis, and rhinitis with hyperemia and enlargement of the bronchial, mediastinal, and retropharyngeal lymph nodes; may see large numbers of Gram-positive or Gram-negative organisms in the mucus of the tracheal and bronchial epithelium.

C CANINE INFECTIOUS RESPIRATORY DISEASE

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—strongly recommended for uncomplicated disease.
- Inpatient—strongly recommended for complicated disease and/or pneumonia.

NURSING CARE

Fluid administration—indicated for complicated disease and/or pneumonia.

ACTIVITY

Enforced rest—14–21 days with uncomplicated disease; for at least the duration of radiographic evidence of pneumonia in severely affected dogs.

DIET

Good-quality commercial food.

CLIENT EDUCATION

- Isolate patient from other animals; infected dogs can transmit the agent(s) before onset of clinical signs and afterward until immunity develops.
- Dogs with uncomplicated disease should respond to treatment in 10–14 days.
- Once infection spreads in a kennel, it can be controlled by evacuation for 1–2 weeks and disinfection with commonly used chemicals, such as sodium hypochlorite (1 : 30 dilution), chlorhexidine, and benzalkonium.



MEDICATIONS

DRUG(S) OF CHOICE

- Amoxicillin/clavulanic acid (12.5–25 mg/kg PO q12h) or doxycycline (5 mg/kg PO q12h or 10 mg/kg PO q24h)—initial treatment of uncomplicated disease.
- Penicillin (ampicillin 10–20 mg/kg IV q6–8h or ticarcillin 40–50 mg/kg IV q6–8h) with aminoglycoside (gentamicin 2–4 mg/kg IV/IM/SC q6–8h or amikacin 6.5 mg/kg IV/IM/SC q8h) or fluoroquinolone (enrofloxacin 5–10 mg/kg PO/IM/IV q24h)—usually effective for severe disease.
- Antimicrobial therapy—continue for at least 10 days beyond radiographic resolution.
- *B. bronchiseptica* and other resistant species—some antimicrobials may not reach adequate therapeutic concentrations in the lumen of the lower respiratory tract, so oral or parenteral administration may have limited effectiveness; nebulization with gentamicin (3–5 mg/kg) can decrease bacterial numbers when administered daily for 3–5 days; use in conjunction with systemic antibiotics in dogs with parenchymal disease.
- Butorphanol (0.55 mg/kg PO q8–12h) or hydrocodone bitartrate (0.22 mg/kg PO q6–8h)—effective suppression of dry, nonproductive cough not associated with bacterial infection.
- Bronchodilators (e.g., terbutaline 0.625–5 mg/dog q8–12h)—may be used to control bronchospasm and wheeze.

CONTRAINDICATIONS

- Do not use cough suppressants in patients with pneumonia.
- Employ glucocorticoids only in cases with significant inflammatory disease refractory to conventional supportive care.

PRECAUTIONS

None

POSSIBLE INTERACTIONS

Fluoroquinolones and theophylline derivatives—concurrent use causes high and possibly toxic plasma theophylline concentration. Dose reduce theophylline while concurrently administering fluoroquinolones.

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Uncomplicated disease—should resolve spontaneously or respond to treatment in 10–14 days; if patient continues to cough 14 days or more after establishment of an adequate treatment plan, question the diagnosis of uncomplicated disease.
- Complicated disease—repeat thoracic radiography until at least 7 days beyond resolution of all clinical signs.

PREVENTION/AVOIDANCE

Shedding of the causative agent(s) of infectious respiratory disease in airway secretions of dogs undoubtedly accounts for the persistence of this problem in kennels, animal shelters, boarding facilities, and veterinary hospitals.

Viral and Bacterial Vaccines

- Modified live CDV and CAV-2 vaccines provide reliable protection and are considered core vaccines for all puppies; can be administered at 6 weeks of age, every 2–4 weeks.
- *B. bronchiseptica* and CPIV vaccine—can vaccinate puppies mucosally or intranasally as early as 2–4 weeks of age without interference from maternal antibody and follow with annual revaccination; can vaccinate mature dogs with a one-dose intranasal vaccination (at the same time as their puppies or when they receive their annual vaccinations).
- Inactivated *B. bronchiseptica* parenteral vaccine—administered as two doses, 2–4 weeks apart; initial vaccination of puppies is recommended at or about 6–8 weeks of age; revaccinate at 4 months of age.
- Inactivated CIV vaccines (H3N2 and H3N8) available to reduce severity and duration of clinical signs but considered noncore; can be administered starting at 6 weeks as two doses, 2–4 weeks apart; results in seroconversion.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Natural course of uncomplicated disease, if untreated—10–14 days; simple restriction of exercise and prevention of excitement

shortens the course.

- Typical course of severe disease—2–6 weeks; patients that die often develop severe pneumonia that affects multiple lung lobes and multiple organ dysfunction due to sepsis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

May accompany other respiratory tract anomalies.

AGE-RELATED FACTORS

Most severe in puppies 6 weeks–6 months old and in puppies from commercial pet shops and humane society shelters.

ZOONOTIC POTENTIAL

Potential zoonotic risk of *Streptococcus equi* subsp. *zooepidemicus* and *B. bronchiseptica* reported in single case reports.

PREGNANCY/FERTILITY/BREEDING

High risk in dogs on extensive medical treatment; especially risky for dogs in overcrowded breeding facilities.

SYNONYMS

- Kennel cough.
- Infectious tracheobronchitis—uncomplicated disease.

ABBREVIATIONS

- CAV-2 = canine adenovirus.
- CDV = canine distemper virus.
- CHV-1 = canine herpesvirus-1.
- CIV = canine influenza virus.
- CnPnV = canine pneumovirus.
- CPIV = canine parainfluenza.
- CRCoV = canine respiratory coronavirus.

INTERNET RESOURCES

<https://www.cdc.gov/flu/other/canine-flu>

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Client Education Handout
available online

CANINE PARVOVIRUS

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BASICS

DEFINITION

- An acute systemic illness characterized by vomiting, hemorrhagic enteritis, and leukopenia.
- Myocardial form was observed in puppies in late 1970s, now rare.
- Most puppies protected against neonatal infection by maternal antibodies.
- Monoclonal antibodies have revealed antigenic changes in canine parvovirus (CPV)-2; CPV2a, b, and c strains have been identified.
- Original virus now virtually extinct in domestic dogs.
- CPV2c viruses are more virulent, and mortality rates higher.
- CPV-2 is closely related to feline panleukopenia virus (FPV).

PATHOPHYSIOLOGY

- Parvoviruses require actively dividing cells for growth.
- After ingestion of virus there is a 2–4-day period of viremia.
- Early lymphatic infection is accompanied by lymphopenia and precedes intestinal infection and clinical signs.
- By postinfection (PI) day 3, rapidly dividing crypt cells of small intestine are infected.
- Viral shedding in feces starts ~3–4 days PI, peaks with clinical signs.
- Virus ceases to be shed in detectable amounts by PI days 8–12.
- Absorption of bacterial endotoxins from damaged intestinal mucosa plays a role in CPV-2 disease.
- Intensity of illness related to viral dose and antigenic type.

SYSTEMS AFFECTED

- Cardiovascular—myocarditis (uncommon), hypovolemia.
- Gastrointestinal.
- Hemic/lymphatic/immune.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Common in breeding kennels, animal shelters, pet stores.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predilections

- Certain breeds are at increased risk, including Rottweiler, Doberman pinscher, American pit bull terrier, Labrador retriever, German shepherd dog, and Yorkshire terrier.

- Higher fatality rates are seen in hounds, gundogs, and nonsporting pedigree groups.

Mean Age and Range

- Illness occurs at any age.
- Most severe in dogs 6–24 weeks of age.

Predominant Sex

None

SIGNS

General Comments

Suspect CPV-2 infection whenever puppies have an enteric illness.

Historical Findings

- Sudden onset of bloody diarrhea, anorexia, and vomiting.
- Some dogs may collapse in a shock-like state and die without enteric signs.
- In breeding kennels, several littermates may become ill simultaneously or within a short period.
- Occasionally, one or two puppies in a litter have minimal signs, followed by death of littermates, which may reflect degree of virus exposure.

Physical Examination Findings

- Hypovolemic shock—weak pulse, tachycardia, dull mentation.
- Severe hemorrhagic diarrhea.
- Fluid-filled intestinal loops may be palpated.
- Dehydration, weight loss, abdominal discomfort.
- May have fever or hypothermia.

CAUSES

CPV-2.

RISK FACTORS

- Unvaccinated dogs.
- Dogs <4 months of age.
- Co-pathogens such as parasites, viruses, and certain bacterial species (e.g., *Campylobacter* spp., *Clostridium* spp.) may exacerbate illness.
- Severe, often fatal parvoviral infections have been demonstrated in puppies exposed simultaneously to CPV-2 and canine coronavirus.
- Crowding and poor sanitation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine coronavirus infection.
- Salmonellosis; colibacillosis; other enteric bacterial infections.
- Gastrointestinal foreign bodies.
- Gastrointestinal parasites.
- Acute hemorrhagic diarrhea syndrome (previously hemorrhagic gastroenteritis).
- Intussusception (may be concurrent).
- Toxin ingestion.

CBC/BIOCHEMISTRY/URINALYSIS

- Lymphopenia—characteristic; commonly occurs PI days 4–6.

- Severely affected dogs exhibit severe neutropenia with onset of intestinal damage.
- Leukocytosis during recovery.
- Serum chemistry profiles help assess electrolyte disturbances (especially hypokalemia), presence of azotemia, panhypoproteinemia, hypoglycemia.

OTHER LABORATORY TESTS

- Virus antigen detection in stool at onset of disease and for 2–4 days afterward; many commercial point-of-care ELISA assays available, also PCR and quantitative PCR methodologies.
- Serologic tests are not diagnostic because dogs often have high titers from vaccination and/or maternal antibodies.

IMAGING

- Abdominal radiographs—generalized small intestinal ileus; exercise caution to prevent misdiagnosis of intestinal obstruction, but intussusception may cause obstructive pattern.
- Abdominal ultrasound—fluid-filled, atonic small and large intestines, duodenal and jejunal mucosal layer thinning with or without indistinct wall layers and irregular luminal-mucosal surfaces, extensive duodenal and/or jejunal hyperechoic mucosal speckling, and duodenal and/or jejunal corrugations; intussusceptions can be identified.

DIAGNOSTIC PROCEDURES

- Electron microscopy detects fecal virus during early stages of infection.
- Samples for virus detection should be submitted during acute phase of infection; ship specimens refrigerated, not frozen.

PATHOLOGIC FINDINGS

- Gross changes include subserosal congestion and hemorrhage or frank hemorrhage into small intestinal lumen, or intestines that are empty or contain yellow or blood-tinged fluid.
- Mesenteric lymph nodes often enlarged and edematous, with hemorrhages in cortex.
- Thymic atrophy in young dogs.
- Pulmonary edema and hydropericardium may be only gross change in dogs with myocarditis and heart failure.
- Histopathology reveals intestinal inflammation and necrosis, with severe villus atrophy.



TREATMENT

APPROPRIATE HEALTH CARE

- Symptomatic and supportive (see Acute Vomiting; Acute Diarrhea; Gastroenteritis, Acute Hemorrhagic Diarrhea Syndrome), including IV fluids, antibiotics, antiemetics, and analgesics.
- Intensity depends on severity of signs; both in- and outpatient treatment protocols exist.

C CANINE PARVOVIRUS

- Goals are to provide intestinal nutrients, restore and maintain fluid and electrolyte balance, and resolve shock, sepsis, and endotoxemia.
- Fecal microbiota transplant may speed resolution of diarrhea.
- Prompt, intensive inpatient care leads to treatment success.
- Proper, strict isolation procedures are essential.
- Exercise care to prevent spread of CPV-2, a very stable virus.
- Antiviral drugs have not yet been shown to be a critical part of treatment.

NURSING CARE

- Hospitalize patients and monitor for dehydration and electrolyte imbalance.
- Fluids are usually supplemented with potassium chloride, 5% dextrose, and possibly sodium bicarbonate (if severe metabolic acidosis due to bicarbonate loss).

ACTIVITY

Restrict until symptoms abate.

DIET

Puppies receiving early enteral nutrition via a nasoesophageal tube (compared to puppies that received nothing enterally until cessation of vomiting) showed earlier clinical improvement, significant weight gain, and improved gut barrier function, which could limit bacterial or endotoxin translocation.

CLIENT EDUCATION

- Inform about need for thorough disinfection, especially if other dogs are on premises; strict sanitation is essential; a 1 : 30 dilution of bleach (5% sodium hypochlorite) destroys CPV-2 in a few minutes.
- If possible, isolate puppies until they reach 3 months of age and vaccinate repeatedly; typical protocols involve vaccination at 6, 9, and 12 weeks of age.
- Puppies can be infected with virulent virus before any vaccine will confer immunity.
- CPV-2 is shed for less than 2 weeks after infection; no carrier state has been substantiated.

SURGICAL CONSIDERATIONS

- Exercise caution to prevent misdiagnosis of intestinal obstruction, especially if vomiting is only clinical sign.
- Intussusceptions can occur.



MEDICATIONS

See Acute Vomiting; Acute Diarrhea; Gastroenteritis, Acute Hemorrhagic Diarrhea Syndrome.

DRUG(S) OF CHOICE

Additional recommended drugs include parenteral antibiotics (ampicillin and gentamicin) and antiemetics (e.g., ondansetron, maropitant).

PRECAUTIONS

Gentamicin may cause renal toxicity in dehydrated puppies.



FOLLOW-UP

PATIENT MONITORING

There is an increased incidence of discospondylitis in puppies that had parvovirus infection.

PREVENTION/AVOIDANCE

- Inactivated and live vaccines are available for prophylaxis, and vaccines differ in their capacity to immunize puppies with maternal antibodies.
- Vaccination with a modified live vaccine at 4 weeks of age in puppies with high maternally derived antibody concentrations resulted in seroconversion rates of up to 80%; this may lead to a decreased window of susceptibility to CPV infection and might be an adjunct control method in contaminated environments.
- Control of CPV-2 requires efficacious vaccines, isolation of puppies, and stringent hygiene.

POSSIBLE COMPLICATIONS

- Septicemia/endotoxemia.
- Bacterial pneumonia.
- Intussusception.
- Discospondylitis.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is guarded in severely affected puppies.
- Prognosis is good for dogs that receive prompt initial treatment and survive initial crisis—approximately 80% survival rate.
- Poor prognosis if a patient is purebred, has a low bodyweight, and if the following biomarker levels are present after 24 hours of intensive therapy: severe persistent leuko- and lymphopenia, persistently elevated or rising serum cortisol concentration ($>8.1 \mu\text{g}/\text{dL}$), severe hypothyroxinemia ($<0.2 \mu\text{g}/\text{dL}$), hypocholesterolemia ($<100 \text{ mg}/\text{dL}$), and persistently elevated serum C-reactive protein ($>97.3 \text{ mg/L}$).
- Conversely, puppies with a good prognosis are of mixed breed, >6 months old, and show the following biomarker values: total leukocyte count $>4.5 \times 10^3/\mu\text{L}$, lymphocyte count $>1 \times 10^3/\mu\text{L}$, and mature neutrophil count $>3 \times 10^3/\mu\text{L}$. Additionally, a serum cortisol concentration $<8.1 \mu\text{g}/\text{dL}$ at 48 hours after

admission is associated with 96% survival, and a serum thyroxine concentration $>0.2 \mu\text{g}/\text{dL}$ at 24 hours after admission is associated with 100% survival. An HDL-cholesterol concentration $>50.2 \text{ mg}/\text{dL}$ at admission is associated with 100% survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Coinfection with intestinal helminths and *Giardia* are indicative of unhygienic housing conditions and can worsen clinical signs and contribute to morbidity.

AGE-RELATED FACTORS

Infection less likely in dogs >1 year of age, but can still occur, especially if unvaccinated.

ZOONOTIC POTENTIAL

Parvovirus per se is not zoonotic, but these puppies may harbor coinfections with *Giardia*, which can be zoonotic.

PREGNANCY/FERTILITY/BREEDING

Pregnant animals are likely to abort.

SEE ALSO

- Acute Diarrhea.
- Acute Vomiting.
- Canine Coronavirus Infections.
- Gastroenteritis, Acute Hemorrhagic Diarrhea Syndrome.
- Sepsis and Bacteremia.
- Shock, Septic.

ABBREVIATIONS

- CPV = canine parvovirus.
- FPV = feline panleukopenia virus.
- PI = postinfection.

Suggested Reading

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Author Johan P. Schoeman

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Client Education Handout
available online

(CONTINUED)

CARDIOMYOPATHY, ARRHYTHMOGENIC RIGHT VENTRICULAR—CATS

C



BASICS

OVERVIEW

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a rare primary cardiomyopathy characterized by progressive atrophy of the right ventricular (RV) and/or right atrial (RA) myocardium, with replacement by fatty or fibrofatty tissue that may act as an arrhythmogenic substrate. The condition in cats typically manifests as signs of right-sided congestive heart failure (CHF) due to progressive RV dysfunction. A variety of arrhythmias have been observed in cats with ARVC; however, sudden death does not appear to be well recognized in this species.

SIGNALMENT

- Cats.
- One study reported mean age at presentation of 7.3 years (range: 1–20 years).
- Breed or sex predilections unknown.

SIGNS

General Comments

Compared to dogs and humans, sudden death does not appear to be as well recognized in cats with ARVC, despite the wide variety of arrhythmias documented with this condition.

Historical Findings

- Lethargy.
- Anorexia.
- Dyspnea.
- Tachypnea.
- Abdominal distention may be noted.

Physical Examination Findings

- Signs consistent with right-sided CHF.
- Dyspnea.
- Tachypnea.
- Jugular venous distention.
- Ascites.
- Heart and/or lung sounds may be muffled.
- Weak femoral pulses.
- Hepatosplenomegaly.
- Thoracic percussion may reveal presence of pleural effusion.
- May auscult arrhythmia.

CAUSES & RISK FACTORS

- Unknown.
- A genetic mutation in the striatin (desmosomal protein) gene is associated with ARVC in some dogs. Genetic mutations are identified in approximately 60% of humans with ARVC, with mutations identified in at least 13 genes. Genetic studies in feline ARVC are lacking.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Uhl's anomaly—a congenital abnormality characterized by partial or complete

absence of myocardium in the RV free wall. Histopathology is required to distinguish this from ARVC and demonstrates apposing endocardial and epicardial surfaces, without any interposed adipose tissue or any evidence of inflammation or necrosis.

CBC/BIOCHEMISTRY/URINALYSIS

Alanine aminotransferase may be elevated secondary to hepatic congestion.

IMAGING

Radiographic Findings

- Cardiomegaly, typically in regions of right atrium and right ventricle; left atrial enlargement may also be noted.
- Pleural effusion.
- Ascites.
- Pericardial effusion.
- Caudal vena caval dilation.

Echocardiographic Findings

- Severe RA and RV dilation.
- RV systolic dysfunction/hypokinesis.
- Tricuspid regurgitation.
- Paradoxical septal motion.
- Focal aneurysms may be observed in the RV wall, often toward the apex.
- Left atrial enlargement sometimes seen.

DIAGNOSTIC PROCEDURES

ECG

- A variety of various arrhythmias have been observed in cats with ARVC.
- Ventricular premature complexes (right-sided or left-sided in origin).
- Ventricular tachycardia.
- Atrial fibrillation.
- Supraventricular tachycardia.
- Ventricular premature complexes.
- Right bundle branch block.
- First-degree atrioventricular block.
- Third-degree atrioventricular block.
- RA and RV enlargement (tall P wave, deep S waves in lead II), right axis deviation.

Paracentesis and Fluid Analysis

Fluid analysis of pleural or abdominal effusions typically reveals modified transudate consistent with right-sided CHF.

PATHOLOGIC FINDINGS

Gross Pathology

- Moderate-to-severe RA and RV dilation.
- Severe thinning of RA and RV walls, which are easily trans-illuminated.
- Left atrial dilation and rarely left ventricular dilation may be seen in some cats.
- Thrombi sometimes identified.

Histopathology

- RV myocardial atrophy with replacement by fatty or fibrofatty tissue.
- Fibrosis may also be observed in right atrium, left ventricular free wall, and interventricular septum.

- Focal or multifocal myocarditis.
- Apoptotic cardiomyocytes.



TREATMENT

- Medical management of right-sided CHF is the mainstay of treatment for clinically affected cats with ARVC.
- Anti-arrhythmic therapy is not routinely required, but in cases with hemodynamically significant arrhythmias, anti-arrhythmic drugs should be selected based on the suspected underlying mechanism of the arrhythmia.



MEDICATIONS

See Congestive Heart Failure, Right-Sided.



FOLLOW-UP

PATIENT MONITORING

Recheck when decompensation or other clinical signs develop.

EXPECTED COURSE AND PROGNOSIS

Prognosis appears to be very poor in cats identified with ARVC. Reported median survival time after development of clinical signs of approximately 1 month (range: 2 days to 4 months). Most cats die or are euthanized due to signs of right-sided CHF or thromboembolic complications.



MISCELLANEOUS

SEE ALSO

- Cardiomyopathy, Arrhythmogenic Right Ventricular—Dogs.
- Congestive Heart Failure, Right-Sided.

ABBREVIATIONS

- ARVC = arrhythmogenic right ventricular cardiomyopathy.
- CHF = congestive heart failure.
- RA = right atrial.
- RV = right ventricular.

SUGGESTED READING

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Spontaneously occurring arrhythmogenic right ventricular cardiomyopathy in the domestic cat: a new animal model similar to the human disease. *Circulation* 2000, 102(15):1863–1870.

Author Michael Aherne

Consulting Editor Michael Aherne

CARDIOMYOPATHY, ARRHYTHMOGENIC RIGHT VENTRICULAR—DOGS



BASICS

OVERVIEW

A myocardial disease commonly characterized by ventricular tachyarrhythmias that can be accompanied by syncope or sudden death. A small percentage (<5%) develop congestive heart failure with systolic dysfunction, comparable to the dilated cardiomyopathy observed in other breeds.

SIGNALMENT

- Dog.
- Specific to the boxer, although a similar presentation is infrequently observed in the English bulldog.
- Usually observed in mature dogs between 5 and 8 years of age. Dogs as young as 6 months have been reported and some affected dogs may not develop clinical signs until >10 years of age.

SIGNS

- Usually one of three presentations:
 - Asymptomatic dog with ventricular premature complexes (VPCs) detected on routine examination.
 - Syncope with VPCs detected on ECG or Holter monitor.
 - Signs of left heart failure (e.g., tachypnea, coughing) or biventricular failure (e.g., ascites, tachypnea, coughing) with VPCs; this presentation is least common.
- Sudden death may occur before development of obvious clinical signs.

CAUSES & RISK FACTORS

- Adult onset, inherited (autosomal dominant).
- A genetic mutation (deletion) in a cardiac desmosomal gene (striatin) is associated with the development of the disease. Dogs that are homozygous for the striatin deletion appear to be more likely to be more severely affected with a higher number of VPCs, and are more likely to have cardiac dilation and myocardial dysfunction. Sudden death is more common. It is not yet known if this is the only genetic cause or if additional genetic mutations will be identified.
- At least one family of boxers with VPCs, ventricular dilation, and systolic dysfunction was found to have decreased myocardial l-carnitine levels and demonstrated some clinical improvement when supplemented with l-carnitine. The cause and effect of this relationship is unclear, and response to this supplementation does not occur in all dogs with myocardial dysfunction.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Aortic stenosis—moderate and severe forms can be associated with VPCs.

- Uncommon forms of acquired cardiac disease (neoplasia, endocarditis).
- Abdominal disease (especially splenic disease) can be associated with VPCs.
- Echocardiography and abdominal ultrasonography can be used to differentiate other causes of cardiac and abdominal disease.

OTHER LABORATORY TESTS

- Genetic testing can now be performed to screen for the genetic mutation (<https://cvm.ncsu.edu/genetics>) associated with arrhythmic right ventricular cardiomyopathy. Submission samples can be either a blood sample in an EDTA tube or a buccal swab of the oral mucosal surface.
- Plasma l-carnitine levels may be evaluated in boxers with ventricular dilation and systolic dysfunction. However, plasma levels are not always reflective of myocardial levels. If plasma levels are not low, it is still possible to have low myocardial levels, and supplementation with l-carnitine might be considered.

IMAGING

Thoracic Radiography

- Normal in most affected dogs.
- Dogs with ventricular dilation and systolic dysfunction may have cardiac enlargement and evidence of heart failure (e.g., pulmonary edema).

Echocardiography

- Normal in most affected dogs.
- A small percentage of dogs have ventricular dilation and systolic dysfunction, particularly if they are homozygous for the deletion mutation.

DIAGNOSTIC PROCEDURES

ECG

- Many dogs will not have VPCs on an ECG of brief duration since the arrhythmia can be intermittent. However, some dogs will have one or more upright VPCs on a brief lead II ECG.
- In either case, if suspicion of disease is present, Holter monitoring is recommended to determine the severity and complexity of the arrhythmia and to have a baseline for comparison once treatment is started. If Holter monitoring is not available and the dog is symptomatic with upright VPCs on an ECG, therapy should be considered.

PATHOLOGIC FINDINGS

- Gross pathology is nonspecific in most cases. In a small percentage of cases, left and right ventricular dilation may be observed.
- Histopathologic abnormalities include a fatty and fibrous infiltrate into the right ventricular (and sometimes interventricular and left ventricular) free wall.



TREATMENT

- The goals of therapy include reduction of the number of VPCs, reduction of clinical signs, and reduction of the risk of sudden cardiac death. Unfortunately, there is no evidence that therapy can reduce the risk of sudden death. The decision to start therapy in the asymptomatic boxer with VPCs is controversial, since all antiarrhythmics have the potential to make the arrhythmia worse. However, dogs with as few as 300 VPCs/24 hours have been observed to die suddenly. In general, initiate antiarrhythmic drugs if there are >1,000 VPCs/24 hours and/or significant runs of ventricular tachycardia or other signs of arrhythmia complexity (e.g., bigeminy, couplets), or clinical signs (syncope, exercise intolerance) related to the VPCs.
- Syncope and sudden cardiac death may be more frequently associated with stress and excitement. Reduce stress and effort when possible. There is no direct relationship between exercise restriction and survivability. Some dogs die while asleep. Thus, strict exercise restriction is not recommended.



MEDICATIONS

DRUG(S) OF CHOICE

- The two best choices for treating the ventricular arrhythmia are sotalol (1.5–2.0 mg/kg PO q12h) or mexiletine (5–6 mg/kg PO q8h). Some cases continue to have significant ventricular ectopy after treatment with one of these; such cases seem to respond well to the combination of sotalol and mexiletine. These drugs have different mechanisms and appear to work in a safe and complementary fashion.
- In dogs with systolic dysfunction and heart failure, consider treatment with furosemide, enalapril, pimobendan, spironolactone, and l-carnitine.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Any antiarrhythmic drug has the potential to make an arrhythmia worse.



FOLLOW-UP

- If possible, repeat the Holter monitor 2–3 weeks after starting therapy to evaluate for a response. Affected dogs can have an 85% day-to-day variability in VPC number before medications; therefore, a good response to therapy would be an 85% reduction in VPC number. It is also anticipated that the complexity of the arrhythmia (bigeminy,

C CARDIOMYOPATHY, ARRHYTHMOGENIC RIGHT VENTRICULAR—DOGS (CONTINUED)

trigeminy, couplets, triplets, runs of ventricular tachycardia) will be reduced once on therapy. It may not always be possible to achieve an 85% reduction in VPC number; in those cases an improvement in arrhythmia complexity and clinical signs would be reasonable goals.

- Annual Holter monitoring and echocardiography are suggested, since in some cases the disease can be progressive.
- Advise owners that dogs are always at risk of sudden death. However, the majority of affected dogs can be maintained on antiarrhythmic

ics for years with good quality of life. Dogs with systolic dysfunction and dilation have the worst prognosis, although some of these dogs do show improvement and a decreased rate of progression on l-carnitine supplementation.

**MISCELLANEOUS****SYNOMYS**

Boxer cardiomyopathy.

SEE ALSO

- Ventricular Premature Complexes.
- Ventricular Tachycardia.

ABBREVIATIONS

- VPC = ventricular premature complex.

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CARDIOMYOPATHY, DILATED—CATS



BASICS

DEFINITION

- Dilated cardiomyopathy (DCM) is a disease of the heart muscle characterized by systolic myocardial failure and a dilated, volume-overloaded heart that leads to signs of congestive heart failure (CHF) or low cardiac output.
- Before 1987, DCM was the second most commonly diagnosed heart disease in cats. Most cats had a secondary DCM as a result of taurine deficiency. Primary idiopathic DCM is now an uncommon cause of heart disease in cats.

PATOPHYSIOLOGY

- Histopathologically, the myocardium of cats with idiopathic DCM has evidence of myocytolysis, fibrosis, myofibril fragmentation, and vacuolization. Gross examination reveals global eccentric enlargement of all four cardiac chambers.
- These anatomic changes are associated with progressive myocardial systolic failure, decreased contractility, decreased compliance, and secondary mitral valve regurgitation due to mitral valve annular dilation. These changes are typically identified by echocardiography.
- Eventually, the chronic myocardial dysfunction leads to CHF and clinical signs.

SYSTEMS AFFECTED

- Cardiovascular**—DCM is a primary myocardial disease and primarily affects the heart and its ability to maintain an adequate cardiac output to maintain the body's needs.
- Musculoskeletal**—cats with DCM can present with aortic thromboembolism (ATE), which causes acute paraparesis or monoparesis.
- Renal/urologic**—cats with DCM and CHF often have poor renal perfusion and commonly have prerenal azotemia.
- Respiratory**—cats usually present with tachypnea or dyspnea due to CHF with DCM. These cats can develop both pulmonary edema and pleural effusion.

GENETICS

Because of the human experience with DCM, it is likely that feline DCM also has a genetic basis, either inherited or de novo, as the cause of the disease. No definitive mutation has been identified in the cat to date; however, a quantitative genetic evaluation of a large cattery suggested an inherited factor in the development of DCM.

INCIDENCE/PREVALENCE

Idiopathic feline DCM is relatively uncommon now that taurine is adequately supplemented in cat foods. A retrospective survey of 106 cats with feline myocardial disease from 1994 to 2001 from Europe revealed that DCM was diagnosed in approximately 10% of the cases

in this series. In the author's experience, the prevalence of feline idiopathic DCM may be less than 10%.

SIGNALMENT

Species

Cat

Breed Predilections

Because the prevalence is low, breed predilections are not clearly defined. That said, the Burmese cat may have an increased incidence.

Mean Age and Range

9 years (5–13 years).

Predominant Sex

None. (One study cites a male predisposition, while another states a female overrepresentation.)

SIGNS

General Comments

- Cats with idiopathic DCM usually present for signs of CHF.
- They are rarely diagnosed prior to onset of clinical signs.

Historical Findings

- Signs related to low cardiac output—anorexia, weakness, depression.
- Signs related to CHF—dyspnea, tachypnea.
- Signs related to ATE—sudden-onset pain and paraparesis.

Physical Examination Findings

- Heart rate can be fast, normal, or slow.
- Soft systolic heart murmur.
- Weak left cardiac impulse.
- Gallop sound.
- Possible arrhythmia.
- Hypothermia.
- Prolonged capillary refill time.
- Tachypnea.
- Quiet lung sounds (pleural effusion).
- Crackles (pulmonary edema).
- Ascites.
- Hypokinetic femoral pulses.
- Possibly, posterior paresis and pain as a result of ATE.

CAUSES

The underlying etiology of idiopathic DCM remains unknown, although a genetic predisposition has been identified in some families of cats. Taurine deficiency was a common cause of secondary myocardial failure before 1987.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Taurine deficiency DCM; because primary idiopathic DCM and taurine deficiency have similar clinical presentations, cats with myocardial failure should be assumed to have

taurine deficiency until shown to be unresponsive to taurine.

- Myocardial failure secondary to long-standing congenital or acquired left ventricular volume overload diseases.
- End-staged remodeled hypertrophic cardiomyopathy may manifest with a dilated hypocontractile heart.
- Arrhythmogenic right ventricular cardiomyopathy.

CBC/BIOCHEMISTRY/URINALYSIS

Many cats will have prerenal azotemia related to low cardiac output.

OTHER LABORATORY TESTS

- Ensure that thyroid concentrations are normal.
- Plasma taurine concentrations less than 40 nmol/L or whole blood taurine concentrations less than 250 nmol/L, are subnormal and suggestive of taurine deficiency DCM. Taurine assays are performed at a limited number of institutions and require special handling.
- Cardiac biomarkers such as plasma amine terminal B-type natriuretic peptide (NT-proBNP) and cardiac troponin I (cTnI) concentrations would be elevated in a cat with CHF due to idiopathic DCM.

IMAGING

Radiography

- Radiography often shows pleural effusion or pulmonary edema.
- Generalized cardiomegaly.

Echocardiography

- Diagnostic modality of choice.
- Characteristic findings include thin ventricular walls, enlarged left ventricular end-systolic and end-diastolic dimensions, left atrial enlargement, and low fractional shortening.
- Pleural and pericardial effusion may be visualized.
- Spontaneous echocardiographic contrast or a thrombus may be visualized.

DIAGNOSTIC PROCEDURES

ECG

- ECG may be normal or may show left atrial or ventricular enlargement patterns.
- Both ventricular and supraventricular arrhythmias can be seen.

Pleural Effusion Analysis

- Pleural effusion typically is a modified transudate with total protein <4 g/dL and nucleated cell counts of less than 2,500/mL; chylous effusion may also be present.
- Analysis of the pleural effusion is important to rule out other causes of pleural effusion such as pyothorax, infectious peritonitis, or lymphosarcoma.

PATHOLOGIC FINDINGS

- Heart : body ratio is increased.
- All four cardiac chambers are dilated;

CARDIOMYOPATHY, DILATED—CATS

(CONTINUED)

C

ventricular walls are thin and left ventricular lumen is enlarged.

- Valve anatomy is normal.
- Histopathology shows myocytolysis and myocardial fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

These cats usually present in CHF and should be treated as inpatients, typically in an intensive care setting until more stable.

NURSING CARE

- Thoracocentesis is often utilized for both therapeutic and diagnostic purposes.
- Supplemental oxygen therapy is beneficial for cats in CHF to decrease the work of breathing.
- If hypothermic, cautious external heat (incubator or heating water pad) is recommended.

ACTIVITY

Indoors only after hospital discharge to reduce stress. Let cat dictate its own activity.

DIET

These cats typically are anorexic, thus tempting their appetite with many types of food may be necessary. Eventually, a low-sodium diet is recommended.

CLIENT EDUCATION

Some cats will need chronic intermittent thoracocentesis to manage significant accumulations of pleural effusion despite medical therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Furosemide is recommended to manage pulmonary edema and pleural effusion. Recommended dose range is 1–4 mg/kg q8–12h. Initially, administer parenterally then switch to oral. Chronically the lowest effective dose of furosemide is recommended.
- Pimobendan, an inodilator, is also recommended to strengthen contractility and provide some vasodilation. Recommended dose range is 0.1–0.3 mg/kg PO q12h. Although pimobendan is not currently licensed for use in cats, several recent publications have demonstrated its safety in cats and possibly a beneficial effect, albeit in retrospective studies. One study in cats with non-taurine-responsive DCM that were treated with pimobendan had a median survival time that was four times longer than the cats not treated with pimobendan (49 vs. 12 days).
- Taurine supplementation is recommended initially in all cats with DCM at 250 mg PO

q12h, until it is demonstrated that the patient is unresponsive to taurine or is not taurine deficient based on diagnostic testing.

- Nitroglycerin (2% ointment) one-fourth to one-half inch applied topically can be used in conjunction with diuretics in the acute management of severe CHF to further reduce preload. Nitroglycerin will lower the dose of furosemide and is particularly useful in patients with hypothermia or dehydration.
- Enalapril or benazepril, at a dose of 0.25–0.5 mg/kg PO q24h, is recommended to reduce afterload and preload as soon as the cat is able to take oral medications and is clinically stable. Use with caution and possibly avoid if creatinine >2.5 mg/dL.
- Digoxin is optionally recommended to strengthen contractility and for its positive neurohumoral effects at a dose of 0.03 mg/cat (one-fourth of a 0.125 mg tablet) or 0.01 mg/kg PO q48h. Digoxin can be given concurrently with pimobendan. However, digoxin is often omitted when pimobendan is given because of the difficulties in giving a cat several pills and digoxin's side-effect profile.

• Dobutamine at extremely low dosages can be given to a patient with severe signs of CHF and low cardiac output that cannot take oral medications. Dose varies 0.25–5 µg/kg/minute IV CRI. ECG monitoring is recommended.

- Because ATE is a concern, an antithrombotic agent is also recommended. Clopidogrel given at a dose of 18.75 mg (one-fourth of a 75 mg tablet) PO q24h is generally the author's preferred antithrombotic agent. Other options include aspirin 81 mg PO q72h (with food) or low molecular weight heparin (e.g., dalteparin 100–150 units/kg SC q8–24h or enoxaparin 1 mg/kg SC q12–24h).

- Antiarrhythmic drugs may also be needed to control supraventricular or ventricular arrhythmias. If hemodynamically significant supraventricular tachycardia or rapid atrial fibrillation is present, diltiazem is recommended. Usually, diltiazem is given orally in either a non-sustained-release formulation (7.5 mg/cat PO q8h) or a sustained-release oral formulation (Cardizem CD® at 10 mg/kg PO q24h or Dilacor XR® 30 mg/cat [or 1/2 of an inner 60 mg tablet] PO q12h). Diltiazem is also available in an injectable formulation for urgent control of a supraventricular arrhythmia in a cat that cannot take oral medications (0.05–0.1 mg/kg slow IV, repeated PRN up to 0.25 mg/kg). If rapid and sustained ventricular tachycardia, lidocaine slow IV 0.2–0.5 mg/kg (repeat once or twice max) or sotalol PO 2 mg/kg q12h is recommended.
- Beta blockers, such as atenolol, may be useful in the chronic management of both

supraventricular and ventricular arrhythmias. Beta blockers are used in the long-term management of DCM in humans because of their positive myocardial effects and survival benefit. Clinical experience is limited in feline DCM and they must be used cautiously, as they acutely decrease contractility and could worsen CHF. Recommended dose ranges from 3.125 to 6.25 mg PO q12–24h. Start low and titrate up based on heart rate and clinical signs.

PRECAUTIONS

- Unless needed for acute cardiac rhythm control, drugs such as calcium channel blockers (diltiazem) or beta-adrenergic blockers may reduce contractility and lower cardiac output. Use cautiously.
- Overzealous diuretic and vasodilation therapy may cause azotemia and electrolyte disturbances.
- Digoxin should not be used if renal insufficiency is documented or suspected.
- Enalapril or benazepril should be used with caution and possibly withheld if serum creatinine is >2.5 mg/dL.
- Dobutamine may cause seizures and cardiac tachyarrhythmias.



FOLLOW-UP

PATIENT MONITORING

- Repeat examination with ideally blood pressure, diagnostic imaging (either a thoracic radiograph or focused thoracic ultrasound for fluid assessment), and chemistry panel within 1 week to determine response of therapy.
- Home resting respiratory rate monitoring is helpful to determine need for diuretic dose adjustment or thoracocentesis.
- Periodically monitor electrolyte and renal parameters. Periodically monitor for CHF fluid accumulation with diagnostic imaging.
- If using digoxin, serum blood concentrations should be measured approximately 10–14 days after initiating therapy. Therapeutic range is 0.5–1.5 ng/dL 8–12 hours post-pill.
- Repeat diagnostic echocardiogram in 2–3 months after initiating taurine supplementation to determine echocardiographic response to therapy. Although echocardiographic response may take 2–3 months to assess, one should see dramatic clinical response within 2 weeks of initiating taurine therapy if cat has taurine-responsive DCM.

PREVENTION/AVOIDANCE

Ensure that cats eat a high-protein diet with sufficient dietary taurine. No vegetarian diets.

(CONTINUED)

CARDIOMYOPATHY, DILATED—CATS**C****POSSIBLE COMPLICATIONS**

ATE is the most feared complication of any feline myocardial disease.

EXPECTED COURSE AND PROGNOSIS

- These cats have a poor prognosis despite intensive therapy. If cat is not taurine responsive, survival is usually weeks to months.
- CHF can be medically refractory and recurrent despite appropriate medical therapy.
- Repeated thoracocentesis may be necessary.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- CHF.
- ATE.
- Pleural effusion.
- Cardiac arrhythmias.

SYNOMYS

Cardiomyopathy

SEE ALSO

- Aortic Thromboembolism.
- Congestive Heart Failure, Left-Sided.
- Congestive Heart Failure, Right-Sided.

ABBREVIATIONS

- ATE = aortic thromboembolism.
- CHF = congestive heart failure.
- cTnI = cardiac troponin I.
- DCM = dilated cardiomyopathy.

Suggested Reading

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CARDIOMYOPATHY, DILATED—DOGS



BASICS

DEFINITION

Dilated cardiomyopathy (DCM) characterized by left- and right-sided dilation, normal coronary arteries, anatomically normal although commonly insufficient atrioventricular valves, significantly decreased inotropic state, and myocardial dysfunction occurring primarily during systole; however, progressive diastolic dysfunction with restrictive physiology may also be present and is a negative predictor of survival.

PATOPHYSIOLOGY

- Myocardial failure leads to reduced cardiac output and congestive heart failure (CHF).
- Atrioventricular (AV) annulus dilation and altered papillary muscle function promote valvular insufficiency.
- Although left-sided signs commonly predominate, evidence of severe right-sided disease can occur and infrequently is the dominant clinical scenario.

SYSTEMS AFFECTED

- Cardiovascular.
- Renal/urologic—prerenal azotemia.
- Respiratory—pulmonary edema, infrequently pulmonary hypertension.
- All organ systems are affected by reductions in cardiac output.

GENETICS

- Genetic cause or heritable susceptibility strongly suspected in most breeds and documented in some (Portuguese water dog, boxer, and Doberman pinscher) with variable forms of inheritance.
- A genetic test is commercially available for causative mutations in boxer dogs (striatin) and Doberman pinscher (NCSU DCM 1—pyruvate dehydrogenase kinase; NCSU DCM 2—titin).
- These mutations are not causative in other predisposed breeds in which they have been evaluated.
- Correlations between genotype and phenotype have shown that Doberman pinschers with both mutations have, on average, an earlier onset of clinical disease with a predisposition to sudden death; boxers homozygous for the mutation are more likely to develop the DCM phenotype.

INCIDENCE/PREVALENCE

Estimated at 0.5–1.1% in predisposed breeds and perhaps higher in specific geographic regions.

GEOGRAPHIC DISTRIBUTION

None with the exception of Chagas' cardiomyopathy, which is limited to the southern United States (Gulf Coast) and both Central and South America.

SIGNALMENT

Species
Dog

Breed Predilections

- Doberman pinscher, boxer.
- Giant breeds—Scottish deerhound, Irish wolfhound, Great Dane, St. Bernard, Newfoundland.
- Cocker spaniel, Portuguese water dog (juvenile).

Mean Age and Range

4–10 years.

Predominant Sex

Males > females in most but not all breeds (minor predisposition).

SIGNS

Historical Findings

- Respiratory—tachypnea, dyspnea, coughing.
- Weight loss, typically of lean muscle mass.
- Weakness, lethargy, anorexia.
- Abdominal distention.
- Syncope, usually associated with arrhythmias (atrial fibrillation; ventricular tachycardia).
- Some dogs are asymptomatic, having what is termed preclinical DCM, the diagnosis of which in specific breeds is well described.
- Breed-specific echocardiographic parameters coupled with cardiac biomarkers (NT-proBNP; cardiac troponin I [$c\text{TnI}$]) may help identify dogs with preclinical DCM.

Physical Examination Findings

- May be completely normal with preclinical DCM.
- Weakness, possibly cardiogenic shock.
- Hypokinetic femoral pulse from low cardiac output.
- Pulse deficits with atrial fibrillation, ventricular or supraventricular premature contractions, and paroxysmal ventricular tachycardia.
- Jugular pulses from tricuspid regurgitation, arrhythmias, or right-sided CHF.
- Breath sounds—muffled with pleural effusion; crackles with pulmonary edema.
- S3 or summation gallop sounds.
- Mitral and/or tricuspid regurgitation murmurs are common but usually focal and soft.
- Auscultatory evidence of cardiac arrhythmia is common.
- Slow capillary refill time, infrequent cyanosis.
- Hepatomegaly with or without ascites.

CAUSES

- Majority of cases represent familial abnormalities of structural, energetic, or contractile cardiac proteins, some of which have been identified.
- Nutritional deficiencies (taurine and/or carnitine) have been documented in several breeds including golden retriever, boxer,

Newfoundland, and cocker spaniel; diet-associated DCM, which may be associated with taurine deficiency, commonly secondary to boutique, exotic-ingredient, or grain free (BEG) diets, is increasing recognized and potentially reversible.

- Viral, protozoal, and immune-mediated mechanisms have been proposed but not proven.
- Doxorubicin toxicity.
- Hypothyroidism and persistent tachyarrhythmias (sometimes associated with congenital tricuspid valve malformation) may cause reversible myocardial failure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Myxomatous valvular degeneration.
- Congenital heart disease.
- Heartworm disease.
- Bacterial endocarditis.
- Cardiac tumors and pericardial effusion.
- Airway obstruction—foreign body, neoplasm, laryngeal paralysis.
- Primary pulmonary disease—bronchial disease, pneumonia, neoplasia, aspiration, vascular disease (e.g., heartworms).
- Noncardiogenic pleural effusions (e.g., pyothorax, hemothorax, chylothorax).
- Trauma resulting in diaphragmatic hernia, pulmonary hemorrhage, hemothorax, pneumothorax.

CBC/BIOCHEMISTRY/URINALYSIS

Routine hematologic tests and urinalysis are usually normal unless altered by severe reductions in cardiac output or severe elevations in venous pressures (e.g., prerenal azotemia, high alanine aminotransferase, hyponatremia), therapy for heart failure (e.g., hyponatremia, hypokalemia, hypochloremia, azotemia, and metabolic alkalosis from diuresis), or concurrent disease.

OTHER LABORATORY TESTS

Cardiac biomarkers including NT-proBNP and $c\text{TnI}$ are elevated in both the preclinical and clinical stages of the disease. Clinical studies investigating use of these markers for diagnosis, prognosis, and optimization of therapy are ongoing.

IMAGING

Radiography

- Typically normal in the preclinical phase.
- Generalized cardiomegaly and signs of CHF are common.
- Left ventricular (LV) enlargement and left atrial enlargement may be most evident in early cases.
- In some cases, the degree of cardiomegaly may be less than expected for the severity of clinical signs; it is also often substantially less than would be expected in a dog with

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CARDIOMYOPATHY, DILATED—DOGS

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primary valvular heart disease and comparable clinical signs.

- Pleural effusion, hepatomegaly, ascites.

Echocardiography

- Gold standard for diagnosis.
- LV dilation often precedes overt reductions in indices of systolic function.
- Ventricular and atrial dilation.
- Indices of myocardial systolic function (fractional shortening [FS%]), ejection fraction, area shortening, and mitral annular motion by tissue Doppler imaging may be reduced.
- Spectral Doppler studies may confirm decreased velocity and/or acceleration of trans-aortic flow as well as mitral regurgitation and/or tricuspid regurgitation.
- Doppler evidence of restrictive LV filling is associated with decreased survival.

DIAGNOSTIC TESTS**ECG**

- Sinus rhythm or sinus tachycardia with isolated atrial or ventricular premature complexes.
- Atrial fibrillation and ventricular tachycardia (paroxysmal or sustained) are very common in Doberman pinschers.
- Boxers commonly have isolated ventricular arrhythmias without evidence of functional or anatomic heart disease.
- Prolonged QRS (>0.06 second), possible increased voltages ($R > 3$ mV lead II), suggesting LV enlargement.
- May have "sloppy" R wave descent with ST-T coving, suggesting myocardial disease or LV ischemia.
- May have low voltages (pleural or pericardial effusion, concurrent hypothyroidism).

PATHOLOGIC FINDINGS

- Dilation of all chambers with or without thinning of chamber walls.
- Slightly thickened endocardium with pale areas within myocardium (necrosis, fibrosis).
- Two histologically distinct forms—fatty infiltration: degenerative type seen in boxers and Doberman pinschers; and attenuated wavy fiber type: seen in many giant-, large-, and medium-sized breeds, including some boxers and Doberman pinschers.

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

With the exception of severely affected dogs (life-threatening arrhythmias, severe pulmonary edema, cardiogenic shock), most therapy can be administered on an outpatient basis.

ACTIVITY

Allow the dog to choose its own level of activity.

DIET

- During initial therapy for clinical signs, simply maintaining adequate caloric intake is paramount.
- Goal—reduce dietary sodium intake to <12–15 mg/kg/day.
- Severe sodium restriction is typically not necessary when using potent cardioactive therapy and may adversely affect appetite.
- Best to use commercially prepared diets.

CLIENT EDUCATION

- Emphasize potential signs associated with progression of disease and adverse side effects of medication.
- Monitoring sleeping respiratory rate often gives insight into impending decompensation.

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

First identify patient problems—CHF (left or right-sided), arrhythmia, hypothermia, renal failure, shock.

Preclinical Disease

- There is clinical evidence (PROTECT Trial) that early intervention with pimobendan monotherapy substantially changes the course of preclinical disease in Doberman pinschers.
- These results are routinely extrapolated to other breeds, but have not been proven.
- Critical evaluation suggests that early intervention with monotherapy using an angiotensin-converting enzyme (ACE) inhibitor is of minimal or no survival benefit in preclinical disease.

Initial Stabilization

- Treat hypoxemia with oxygen administration; prevent heat loss if hypothermic (warm environment).
- If pulmonary edema—furosemide (1–4 mg/kg IM/IV, then 1–2 mg/kg q6–12h for first 1–3 days), or CRI 1–2 mg/kg/h (author's preference).
- 2% topical nitroglycerin for first 24–48h for severe pulmonary edema—apply 1 inch–2 inches q8h (beware of hypotension in both patients and staff).
- If significant pleural effusion—drain each hemithorax.
- If severe heart failure and cardiogenic shock—dobutamine may be indicated; this drug may exacerbate arrhythmias, particularly in hypoxic dogs; oral pimobendan (see dosing below) may have important acute (2–4h) hemodynamic benefit as well; IV pimobendan (0.15 mg/kg) is available in select countries.
- Dobutamine 5–15 µg/kg/min infused for 24–72h with care (start low and gradually up-titrate based on response).

- If paroxysmal ventricular tachycardia is present—administer lidocaine slowly in 2 mg/kg boluses (up to 8 mg/kg total over 30 min) to convert to sinus rhythm; follow with lidocaine infusion (50–100 µg/kg/min).
- If lidocaine is ineffective—administer procainamide slowly at dose of 2–5 mg/kg (up to 15 mg/kg) IV to convert to sinus rhythm; follow with 25–50 µg/kg/min CRI (beware of proarrhythmia and infrequent hypotension).

Maintenance Therapy

- ACE inhibitors (enalapril, benazepril, lisinopril) are considered cornerstone of therapy for DCM.
- Enalapril (0.25–0.5 mg/kg PO q12h), benazepril (0.5 mg/kg PO q12–24h), or lisinopril (0.5 mg/kg PO q 12–24h) should be initiated early in the therapeutic regimen.
- Furosemide (1–4 mg/kg PO q8–12h) is used to control signs of congestion.
- Torsemide (0.1–0.4 mg/kg PO q8–12h) is commonly employed as an alternative to furosemide, particularly in later-stage disease.
- Spirostanolactone (1–2 mg/kg PO q12h) may impart an independent survival benefit by blocking aldosterone; higher doses can be used for refractory heart failure (2–4 mg/kg PO q12h).
- Hydrochlorothiazide (1–2 mg/kg PO q12h) may be beneficial as a third diuretic.
- Beta blockers can be used cautiously once heart failure is controlled with other drugs (see Precautions); if tolerated, they may improve myocardial function with chronic use; carvedilol (0.25–1.25 mg/kg PO q12h) is an alpha and beta blocker with antioxidant activity: start at the low end of the dose range and gradually up-titrate over a 6-week period if tolerated; consult with a cardiologist before using beta blockers in clinical DCM patients as can result in rapid and profound clinical deterioration.
- Pimobendan (0.25–0.3 mg/kg PO q12h) is a calcium-sensitizing drug and a vasodilating, positive inotrope (inodilator) that, when added to furosemide, ACE inhibitors, and spirostanolactone improves functional heart failure class and in Doberman pinschers increases survival time; the author has administered pimobendan 0.5 mg/kg PO q8h in refractory cases with perceived clinical benefit.
- The role of carnitine and taurine in therapy of DCM remains controversial; however, American cocker spaniels with DCM generally respond favorably to taurine and L-carnitine supplementation, but still require additional cardiac medications.

Arrhythmias

- In atrial fibrillation, slowing of ventricular rate response typically achieved with chronic administration of extended-release diltiazem

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- (Dilacor[®]) 2–7 mg/kg PO q12h, or atenolol 0.75–1.5 mg/kg PO q12h (never start in patient with active CHF), occasionally combined with digitalis at dose of 0.005 mg/kg PO q12h; therapeutic drug monitoring recommended when administering digoxin.
- Therapeutic goal is obtaining resting ventricular rate of 100–140 bpm.
 - At-home monitoring with AliveCor Kardia device.
 - This therapy merely controls ventricular rate, by depressing atrioventricular nodal conduction; generally does not convert rhythm from atrial fibrillation to sinus rhythm.
 - Amiodarone (10–15 mg/kg PO q24h for 7–10 days followed by 5–10 mg/kg PO q24h) may either control ventricular response rate or in some cases result in conversion to normal sinus rhythm.
 - Chronic oral therapy for ventricular tachycardia includes sotalol (1–2 mg/kg PO q12h), mexiletine (5–10 mg/kg PO q8h), or amiodarone (5–10 mg/kg PO q24h).
 - Mexiletine can be combined with sotalol if necessary.

CONTRAINDICATIONS

Digoxin should be avoided in severe uncontrolled paroxysmal ventricular tachycardia, in animals with compromised renal function, and in animals with important hypokalemia.

PRECAUTIONS

- Calcium channel blockers and notably beta blockers are negative inotropes and may have acute adverse effect on myocardial function; numerous human studies, however, have suggested that chronic administration of beta blockers may be of benefit in DCM.
- Combination of diuretics and ACE inhibitors may result in azotemia, especially in patients with severe heart failure or preexisting renal dysfunction, and must be closely monitored.

POSSIBLE INTERACTIONS

- Quinidine, amiodarone, and diltiazem may increase serum digoxin levels and predispose to digitalis intoxication.
 - Renal dysfunction, hypothyroidism, and hypokalemia predispose to digitalis intoxication.
- ALTERNATIVE DRUG(S)**
- Other vasodilators, including hydralazine and amlodipine, may be used instead of or in addition to ACE inhibitors (beware of hypertension).
 - Role of co-enzyme Q10, fish oil, and arginine remains to be determined.



FOLLOW-UP

PATIENT MONITORING

- Serial clinical examinations, thoracic radiographs, blood pressure measurements, routine serum biochemical evaluations (including electrolytes), and electrocardiography are most helpful.
- Repeat echocardiography is rarely informative or indicated.
- Serial evaluation of serum digoxin levels (therapeutic range: 0.5–1 ng/mL) taken 6–8 hours post-pill and serum biochemistries may help prevent iatrogenic problems.

POSSIBLE COMPLICATIONS

- Sudden death due most commonly to arrhythmias.
- Iatrogenic problems associated with medical management (see above).

EXPECTED COURSE AND PROGNOSIS

- Always fatal unless associated with nutritional deficiencies.
- Death usually occurs 6–24 months following diagnosis.
- Dobermanns typically have worst prognosis; however, with addition of pimobendan,

survival following identification in *preclinical* phase averages over 700 days.

- Atrial fibrillation, paroxysmal ventricular tachycardia, Doppler evidence of restrictive LV filling, markedly decreased FS%, homozygosity for known mutations (boxer), or presence of multiple mutations (Doberman pinschers) are believed to be markers for shortened survival and increased risk for sudden arrhythmogenic death.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Prevalence increases with age.

SYNOMYMS

- Congestive cardiomyopathy.
- Giant-breed cardiomyopathy.

SEE ALSO

- Atrial Fibrillation and Atrial Flutter.
- Ventricular Tachycardia.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- AV = atrioventricular.
- BEG = boutique, exotic-ingredient, or grain free.
- CHF = congestive heart failure.
- cTnI = cardiac troponin I.
- DCM = dilated cardiomyopathy.
- FS% = percent fractional shortening.
- LV = left ventricular.

INTERNET RESOURCES

<https://cardiaceducationgroup.org>

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Client Education Handout
available online

CARDIOMYOPATHY, HYPERTROPHIC—CATS



BASICS

DEFINITION

Inappropriate concentric hypertrophy of the ventricular free wall and/or the interventricular septum of the nondilated left ventricle. The disease occurs independently of other cardiac or systemic disorders.

PATHOPHYSIOLOGY

- Diastolic dysfunction results from a thickened, less compliant left ventricle.
- High left ventricular filling pressure develops, causing left atrial (LA) enlargement.
- Pulmonary venous hypertension causes pulmonary edema. Some cats develop biventricular failure (i.e., pulmonary edema, pleural effusion, small volume pericardial effusion without tamponade, and infrequently ascites).
- Stasis of blood in the large left atrium predisposes the patient to aortic thromboembolism (ATE).
- Dynamic aortic outflow obstruction and systolic anterior mitral motion (SAM) with secondary mitral insufficiency may occur, but unlike in humans, appears not to affect prognosis.
- Recent evidence suggests that some cats with apparent hypertrophic cardiomyopathy (HCM) and congestive heart failure (CHF) actually have transient myocardial thickening, often associated with high serum troponin I concentrations. These cats are younger than average for HCM, with on average less severe left ventricular (LV) hypertrophy, and they can experience resolution of both CHF and LV hypertrophy.

SYSTEMS AFFECTED

- Cardiovascular—CHF, ATE, and arrhythmias.
- Pulmonary—dyspnea if CHF develops.
- Renal/urologic—prerenal azotemia.

GENETICS

Some families of cats have been identified with a high prevalence of the disease, and the disease appears to be an autosomal dominant trait in Maine coon cats and ragdoll cats, due to a mutation in the myosin-binding protein C (MyBPC) gene. The genetics have not been definitively determined in other breeds; however, the Maine coon and ragdoll mutations have not been identified in affected Sphynx, Norwegian forest cats, Bengals, Siberians, or British shorthair cats.

INCIDENCE/PREVALENCE

Unknown, but relatively common. May be as high as 15% of the population.

SIGNALMENT

Species

Cat

Breed Predilections

Maine coon cats, ragdolls, Sphynx, British and American shorthairs, and Persians.

Mean Age and Range

- 5–7 years, with reported ages of 3 months–17 years. Some breeds of cats including ragdolls and Sphynx may develop the disease at a younger age (average of 2 years).
- HCM is most often a disease of young to middle-aged cats; unexplained murmurs in geriatric cats are more likely associated with hyperthyroidism or hypertension.

Predominant Sex

Male

SIGNS

Historical Findings

- Dyspnea, tachypnea.
- Anorexia.
- Exercise intolerance.
- Vomiting.
- Collapse.
- Sudden death.
- Coughing is uncommon in cats with HCM and suggests primary pulmonary disease.

Physical Examination Findings

- Gallop rhythm (S3 or S4).
- Systolic murmur in approximately half of affected cats.
- Apex heartbeat may be exaggerated.
- Muffled heart sounds, lack of chest compliance, and dyspnea characterized by rapid shallow respirations may be associated with pleural effusion.
- Dyspnea and crackles if pulmonary edema is present.
- Weak femoral pulse.
- Acute pelvic limb paralysis with cyanotic pads and nailbeds, cold limbs, and absence of femoral pulse in animals with ATE; emboli rarely affect thoracic limbs.
- Arrhythmia in some animals.
- May have no clinical signs.

CAUSES

- Usually unknown—multiple causes exist.
- MyBPC mutations in some cats with HCM.

Possible Causes

- Abnormalities of contractile protein myosin or other sarcomeric proteins (e.g., troponin, myosin-binding proteins, tropomyosin).
- Abnormality affecting catecholamine-influenced excitation contraction coupling.
- Abnormal myocardial calcium metabolism.
- Collagen or other intercellular matrix abnormality.
- Growth hormone excess.
- Dynamic LV outflow obstruction may contribute to secondary LV hypertrophy.

RISK FACTORS

Offspring of animals with familial mutations of MyBPC.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other forms of cardiomyopathy.
- Hyperthyroidism.
- Aortic stenosis.
- Systemic hypertension.
- Acromegaly.
- Noncardiac causes of pleural effusion.

CBC/BIOCHEMISTRY/URINALYSIS

- Results usually normal.
- Prerenal azotemia in some animals.

OTHER LABORATORY TESTS

- MyBPC assay; mutation differs for Maine coon cats and ragdoll cats.
- In cats >6 years old, check thyroid hormone concentration; hyperthyroidism causes myocardial hypertrophy that might be confused with HCM.
- Serum NT-proBNP concentrations higher in cats with HCM than in normal cats, and higher still in cats with symptomatic HCM. SNAP NT-proBNP point-of-care testing is also available to help differentiate symptomatic cats with HCM from those that are symptomatic from other causes. Send-out serum NT-proBNP testing is useful in identifying cats with suspicion of HCM from asymptomatic cats with abnormal physical exam findings (e.g., murmur). Follow-up echocardiography indicated in cats with serum NT-proBNP concentrations in “equivocal” or “high” range, or positive SNAP results.

IMAGING

Radiography

- Dorsoventral radiographs often reveal a valentine-appearing heart because of atrial enlargement and a left ventricle that comes to a point.
- Pulmonary edema, pleural effusion, or both in some animals.
- Radiographs may be normal in asymptomatic cats.
- Different forms of cardiomyopathy cannot be reliably differentiated by radiography.

Echocardiography

- Hypertrophy of interventricular septum (IVS) or LV posterior wall (diastolic wall thickness >6 mm).
- Hypertrophy may be symmetric (affecting IVS and posterior wall) or asymmetric (affecting IVS or posterior wall, but not both).
- Hypertrophy of papillary muscles.
- Normal or high fractional shortening.
- Normal or reduced LV lumen.
- LA enlargement.
- Systolic anterior motion of mitral valve (some animals).
- LV outflow obstruction (some animals); specialized Doppler studies performed by

CARDIOMYOPATHY, HYPERTROPHIC—CATS

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experienced sonographers often reveal LV relaxation abnormalities (e.g., mitral inflow E : A wave reversal).

- Thrombus in left atrium (rare).
- Note: there is some overlap between normal cats (especially ketaminized or dehydrated) and cats with mild HCM. Correlate echo findings with physical findings. Presence of LA enlargement favors HCM.

DIAGNOSTIC PROCEDURES

ECG

- Sinus tachycardia (heart rate >240) common with heart failure; however, some cats with severe heart failure and hypothermia are bradycardic.
- Atrial and ventricular premature complexes seen more often in cats with cardiomyopathy, but also occasionally seen in normal cats.
- Atrial fibrillation seen in some advanced cases.
- Left axis deviation often seen.
- Prolongation of QT interval and QTc (QT interval corrected for heart rate) often seen with LV hypertrophy.
- Cannot differentiate different forms of cardiomyopathy; may be normal.

Systemic Blood Pressure

- Normotensive or hypotensive.
- Evaluate blood pressure in all patients with myocardial hypertrophy to rule out systemic hypertension as cause of hypertrophy.

PATHOLOGIC FINDINGS

- Nondilated left ventricle with hypertrophy of IVS or LV free wall.
- Hypertrophy of papillary muscles.
- LA enlargement.
- Mitral valve thickening.
- Myocardial hypertrophy with disorganized alignment of myocytes (myofiber disarray).
- Interstitial fibrosis.
- Myocardial scarring.
- Hypertrophy and luminal narrowing of intramural coronary arteries.



TREATMENT

APPROPRIATE HEALTH CARE

Cats with CHF should be hospitalized.

NURSING CARE

- Minimize stress.
- Oxygen if dyspneic.
- Warm environment if hypothermic.

ACTIVITY

Restricted with CHF.

DIET

Modest to moderate sodium restriction in animals with CHF.

CLIENT EDUCATION

- Many cats diagnosed while asymptomatic eventually develop CHF and may develop ATE and die suddenly.
- If cat is receiving warfarin, dalteparin, enoxaparin (Lovenox®), or combination of

clopidogrel and any of those medications, minimize potential for trauma and subsequent hemorrhage.



MEDICATIONS

DRUG(S) OF CHOICE

Furosemide

- Dosage—1–2 mg/kg PO/IM/IV q8–24h.
- Critically dyspneic animals often require high dosage (4 mg/kg IV); this dose can be repeated in 1 hour if cat still severely dyspneic; indicated to treat pulmonary edema, pleural effusion, and ascites.
- Cats are sensitive to furosemide and prone to dehydration, prerenal azotemia, and hypokalemia.
- Once pulmonary edema resolves, taper to lowest effective dose.

Pimobendan

- Dosage—0.25–0.3 mg/kg PO q12h.
- Appears to be useful in management of CHF (e.g., pulmonary edema or pleural effusion) in cats with HCM, possibly by enhancing diastolic function and LA fractional shortening; not used in management of asymptomatic HCM at this time.
- Not currently licensed for use in cats.

Angiotensin-Converting Enzyme (ACE) Inhibitors

- Dosage—enalapril or benazepril 0.25–0.5 mg/kg PO q24h.
- Indications in cats with HCM not well defined—authors currently use for CHF.

Beta Blockers

- Dosage—atenolol (6.25–12.5 mg/cat PO q12h).
- Beneficial effects may include slowing of sinus rate, correcting atrial and ventricular arrhythmias, platelet inhibition.
- More effective than diltiazem in controlling dynamic outflow tract obstruction.
- Role in asymptomatic patients unresolved, but many clinicians use if dynamic outflow obstruction and hypertrophy present.
- Contraindicated in presence of CHF.

Diltiazem

- Dosage—7.5–15 mg/cat PO q8h or 10 mg/kg PO q24h (Cardizem® CD) or 30 mg/cat q12h (Dilacor XR®).
- Beneficial effects may include slower sinus rate, resolution of supraventricular arrhythmias, improved diastolic relaxation, coronary and peripheral vasodilation, platelet inhibition.
- May reduce hypertrophy and LA dimensions in some cats.
- Role in asymptomatic patients unresolved.

Aspirin

- Dosage—81 mg/cat q2–3 days if severe atrial enlargement.

- Depresses platelet aggregation, hopefully minimizing risk of thromboembolism.
- Warn owners that thrombi can still develop despite aspirin administration; aspirin appears to be not as effective as clopidogrel (1/4 of 75 mg tablet PO q24h) in prevention of ATE, at least in cats with previous embolic episode.

Nitroglycerin Ointment

- Dosage—one-fourth inch/cat topically applied q6–8h or 2.5 mg/24h patch.
- Often used in acute stabilization of cats with severe pulmonary edema or pleural effusion.
- When used intermittently, may be useful for long-term management of refractory cases.

CONTRAINDICATIONS

Avoid beta blockers in cats with emboli; these agents cause peripheral vasoconstriction. If beta blockers must be used in this setting for arrhythmia control, choose beta-1 selective blocker such as atenolol.

PRECAUTIONS

Use ACE inhibitors cautiously in azotemic animals.

ALTERNATIVE DRUG(S)

Torsemide

- Dosage—0.1–0.5 mg/kg q24h, sometimes with dose escalation to q12h.
- Used as substitute for furosemide in refractory pulmonary edema or pleural effusion in cats with apparently normal (or at least stable) renal function.
- Monitor renal function closely in first days after switching to torsemide.

Spirostanolactone

- Dosage—1 mg/kg q12–24h.
- Used in conjunction with furosemide in cats with CHF, especially refractory effusions.
- May cause facial pruritis.

Warfarin and Low Molecular Weight Heparin

- Used sometimes in cats at high risk for thromboembolism.
- See Aortic Thromboembolism.

Clopidogrel

- Dosage—18.75 mg/cat/day.
- Platelet function inhibitor, superior to aspirin in cats with previous ATE.

Beta Blocker plus Diltiazem

- Cats that remain tachycardic on a single agent can be treated cautiously with a combination of a beta blocker and diltiazem.
- Monitor for bradycardia and hypotension.



FOLLOW-UP

PATIENT MONITORING

- Observe closely for dyspnea, lethargy, weakness, anorexia, and painful posterior paralysis or paresis.

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- If treating with warfarin, monitor prothrombin time.
- If treating with ACE inhibitor or spironolactone, monitor renal function and electrolytes.
- Repeat echocardiogram in 6 months to assess efficacy of treatment for hypertrophy. If beta blocker or diltiazem was prescribed in asymptomatic animal and there is evidence of progressive hypertrophy/LA enlargement, consider switching to another class of medications (or adding an ACE inhibitor) and recheck 4–6 months later.
- Echocardiographic evaluations that reveal LA diameters >2 cm or loss of LV systolic function should prompt more aggressive prophylaxis against ATE (e.g., clopidogrel with low molecular weight heparin).

PREVENTION/AVOIDANCE

Avoid stressful situations that might precipitate CHF.

POSSIBLE COMPLICATIONS

- Heart failure.
- ATE and paralysis.
- Cardiac arrhythmias/sudden death.

EXPECTED COURSE AND PROGNOSIS

- Animals homozygous for MyBPC mutations more likely to develop severe HCM and at earlier age than heterozygous animals.
- Prognosis varies considerably, probably because there are multiple causes. In one study of cats with HCM living at least 24 hours following presentation:

- Asymptomatic cats—median survival 563 days (range: 2–3,778 days).
- Cats with syncope—median survival 654 days (range: 28–1,505 days).
- Cats with CHF—median survival 563 days (range: 2–4,418 days).
- Cats with ATE—median survival 184 days (range: 2–2,278 days).
- Older age and larger left atria predicted shorter survival.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Aortic thromboembolism.

PREGNANCY/FERTILITY/BREEDING

- High risk of complications.
- Avoid aspirin.

SEE ALSO

- Aortic Thromboembolism.
- Congestive Heart Failure, Left-Sided.
- Hypersomatotropism/Acromegaly in Cats.
- Hypertension, Systemic Arterial.
- Hyperthyroidism.
- Murmurs, Heart.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- ATE = aortic thromboembolism.
- CHF = congestive heart failure.
- HCM = hypertrophic cardiomyopathy.
- IVS = interventricular septum.

- LA = left atrial.
- LV = left ventricular.
- MyBPC = myosin-binding protein C.
- QTc = QT interval corrected for heart rate.
- SAM = systolic anterior mitral motion.

Suggested Reading

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International collaborative study to assess cardiovascular risk and evaluate long-term health in cats with preclinical hypertrophic cardiomyopathy and apparently healthy cats: the REVEAL study. *J Vet Intern Med* 2018, 32(3):930–943.

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**Client Education Handout
available online**

CARDIOMYOPATHY, HYPERTROPHIC—DOGS



BASICS

OVERVIEW

Hypertrophic cardiomyopathy (HCM) is defined as inappropriate myocardial hypertrophy of a nondilated left ventricle, occurring in the absence of an identifiable stimulus. HCM is rare in dogs, and is characterized by left ventricular (LV) concentric hypertrophy (increased wall thickness). The primary disease process is confined to the heart and only affects other organ systems when congestive heart failure (CHF) is present. Increased LV wall thickness leads to impaired ventricular filling (due to lack of compliance and abnormal relaxation), with resultant increases in LV end-diastolic pressure and left atrial (LA) pressure. LA enlargement is usually in response to increased LV end-diastolic pressure. Mitral insufficiency and/or dynamic LV outflow tract obstruction commonly occur secondary to structural and/or functional changes of the mitral valve apparatus caused by papillary muscle malalignment due to hypertrophy.

SIGNALMENT

- The incidence of HCM in dogs is very low, thus accurate accounts of signalment are lacking.
- Young (<3 years) male dogs.
- Rottweiler, Dalmatian, German shepherd, pointer breeds and Boston terriers have been reported.

SIGNS

Historical Findings

- Most are asymptomatic.
- Signs of left CHF predominate in symptomatic dogs.
- Syncope, generally during activity or exercise.
- Sudden death is the most commonly reported clinical sign.

Physical Examination Findings

- ± Systolic heart murmur.
- ± Gallop heart sound.
- ± Signs of left CHF (e.g., dyspnea, cyanosis, exercise intolerance, cough).

CAUSES & RISK FACTORS

The cause of canine HCM is unknown. Genetic abnormalities in genes coding for myocardial contractile proteins have been documented in humans and cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Systemic hypertension.
- Infiltrative cardiac disorders.

- Thyroid toxicosis.
- Mitral dysplasia.

IMAGING

Radiography

- May be normal or may show LA or LV enlargement.
- Pulmonary edema present with left CHF.

Echocardiography

- Severe cases usually have marked LV and papillary muscle hypertrophy, and LA enlargement. Hypertrophy is usually global, but can be more regional or segmental (asymmetric). Milder forms may have subtle LV hypertrophy.
- Systolic anterior motion of the mitral valve, suggesting dynamic LV outflow tract obstruction (LVOTO), is common in dogs with HCM.

DIAGNOSTIC PROCEDURES

ECG

- May be normal.
- ST segment and T wave abnormalities have been reported.
- Atrial or ventricular ectopic arrhythmias may rarely occur.

Blood Pressure

Usually normal. Should be evaluated to rule out systemic hypertension as the cause of LV hypertrophy.

PATHOLOGIC FINDINGS

- Abnormal heart : body weight ratio.
- LV concentric hypertrophy.
- The interventricular septum may have an impact lesion, varying from a small opaque lesion to a thickened plaque.
- The mitral valve is often thickened and elongated.
- Varying degrees of LA enlargement may be present.



TREATMENT

Treatment is generally only pursued if there is evidence of CHF, severe arrhythmias, or frequent syncope. Exercise restriction and sodium restriction are beneficial.



MEDICATIONS

DRUG(S) OF CHOICE

- In patients with left CHF, diuretics and angiotensin-converting enzyme (ACE) inhibitor therapy are advocated.
- In dogs with severe dynamic LVOTO, administration of beta blockers or calcium

channel blockers has been advocated; however, benefit has not been proven.

- Beta blockers or calcium channel blockers may also improve myocardial oxygenation, reduce heart rate, improve LV diastolic function, and control arrhythmias, and therefore may be useful in dogs with left CHF; however, benefit has also not been proven.

CONTRAINdications/POSSIBLE INTERACTIONS

- Positive inotropes may worsen dynamic LVOTO.
- Avoid calcium channel blockers in combination with beta blockers, as clinically significant bradyarrhythmias can develop.
- Avoid potent arteriolar dilators in cases with dynamic LVOTO. The use of milder vasodilators such as ACE inhibitors in dogs with CHF is generally well tolerated.



FOLLOW-UP

- Depends on clinical severity. Serial radiography and/or echocardiography may help characterize disease progression and guide medication adjustments.
- Due to the rarity of canine HCM, prognostic information is lacking. In dogs with severe CHF or other complications, prognosis is generally guarded.



MISCELLANEOUS

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- CHF = congestive heart failure.
- HCM = hypertrophic cardiomyopathy.
- LA = left atrial.
- LV = left ventricular.
- LVOTO = left ventricular outflow tract obstruction.

Suggested Reading

Oyama MA. Canine cardiomyopathy. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2016, pp. 141–152.

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Author Michael Aherne

Consulting Editors Michael Aherne

Acknowledgment The author and book editors acknowledge the prior contribution of Larry P. Tilley.

C CARDIOMYOPATHY, NUTRITIONAL

(CONTINUED)

C myocardial or skeletal muscle carnitine deficiency. Plasma free carnitine concentrations of less than 8 μmol/L are considered diagnostic of systemic carnitine deficiency; plasma concentrations in the normal or supernormal range do not rule out myocardial carnitine deficiency or insufficiency.

- There is no confirmatory laboratory test currently available to diagnose nutritional DCM associated with BEG diets; dogs should be assessed for taurine and carnitine deficiency, and the diagnosis is solidified by response to nutritional management.

IMAGING

Echocardiography is used to diagnose DCM.

DIAGNOSTIC PROCEDURES

- Endomyocardial biopsy is the gold standard to assess myocardial carnitine levels, since plasma carnitine concentrations are an insensitive indicator of muscle carnitine deficiency.
- Myocardial free carnitine concentrations <3.5 nmol/mg of noncollagenous protein are considered diagnostic of myocardial carnitine deficiency.
- Ratio of esterified to free carnitine >0.4 is considered diagnostic of carnitine insufficiency.



TREATMENT

- Response to nutritional manipulation and supplementation can take months, so patients will require medications to support myocardial function (e.g., pimobendan), antagonize neurohormonal activation (e.g., angiotensin-converting enzyme inhibitors and spironolactone), and diuretic therapy if congestive heart failure is present (e.g., furosemide).
- Taurine supplementation if taurine deficiency is diagnosed; if blood concentrations are not measured, it is

reasonable to trial with supplementation and assess response to treatment; taurine deficiency associated with DCM in American cocker spaniels is reported to respond to both taurine and L-carnitine supplementation.

- Treatment with L-carnitine is indicated in addition to conventional treatment for DCM; however, some dogs, including some families of carnitine-deficient boxers, fail to respond clinically to supplementation. While supplementation dramatically improves a small percentage of dogs with DCM, the overall efficacy of L-carnitine supplementation for treatment of DCM is untested. If a trial of metabolic supplementation is desired in the absence of known L-carnitine deficiency, the combination of L-carnitine with taurine and CoQ10 (100 mg as ubiquinol q8–12h) seems prudent.
- Transition to a high-quality, scientifically backed, grain-based food with a well-studied protein source is critical to the recovery of nutritional DCM associated with BEG diets. The role of taurine supplementation in the absence of deficiency is uncertain; however, there is no known detriment to empiric supplementation, and taurine may have therapeutic benefits apart from correction of deficiency.



MEDICATIONS

DRUG(S) OF CHOICE

Taurine

- Dogs—250 mg PO q12h if <10 kg; 500 mg PO q12h if 10–25 kg; 1000 mg PO q12h if >25 kg.
- Cats—250 mg PO q12h.

L-Carnitine

- Large-breed dogs—2 g (approximately 1 tsp L-carnitine powder) q8–12h.

- American cocker spaniels—in combination with taurine) 1 g (approximately 0.5 tsp L-carnitine powder) q8–12h.



FOLLOW-UP

Repeat echocardiogram 3–6 months after nutritional manipulation, including amino acid supplementation and/or diet change. Improvement in myocardial function may take up to a year for dogs with nutritional cardiomyopathy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Taurine deficiency may cause reproductive failure in cats.

SEE ALSO

- Cardiomyopathy, Dilated—Cats.
- Cardiomyopathy, Dilated—Dogs.

ABBREVIATIONS

- BEG = boutique, exotic-ingredient, grain-free.
- DCM = dilated cardiomyopathy.

Suggested Reading

Adin D, DeFrancesco T, Keene B, et al. Echocardiographic phenotype of DCM differs based on diet type. *J Vet Cardiol* 2019; 21:1–9.

Authors Darcy B. Adin and Bruce W. Keene
Consulting Editor Michael Aherne

CARDIOMYOPATHY, RESTRICTIVE—CATS

C



BASICS

DEFINITION

A rare, primary heart muscle disease characterized *functionally* by severe diastolic dysfunction with restrictive left ventricular (LV) filling and normal to near normal systolic function, *morphologically* by a nondilated, nonhypertrophied left ventricle with increased endocardial and/or myocardial fibrosis and severe atrial enlargement, and *clinically* by congestive heart failure (CHF), thromboembolic disease, and cardiac death.

PATOPHYSIOLOGY

- Increased cardiomyofilament Ca^{2+} sensitivity leading to severely impaired myocardial relaxation, high myocardial stiffness due to endomyocardial fibrosis (endomyocardial type) and/or interstitial fibrosis (myocardial type), and disorganized myofiber architecture (disarray) are main characteristics of primary restricted cardiomyopathy (RCM); RCM-like myocardial changes and clinical syndromes can result from myocardial remodeling and dysfunction secondary to other causes (e.g., endomyocarditis, immune-mediated disease, or end-stage hypertrophic cardiomyopathy).
- Diastolic heart failure and cardiogenic arterial thromboembolism (ATE) lead to high mortality.

SYSTEMS AFFECTED

- Cardiovascular.
- Respiratory.

GENETICS

Primary RCM can be a spontaneous or familial disease, but is generally considered of genetic cause in humans with an autosomal dominant pattern of inheritance; several genes encoding sarcomeric and nonsarcomeric proteins can be affected; RCM-causing mutations have not been identified in cats.

INCIDENCE/PREVALENCE

Primary feline RCM is rare—prevalence ranging from 1% to 5% of all myocardial diseases in cats.

SIGNALMENT

- Cats.
- Higher prevalence in Siamese and oriental cats.
- Middle-aged to older cats.
- Male predisposition.

SIGNS

Historical Findings

- Lethargy.
- Weight loss.
- Paresis or paralysis (i.e., signs of ATE).
- Labored breathing.
- Tachypnea.
- Ascites.
- Jugular venous distension.
- Cyanosis.

Physical Examination Findings

- If not in CHF—arrhythmias.
- Prominent gallop sounds are a hallmark.
- Heart murmur uncommon.
- If in CHF—above signs plus the following:
- Tachypnea.
- Labored breathing.
- Cyanosis.
- Hepatomegaly or ascites with jugular venous distension.
- Pulmonary

crackles.

- Muffled cardiac or respiratory sounds if pleural effusion.
- Paralysis or paresis with loss of femoral pulses; one or more extremities cold and painful (ATE).

CAUSES

- Primary RCM—currently unknown; genetic cause documented in humans.
- Secondary RCM—late or end stage of underlying disease (e.g., hypertrophic cardiomyopathy); link between prior interstitial pneumonia and feline endomyocarditis leading to RCM suspected in one study.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Advanced stages of other feline cardiomyopathies:
 - Hypertrophic, dilated, arrhythmic right ventricular, non-specific phenotype, and tachycardia-induced cardiomyopathy.
 - Myocardial infarct.
 - CHF secondary to thyrotoxicosis or hypertensive heart disease.

CBC/BIOCHEMISTRY/URINALYSIS

Routine chemistry panel and urinalysis helpful to document concurrent or complicating conditions (e.g., renal failure and potassium depletion).

OTHER LABORATORY TESTS

- Plasma T_4 concentration in cats ≥ 6 years old.
- Plasma cardiac troponin I concentration (more specific if ischemic heart disease or myocarditis suspected).

IMAGING

Thoracic Radiography

- Cardiomegaly with severe biatrial enlargement (“valentine” heart on v/d projections).
- Interstitial or alveolar infiltrates or pleural effusion with pulmonary venous distention if in CHF.

Echocardiography

- Note: definitive diagnostic criteria are poorly defined and remain controversial. Early (noncongestive) RCM has rarely been documented in cats.
- Anatomic findings characterizing the RCM phenotype include:
 - Severe biatrial enlargement.
 - Nonhypertrophied, nondilated left ventricle (normal chamber dimension, normal wall thickness).
 - Severe enlargement of the left atrium with spontaneous echocardiographic contrast or thrombi frequently seen.
 - Prominent, often diffuse echogenic scar (“moderator bands,” false tendons) leading to a small LV lumen and narrowing at the mid-ventricle (endomyocardial fibrosis or “bridging” fibrosis).
 - Focal areas of highly echogenic and often thin myocardium indicative of ischemia or scarring.
 - Myocardium can appear normal with pure myocardial form of RCM.
 - Pleural effusion and pericardial effusion may be present.

- Functional findings (echocardiographic):
- Severe LV diastolic dysfunction on Doppler echocardiography—restrictive LV filling with a peak velocity of early : late transmural flow ($E : A$) ratio >2.0 , short isovolumic relaxation time (<37 msec), shortened deceleration time of E (<45 msec), low peak velocity of mitral annular motion (E'), and $E : E' \gg 15$.
- Normal to low normal LV systolic function (in some cases LV systolic dysfunction is present).
- Regional wall motion abnormalities possible.
- Left atrial dysfunction.
- Severe left atrial appendage enlargement with evidence of blood stasis.
- Midventricular obstruction with flow turbulence in cats with bridging endomyocardial fibrosis.
- In cats with other causes of restrictive physiology, characteristics of the underlying disease can predominate; however, severe atrial enlargement and restrictive LV filling will be present in nearly all cats.

DIAGNOSTIC PROCEDURES

ECG

- Note: ECG findings are neither sensitive nor specific.
- Sinus tachycardia is common, but cats with severe CHF and hypothermia may be bradycardic.
- Ventricular or supraventricular ectopic beats, paroxysmal or sustained supraventricular or ventricular tachycardia, or atrial fibrillation.
- Atrial or ventricular enlargement patterns.
- ST segment changes.

Pathology

- Note: histopathologic confirmation is needed to diagnose RCM.
- Increased heart weight (>19 g).
- Severe biatrial dilatation.
- Locally or diffusely thickened opaque endocardium.
- False tendons (“moderator bands”) present in some cats.
- Normal luminal size of the left and right ventricles.
- Diffuse or focal cardiomyocyte disarray.
- Increased interstitial and replacement fibrosis.
- Abnormal intramural coronary arterioles with medial hypertrophy and narrowed lumen.
- Increased number of inflammatory cells seen only in cats with acute endomyocarditis—this finding is commonly absent in cats with endocardial fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with severe CHF are hospitalized for emergency care.
- Mildly symptomatic animals can be treated with outpatient medical management.

NURSING CARE

- Cats with respiratory distress should receive oxygen.
- Sedation is usually beneficial.
- Thoracocentesis if relevant pleural effusion.
- Maintain a low-stress environment (e.g., cage rest, minimize handling).
- Heating pad for hypothermic patients.
- Respiratory rate should be used to monitor immediate treatment success.

CARDIOMYOPATHY, RESTRICTIVE—CATS

(CONTINUED)

C

ACTIVITY

Cage rest for CHF patients.

DIET

In acute heart failure, maintain intake with hand feeding if necessary.

CLIENT EDUCATION

Owner should be counseled regarding technique of pill administration in cats, possible adverse effects of medications, importance of maintaining stable food and water intake, and monitoring their cat's resting respiratory rate at home.



MEDICATIONS

DRUG(S) OF CHOICE

Acute CHF

- Parenteral administration of furosemide (1–2 mg/kg IV/IM/SC q2–6h); CRI may be considered.
- Dermal application of nitroglycerin ointment (2%, one-fourth inch q12h).
- Oxygen delivered by cage, mask, nasal prongs, or flow-by.
- Thoracocentesis if relevant pleural effusion.
- Dobutamine only if cats are hypotensive (systolic blood pressure <90 mmHg); 1–5 µg/kg/minute as CRI, start a lower dose and increase over 0.5–1h.
- Severe supraventricular tachyarrhythmias can be treated with diltiazem CRI (2–6 µg/kg/min IV).
- Ventricular tachycardia may resolve with resolution of CHF.
- Acute therapy of ventricular tachycardia may include lidocaine (0.25–0.5 mg/kg IV *slowly*); monitor closely for neurologic signs of toxicity.
- Pimobendan (0.25 mg/kg PO q12h) may be helpful to increase cardiac performance in acute heart failure, but is only used in animals that cannot be stabilized and systemic hypotension cannot be corrected.
- Note:* pimobendan is not approved for clinical use in cats and clinical safety and efficacy data are limited.
- Antiplatelet medication (clopidogrel bisulfate 18.75 mg PO q24h) or anticoagulants (e.g., unfractionated heparin 150–250 IU/kg SC q6h) may be administered, in particular in cats with severe left atrial enlargement and spontaneous echocardiographic contrast.

Chronic Therapy

- Furosemide is gradually decreased to lowest effective dose.
- Angiotensin-converting enzyme (ACE) inhibitors may reduce fluid retention, decrease the need for diuretics, and counterbalance adverse effects of diuretics (e.g., enalapril 0.25–0.5 mg/kg PO q12–24h).
- Diltiazem (1.5–2.5 mg/kg regular diltiazem or 10 mg/kg q24h extended-release diltiazem) decreases heart rate and improves supraventricular arrhythmias in affected cats; the addition of digoxin (0.007 mg/kg PO

q48h) may allow better control of ventricular response rate in cats with atrial fibrillation; cats with hemodynamically important ventricular and supraventricular ectopy can also benefit from sotalol (1.0–2.0 mg/kg PO q12h). • Pimobendan (0.25 mg/cat PO q12h) may be helpful in the management of chronic heart failure; *note:* pimobendan is not approved for clinical use in cats.
- Treat associated conditions (e.g., dehydration, hypothermia, hypokalemia).
- Clopidogrel (one-fourth of a 75 mg tablet PO q24h) to inhibit platelets chronically; aspirin (25 mg/kg PO q72h) may also be considered, but efficacy is questionable; in cases of echogenic smoke or prior ATE, dual platelet inhibition (clopidogrel and aspirin) may be used.
- Addition of low molecular weight heparin (enoxaparin [Lovenox®] at 1–2 mg/kg q12h SC) may be considered in cats at high risk for thromboembolic disease; apixaban (Eliquis®) at 0.625 mg/cat q12h in cats <5 kg body-weight and 1.25 mg/cat q12h in cats ≥5 kg has been recommended, but published evidence is not available.
- Treatment of cats with preclinical RCM has rarely been reported, but includes ACE inhibitors and antiplatelet drugs; there is currently no specific drug for LV diastolic dysfunction.

CONTRAINdications

- Beta blockers should never be administered in cats with RCM.
- For diltiazem—bradycardia, atrioventricular block, myocardial failure, and hypotension.
- For furosemide—severe dehydration, severe hypokalemia, and moderate to severe azotemia.
- For ACE inhibitors—moderate to severe azotemia, hypotension, and hyperkalemia.

POSSIBLE INTERACTIONS

- Combination of ACE inhibitors and furosemide—hypotension and renal failure.
- Chronic aspirin therapy may increase risk of renal side effects of ACE inhibitors and may lead to inappetence and gastrointestinal upset.
- Combining antiplatelets and anti-coagulants may increase risk of bleeding.



FOLLOW-UP

PATIENT MONITORING

- Frequent physical reexaminations to assess response to treatment.
- Frequent reevaluation of hydration status and renal function, particularly in first few days of therapy to avoid dehydration, hypokalemia, and azotemia.
- Repeated thoracocentesis if necessary.
- “Hands-off” hourly assessment of respiratory rate in first 12–24 hours can be used to monitor efficacy of CHF therapy.
- Radiographs may be repeated in 12–24

hours to monitor pulmonary infiltrate resolution.

- Repeat physical examination and analysis of blood biochemistries after 3–7 days' treatment of acute CHF.
- Stable patients reevaluated every 2–4 months or more frequently if problems occur.

PREVENTION/AVOIDANCE

No known preventative measures for RCM.

POSSIBLE COMPLICATIONS

Tissue necrosis or loss of function in limbs affected by thromboembolic complications, adverse effects of medications, sudden death, and euthanasia due to refractory heart failure.

EXPECTED COURSE AND PROGNOSIS

Variable, but most cats have a grave prognosis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Aortic thromboembolism and CHF.

AGE-RELATED FACTORS

Hyperthyroidism should be ruled out with appropriate testing in feline patients with heart disease ≥6 years of age.

SYNOMYS

- Intermediate cardiomyopathy.
- Unclassified cardiomyopathy.

SEE ALSO

- Aortic Thromboembolism.
- Congestive Heart Failure, Left-Sided.
- Congestive Heart Failure, Right-Sided.

ABBREVIATIONS

- A = peak velocity of late transmural flow.
- ACE = angiotensin-converting enzyme.
- ATE = arterial thromboembolism.
- CHF = congestive heart failure.
- E = peak velocity of early transmural flow.
- E' = peak velocity of mitral annular motion.
- LV = left ventricular.
- RCM = restrictive cardiomyopathy.

Suggested Reading

Charles PY, Li YJ, Nan CL, Huang XP. Insights into restrictive cardiomyopathy from clinical and animal studies. J Geriatr Cardiol 2011; 8:168–183.

Fox PR. Endomyocardial fibrosis and restrictive cardiomyopathy: pathologic and clinical features. J Vet Cardiol 2004; 6:25–31.

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Consulting Editor Michael Aherne



Client Education Handout
available online

CARDIOPULMONARY ARREST



BASICS

DEFINITION

- Cessation of effective perfusion and ventilation because of loss of coordinated cardiac and respiratory function.
- Cardiac arrest invariably follows respiratory arrest if not recognized and corrected.

PATHOPHYSIOLOGY

- Generalized or cellular hypoxia may be cause or effect of sudden death.
- After 1–4 minutes of airway obstruction, breathing efforts stop while circulation remains intact.
- If obstruction continues for 6–9 minutes, severe hypotension and bradycardia lead to dilated pupils, absence of heart sounds, and lack of palpable peripheral pulse.
- After 6–9 minutes, myocardial contractions cease even though ECG may look normal—pulseless electrical activity (formerly electrical mechanical dissociation).
- Ventricular fibrillation, ventricular asystole, and pulseless electrical activity are rhythms indicating cessation of myocardial contractility.

SYSTEMS AFFECTED

- All systems are affected, but those requiring greatest supply of oxygen and nutrients affected first.
- Cardiovascular.
- Renal/urologic.
- Neurologic.

SIGNALMENT

- Dog and cat.
- Any age, breed, or sex.

SIGNS

- Lack of response to stimulation.
- Loss of consciousness.
- Dilated pupils.
- Cyanosis.
- Agonal gasping or absence of ventilation.
- Absence of peripheral pulses.
- Hypothermia.
- Absence of audible heart sounds.

CAUSES

- Hypoxemia caused by ventilation-perfusion mismatch, diffusion barrier impairment, hypoventilation, or shunting.
- Poor oxygen delivery due to anemia or vasoconstriction.
- Myocardial disease—*infectious, inflammatory, infiltrative, traumatic, neoplastic, or embolic*.
- Acid-base abnormalities.
- Electrolyte derangements—hyperkalemia, hypocalcemia, and hypomagnesemia.
- Hypovolemia.
- Shock.
- Anesthetic agents.
- Sepsis/septic shock.
- CNS trauma.
- Electrical shock.

RISK FACTORS

- Cardiovascular disease.
- Respiratory disease.
- Trauma.
- Anesthesia.
- Septicemia.
- Endotoxemia.
- Ventricular arrhythmias—ventricular tachycardia, R on T phenomenon, multifocal ventricular complexes.
- Increased parasympathetic tone—gastrointestinal disease, respiratory disease, manipulation of eyes, larynx, or abdominal viscera.
- Prolonged seizing.
- Invasive cardiovascular manipulation—pericardiocentesis, surgery, angiography.



DIAGNOSIS

- Sudden cardiovascular collapse associated with inadequate cardiac output leading to severe consequences.
- Quick assessment and diagnosis are critical.
- Assess the ABCs—airway, breathing, circulation.

DIFFERENTIAL DIAGNOSIS

- Severe hypovolemia and absence of palpable pulses.
- Pericardial effusion with cardiac tamponade, decreased cardiac output, and muffled heart sounds.
- Pleural effusion with respiratory arrest.
- Respiratory arrest can be confused with cardiopulmonary arrest (CPA).
- Upper airway obstruction can rapidly progress to CPA.

CBC/BIOCHEMISTRY/URINALYSIS

May help identify underlying cause for CPA, but should not be part of initial triage.

OTHER LABORATORY TESTS

- Arterial blood gas evaluation may be useful during or after resuscitative procedures, but is not part of initial emergency management.
- Venous blood gas evaluation may be more useful during cardiopulmonary resuscitation (CPR) than arterial blood gas and provides electrolyte and lactate concentrations.

IMAGING

- Thoracic/abdominal focused assessment with sonography for trauma (TFAST®/AFAST®) may be useful in identifying underlying disease; additional terminology being introduced, such as POCUS (point of care ultrasound) and eFAST (extended FAST).
- Thoracic or abdominal radiographs or abdominal ultrasound may help identify underlying disease processes, but only consider after patient has been stabilized.
- Echocardiography may confirm pericardial effusion or underlying myocardial disease, but

should not interfere with resuscitative procedures.

DIAGNOSTIC PROCEDURES

Once CPA has developed, continuous ECG monitoring, blood pressure monitoring, pulse oximetry, and capnography are useful in monitoring effectiveness of resuscitative procedures.



TREATMENT

Institute CPR immediately upon diagnosing CPA; CPR in veterinary patients should follow Reassessment Campaign on Veterinary Resuscitation (RECOVER) evidence-based guidelines, published in 2012 and divided into five domains. It is recommended the reader read the original publication.

Basic Life Support (Domain 2)

Immediate Recognition of CPA

If patient is identified as being nonresponsive and apneic, start CPR immediately, do not take time to confirm via palpation of pulse or ECG.

Chest Compressions

- Perform CPR in continuous, uninterrupted, 2-minute cycles when possible.
- Use the cardiac pump in patients weighing <10 kg bodyweight; with the patient in right lateral recumbency, perform compressions directly over the heart (intercostal spaces 3–5); this can be performed using one or two hands.
- Use the thoracic pump for patients weighing >10 kg bodyweight; with the patient in right lateral recumbency, apply thoracic compressions at the widest portion of the thorax.
- Different compression and ventilation regimes have been reported.
- Providing appropriate compressions (100–120 per minute) and appropriate ventilations (10 per minute) without stopping compressions for ventilations and without trying to synchronize ventilations with compressions is the goal; the chest should be displaced ~30–50%.
- Try to minimize discontinuing compressions to interpret ECG.
- Avoid leaning on the patient during chest compressions and allow full chest wall recoil.
- Interposing abdominal compressions between chest compressions enhances cerebral and coronary blood flow by increasing aortic diastolic pressure; this technique has not been shown to improve survival, but should be considered if adequate personnel are available.

Airway and Ventilation

- Visualize the airway by extending the patient's head and neck and pulling the tongue forward; clear any debris (e.g., secretions,

C CARDIOPULMONARY ARREST

(CONTINUED)

C blood, or vomitus) manually or with suction; use of a laryngoscope is advised.

- Establish an airway by either oral endotracheal intubation or, if complete obstruction, emergency tracheostomy.
- Correct endotracheal tube placement should be confirmed visually, by auscultation and/or capnography.
- 10 breaths per minute with a tidal volume of 10 mL/kg and an inspiratory time of 1 second; peak airway pressures should not exceed 20 cm H₂O.
- Techniques for ventilation include mouth to mouth, mouth to nose, or mouth to endotracheal tube; these techniques provide ~16% oxygen; use of a mechanical resuscitator (Ambu® bag) and room air provides 21% oxygen.
- The preferred technique is endotracheal intubation and ventilation with 100% oxygen using an Ambu bag or an anesthesia machine.
- The suggested rate of oxygen administration is 150 mL/kg/minute.

Circulation

- Assessment—palpate peripheral pulses and auscultate heart to confirm CPA.
- External thoracic compression provides at best ~30% of normal cardiac output; internal cardiac compression is two to three times more effective in improving cerebral and coronary perfusion.

Open-Chest CPR

- Indicated if closed-chest CPR is ineffective or preexisting conditions such as flail chest, obesity, diaphragmatic hernia, pericardial effusion, or other significant intrathoracic disease preclude closed-chest techniques.
- Perform through a left thoracotomy at the fifth or sixth intercostal space.
- Perform a pericardectomy.
- The palmar surface of the fingers and thumb is used to push the ventricular blood toward the great vessel; digital compression of the descending aorta may help improve coronary and cerebral perfusion.

Advanced Life Support (Domain 4)

This includes drug therapy and additional resuscitation techniques. Drugs should be administered every other CPR cycle (~q4 minutes).

Epinephrine

- Epinephrine low dose—0.01 mg/kg IV (1 : 10,000) 1 mL/10 kg patient.
- Epinephrine high dose—0.1 mg/kg IV (1 : 1000) can be used in protracted CPR.

Vasopressin

May be used as alternative to epinephrine 0.8 U/kg IV (20 U/ml; ~0.5 mL/10 kg patient); may be used in combination with epinephrine, especially if protracted CPR.

Atropine

- Atropine—0.04 mg/kg IV (0.4 mg/mL) 1 mL/10 kg patient.
- Limited data to suggest benefit unless arrest is due to increased vagal tone.

Fluids

Administer fluids cautiously unless known hypovolemia has led to CPA. Crystalloids, colloids, or blood products may be considered, including Oxyglobin®.



MEDICATIONS

DRUG(S) OF CHOICE

- See Advanced Life Support.
- Administer drugs via intravenous, intraosseous, or intratracheal routes in descending order of preference; volumes should be doubled if administering via the intratracheal route and diluted in saline.
- Intracardiac administration should not be used unless open-chest CPR is being performed; administration of epinephrine into the left ventricle with concurrent digital or mechanical compression of descending aorta is optimal.

PRECAUTIONS

Fluid administration should be used cautiously and only if there is a known history of hypovolemia; excessive fluid administration may lead to decreased coronary perfusion.



FOLLOW-UP

PATIENT MONITORING

- Maintain normal heart rate and blood pressure with fluids and inotropic agents.
- Arterial blood pressure.
- Central venous pressure.
- Blood gas analysis.
- Support respiration with artificial ventilation and supplemental oxygen.
- Neurologic status—if signs of increased intracranial pressure develop, consider mannitol, corticosteroids, and furosemide.
- ECG—continuously.
- Urine output.
- Body temperature.
- Radiograph thorax to assess resuscitative injury.

- Diagnose and correct factors that led to initial CPA.

PREVENTION/AVOIDANCE

Careful monitoring of all critically ill patients.

POSSIBLE COMPLICATIONS

- Vomiting.
- Aspiration pneumonia.
- Fractured ribs or sternebrae.
- Pulmonary contusions and edema.
- Pneumothorax.
- Acute renal failure.
- Neurologic deficits.
- Cardiac arrhythmias.

EXPECTED COURSE AND PROGNOSIS

- Prognosis depends on underlying disease process.
- Rapid return to spontaneous cardiac and respiratory function improves the prognosis.
- Overall prognosis is poor; <10% of patients are discharged.



MISCELLANEOUS

ZOONOTIC POTENTIAL

None

SYNOMYMS

- For CPA—cardiac arrest, heart attack.
- For CPR—cardiopulmonary cerebral resuscitation (CPCR).

SEE ALSO

- Ventricular Fibrillation.
- Ventricular Standstill (Asystole).

ABBREVIATIONS

- CPA = cardiopulmonary arrest.
- CPCR = cardiopulmonary cerebral resuscitation.
- CPR = cardiopulmonary resuscitation.
- FAST = focused assessment with sonography for trauma.
- POCUS = point of care ultrasound.
- RECOVER = Reassessment Campaign on Veterinary Resuscitation.

Suggested Reading

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McIntyre RL, Hopper K, Epstein SE, et al. Assessment of cardiopulmonary resuscitation in 121 dogs and 30 cats at a university teaching hospital (2009–2012). J Vet Emerg Crit Care 2014, 24(6):693–704.

Author Steven L. Marks

Consulting Editor Michael Aherne

CATARACTS

C



BASICS

DEFINITION

Opacification of the lens (focal or diffuse).

PATHOPHYSIOLOGY

- The normal lens is composed of perfectly aligned lens fibers that create a transparent structure. A clear capsule surrounds the cortex and nucleus. New lens fibers are continually produced at the equator of the lens cortex throughout life. The aqueous humor provides nutrition to the lens.
- A cataract occurs when there is derangement of lens fibers due to changes in lens nutrition, energy metabolism, protein synthesis or metabolism, or osmotic balance.
- Anterior uveitis is a common cause of altered lens nutrition.
- Genetics can result in altered protein and energy metabolism, or protein synthesis, in the lens.
- Diabetes mellitus affects the osmotic balance in the lens. Hyperglycemia increases glucose in the aqueous and lens overwhelming the glycolysis pathway; glucose is shunted to the sorbitol pathway; sorbitol creates an osmotic gradient that draws water into the lens and rapid cataract formation. The sorbitol pathway requires aldose reductase enzyme and dogs have more aldose reductase than cats, making cats more resistant to developing diabetic cataracts. The enzyme levels vary between individuals, which may explain dogs that are resistant to cataract development.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- Inheritance has been established for many dog breeds; the most common mode of inheritance is autosomal recessive.
- Inheritance has been established in the Himalayan cat (autosomal recessive).

INCIDENCE/PREVALENCE

- One of the leading causes of blindness in dogs.
- The prevalence of genetic cataracts varies significantly; up to 10% in some breeds.
- Most diabetic dogs will develop cataracts regardless of their diabetic control.
- Cataracts are rare in cats.

SIGNALMENT

Species

Dogs and cats.

Breed Predilections

Over 135 dog breeds are suspected as being predisposed to hereditary cataracts.

Mean Age and Range

Cataracts can develop at any age; genetic cataracts can develop as early as 6 months of age.

SIGNS

Historical Findings

- Cloudy/white appearance of the lens.
- Vision loss when the cataracts are bilateral and diabetic cataracts with a rapid, bilateral onset.
- Polyuria/polydipsia is noticed prior to cataract development in diabetic dogs.

Physical Examination Findings

- General physical examination findings—unremarkable unless the dog is an undiagnosed diabetic.
- Ophthalmic examination findings—opacification in one or both lenses.
 - Incipient stage—small, focal opacity/opacities in the lens that does not interfere with the view of the fundus; no vision deficits.
 - Immature stage—diffusely cloudy appearance to the lens with the tapetal reflection still visible and some portions of the fundus visible through a dilated pupil; the menace reflex is positive.
 - Mature stage—completely opaque lens with no tapetal reflection visible; blind.
 - Hypermature stage—wrinkled lens capsule, areas of dense white mineralization, may have portions of liquefied cortex (white, sparkly to clear); deep anterior chamber; blind unless there is a large area of clear liquefied cortex.
 - Intumescent mature cataract—opaque, swollen lens usually due to the hyperosmotic effect of diabetes; shallow anterior chamber.

CAUSES

- Hereditary—most common cause in dogs.
- Diabetes mellitus.
- Anterior uveitis—either by altered nutrition of the lens from the abnormal aqueous, or by posterior synechia and inflammatory debris causing opacification of the anterior lens capsule.
- Trauma—perforating injury that disrupts the anterior lens capsule, most commonly a cat claw injury, especially in puppies and kittens.
- Senile—slowly progressive cataract in geriatric animals, usually beginning as dense nuclear sclerosis followed by gradual spoke-like opacities extending into the cortex.
- Congenital—due to heredity, in utero insult, or associated with other congenital ocular anomalies such as persistent pupillary membranes, persistent hyperplastic primary vitreous/persistent tunica vasculosa lentis, or a hyaloid artery attachment.
- Surgery—transpupillary laser energy, intraocular instrument trauma.
- Toxic—long-term ketoconazole therapy; suspected secondary to toxic by-products of degenerating photoreceptors in dogs with progressive retinal atrophy.
- Radiation—when the eye is in the radiation treatment field for neoplasia of the mouth or head.

- Hypocalcemia—can cause bilateral, diffuse punctate or incipient cataracts.
- Nutritional—use of unbalanced milk replacers in bottle-fed puppies and kittens.
- Electrical shock—chewing electrical cords or lightning strike.

RISK FACTORS

- Diabetes mellitus (dogs).
- Chronic anterior uveitis.
- Progressive retinal atrophy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Lenticular nuclear sclerosis—normal aging change in the lens of dogs and cats starting at 6 years of age due to compression of older lens fibers in the center of the lens; gradually becomes more visible with age and can be mistaken for a cataract in geriatric patients; definitive diagnosis can be made using mydriasis (1% tropicamide) and the observation of a perfectly round, bilaterally symmetric, homogeneous nucleus in the center of each lens, and the ability to view the fundus through the lens; vision is rarely affected and treatment is not indicated.

CBC/BIOCHEMISTRY/JRINALYSIS

Dogs with diabetic cataracts may have hyperglycemia and glucosuria.

IMAGING

Ocular ultrasound can be used to evaluate the posterior lens capsule for any sign of rupture and can evaluate for retinal detachment prior to cataract surgery.

DIAGNOSTIC PROCEDURES

ERG is performed prior to cataract surgery to evaluate for retinal degeneration when the fundus is not visible due to the cataract.



TREATMENT

ACTIVITY

For safety, blind animals should not be allowed access to an in-ground swimming pool or elevated decks with open railings; use caution near stairs; restrict outside activity to fenced yards or leash walks.

CLIENT EDUCATION

- Cataract surgery is routinely performed, with an overall 80–90% success rate.
- Once the cataracts are removed they cannot return.
- Artificial lens implants will restore essentially normal vision.
- Evaluation for surgery should be done early in the course of cataract development to avoid complications that may result in the cataract becoming inoperable, to allow time to plan

CATARACTS

C

for the surgery, and in some cases to eliminate the need and extra cost for an ocular ultrasound and ERG.

SURGICAL CONSIDERATIONS

- Phacoemulsification (removal of the cataract through a corneal incision using ultrasonic waves to emulsify and aspirate the lens) is the most common technique for cataract removal.
- The ideal time for cataract surgery is the immature/early mature stage.
- Inherited, diabetic, and senile cataracts are potentially good candidates for surgery; cataracts secondary to anterior uveitis are normally poor surgical candidates.
- Artificial intraocular lenses are routinely placed inside the patient's lens capsule; lens implants restore normal focus and help minimize posterior capsular fibrosis; if a lens cannot be implanted (e.g., due to an unstable lens capsule or luxated lens), the dog or cat will still have functional vision.
- Traumatic lens perforation with release of lens cortex into the anterior chamber may require surgery to remove the lens, depending on the size of the capsular tear.



MEDICATIONS

DRUG(S) OF CHOICE

- Topical anti-inflammatory medication is recommended q6–24h to help prevent or treat lens-induced uveitis with immature, mature, and hypermature cataracts; this can be a topical nonsteroidal anti-inflammatory drug (NSAID) such as flurbiprofen, diclofenac, or ketorolac, or a topical steroid such as prednisolone acetate 1% or dexamethasone 0.1%; topical NSAIDs may be preferable in diabetic patients.
- Topical atropine q8–24h is indicated for lens-induced uveitis; *contraindicated with glaucoma*.
- Oral NSAIDs (carprofen, meloxicam, deracoxib) are also used to treat lens-induced uveitis.
- Topical antioxidants are advertised as able to reverse cataract changes; to date there have

been no published data conclusively showing a significant reversal, or delay in progression; time spent trying medical therapy will delay evaluation for surgery, resulting in surgery being performed at a suboptimal stage, or complications from the cataract making it inoperable.

- A topical aldose reductase inhibitor, Kinostat®, is in the final stage of FDA approval. When made available, it may prove helpful in delaying the onset of diabetic cataracts in dogs.



FOLLOW-UP

PATIENT MONITORING

- Incipient or early immature cataracts should be monitored regularly for progression in order to select the ideal time for surgery and to avoid complications associated with cataracts.
- Postoperative monitoring by the surgeon is critical for the success of surgery and should be clearly discussed with the owner prior to surgery.

PREVENTION/AVOIDANCE

Do not breed animals with cataracts.

POSSIBLE COMPLICATIONS

- Lens-induced uveitis—associated with hypermature cataracts and cataracts that progress rapidly; caused by antigenic lens proteins leaking through the lens capsule. Clinical signs can be subtle (e.g., low intraocular pressure) to extreme (granulomatous uveitis with aqueous flare, miosis, synechia, keratic precipitates); preoperative uveitis increases postoperative complications.
- Secondary glaucoma—impaired aqueous outflow from intraocular changes associated with lens-induced uveitis, or from an intumescent cataract causing a forward displacement of the iris, narrowing the iridocorneal angle.
- Retinal detachment—associated with hypermature cataracts and cataracts in young dogs with a rapid onset and cortical liquefaction.
- Lens luxation—associated with hypermature cataracts in which the lens and capsule shrink,

causing the zonules to stretch and break, resulting in a lens subluxation or luxation.

EXPECTED COURSE AND PROGNOSIS

- Most cataracts are progressive, although the rate of progression can vary widely depending on age, breed, and location of the cataract.
- Long-term prognosis following cataract surgery is very good; however, some patients have increased risk for postoperative complications.
- Those that do not pursue surgery should be monitored for uveitis and glaucoma.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Retinal detachment.
- Lens-induced uveitis.
- Congenital ocular anomalies.

AGE-RELATED FACTORS

- Immediate referral for cataracts in young dogs (<2 years of age) is recommended because the cataract can progress very rapidly, with partial cortical liquefaction followed by retinal detachment.
- Nuclear sclerosis is prominent in geriatric animals; a dilated exam may be necessary to definitively distinguish nuclear sclerosis from cataract.

SEE ALSO

- Anterior Uveitis—Cats.
- Anterior Uveitis—Dogs.
- Diabetes Mellitus Without Complication—Cats.
- Diabetes Mellitus Without Complication—Dogs

ABBREVIATION

- NSAID = nonsteroidal anti-inflammatory drug.

Author Margi A. Gilmour

Consulting Editor Katheren E. Myrna



Client Education Handout
available online

CEREBROVASCULAR ACCIDENTS

(CONTINUED)

C kidney disease, or hypothyroidism. • Single hemorrhagic lesion—most often associated with *Angiostrongylus vasorum*. • Multiple hemorrhagic lesions ≥ 5 mm—most often associated with *Angiostrongylus vasorum*, primary extracranial neoplasia with metastases (haemangiosarcoma).

DIAGNOSTIC PROCEDURES

Diagnosis of potential underlying causes.

Ischemic Stroke

Evaluate for hypertension (and potential underlying causes), endocrine disease (hyperadrenocorticism, hypothyroidism, hyperthyroidism, diabetes mellitus), chronic kidney disease (especially protein-losing nephropathy), protein-losing enteropathy, heart disease, and metastatic diseases (particularly hemangiosarcoma).

Hemorrhagic Stroke

Evaluate for coagulopathy (and potential underlying causes), hypertension (and potential underlying causes), and metastatic diseases (particularly hemangiosarcoma).

PATHOLOGIC FINDINGS

Ischemic Stroke

- Ischemic necrosis centered on gray matter due to selective vulnerability. • Lesions limited to brain area vascularized by the affected vessel with sharply demarcated borders; normal surrounding brain tissue; minimal to no mass effect. • Global brain ischemia usually affects a dense area of selectively vulnerable neurons; specific anatomic areas including cerebral cortex, hippocampus, certain basal nuclei (e.g., caudate nuclei), thalamus, and cerebellar Purkinje cell layers are more susceptible to hypoxic injury. • Early ischemic cell changes occur rapidly and are a result of energy deprivation with swelling of the mitochondria and endoplasmic reticulum, which causes cytoplasmic microvacuolation; more chronic lesions are characterized by postnecrotic atrophy of the brain parenchyma, endothelial proliferation in viable capillaries, and accumulation of Gitter cells.

Hemorrhagic Stroke

- Parenchymal bleeding results from rupture of the small penetrating brain arteries; most acute cases reveal fresh hemorrhage and acute neuronal necrosis that is slowly removed by macrophages, leaving over time a cystic cavity lined by fibrillary astrocytes. • Histology is characterized by presence of edema, neuronal damage, macrophages, and neutrophils in the region surrounding the hematoma. • While some cerebral hemorrhages stop quickly as a result of clotting and tamponade by the surrounding regions, others tend to expand over time; the latter is a result of continued bleeding from the primary source and to the mechanical disruption of surrounding vessels;

the hemorrhage spreads between planes of white matter cleavage with minimal destruction, leaving nests of intact neural tissue within and surrounding the hematoma.



TREATMENT

NURSING CARE

Ischemic Stroke

- Monitoring and correction of basic physiologic variables (e.g., oxygen level, fluid balance, blood pressure, body temperature). • Maintenance of systemic arterial blood pressure within physiologic range; aggressive lowering of blood pressure should be avoided during acute stages unless the patient is at high risk of end-stage organ damage (systolic blood pressures >180 mmHg); hypertension can develop as a physiologic response to a stroke to ensure adequate cerebral perfusion pressure; elevated blood pressure can persist for up to 72 hours after the onset of injury.
- No evidence that glucocorticoid provides beneficial neuroprotection; most neuroprotective agents tested have either failed to prove their efficacy in clinical trials or are awaiting further investigation.

Hemorrhagic Stroke

- Patient stabilization (airway protection, monitoring and correction of vital signs).
- Assessment and monitoring of neurologic status. • Determination and treatment of potential underlying causes of hemorrhage.
- Assessment for the need of specific treatment measures including management of raised ICP, which revolves around reducing cerebral edema, optimizing cerebral blood volume, and eliminating space-occupying mass. • Risk of neurologic deterioration and cardiovascular instability highest during the first 24 hours after onset of intracranial hemorrhage, as the space-occupying lesion slowly expands and cerebral vasogenic edema develops.



MEDICATIONS

DRUG(S) OF CHOICE

Ischemic Stroke

- Antihypertensive—consider if systemic BP >180 mmHg on serial evaluation and/or severe ocular manifestations of hypertension.
- Angiotensin-converting enzyme (ACE) inhibitor—enalapril (0.25–0.5 mg/kg q12h) or benazepril (0.25–0.5 mg/kg q12h) and/or calcium channel blockers such as amlodipine (0.1–0.25 mg/kg q24h); amlodipine is more effective in severe hypertension. • Prevention of clot formation—consider in proven cardiac sources of embolism; antiplatelet therapy with low-dose aspirin (0.5 mg/kg PO q24h) or

clopidogrel (2–4 mg/kg PO q24h) and low molecular weight heparin can be used prophylactically; low molecular weight heparin 80–150 IU/kg SC can be used in suspected or confirmed case of hypercoagulable state; anti-factor Xa activity should be monitored, although this may not be practical.

Hemorrhagic Stroke

Mannitol—if suspected elevated ICP unresponsive to extracranial stabilization measures (0.25–2 g/kg IV over 10–20 min up to q4-8h).



FOLLOW-UP

PATIENT MONITORING

Frequent neurologic evaluations in the first 48–72 hours to monitor progress.

EXPECTED COURSE AND PROGNOSIS

- Maximum severity of signs usually reached within 24h for ischemic stroke. • Resolution of signs—gradual within 2–10 weeks; some dogs/cats may be left with permanent neurologic signs due to irreversible brain damage. • Dogs with causal medical condition significantly more likely to relapse and have significant shorter survival time than dogs with no identifiable medical condition. • Despite having a high likelihood of concurrent disease, cat with ischemic stroke have been reported to have a favorable short-term outcome, if neither clinical presentation nor concurrent disease was severe. • Prognosis for global brain ischemia difficult to predict as there are no controlled studies.



MISCELLANEOUS

SYNOMYMS

Stroke

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- CVA = cerebrovascular accident. • DWI = diffusion-weighted imaging. • FLAIR = fluid-attenuated inversion recovery. • ICP = intracranial pressure. • MRA = magnetic resonance angiography. • TIA = transient ischemic attack.

Suggested Reading

Lowrie M, De Risio L, Dennis R, et al. Concurrent medical conditions and long-term outcome in dogs with nontraumatic intracranial hemorrhage. Vet Radiol Ultrasound, 2012, 53:381–388.

Whittaker DE, Drees R, Beltran E. MRI and clinical characteristics of suspected cerebrovascular accident in nine cats. J Feline Med Surg, 2017, 20:674–684.

Author Laurent Garosi

CERUMINOUS GLAND ADENOCARCINOMA, EAR



BASICS

OVERVIEW

- Most common primary malignant tumor of the external ear canal, arising from modified apocrine sweat glands (ceruminous glands).
- Often locally invasive, but associated with a low metastatic rate.

SIGNALMENT

- Uncommon overall, but the most common malignant tumor of the ear canal in both dogs and cats, followed by carcinoma of undetermined origin and squamous cell carcinoma.
- Cocker spaniels and German shepherd dogs are overrepresented.
- Mean age—dogs, 10 years; cats, 11 years.
- No known sex predisposition.

SIGNS

- Progressive hearing loss.
- Similar to chronic, recurrent otitis externa—discharge, odor, pruritus, inflammation.
- Early appearance—pale pink, friable, ulcerative, bleeding nodular mass(es) within the external ear canal.
- Late appearance—large mass(es) filling the canal and invading through canal wall into surrounding structures.
- Regional lymph node enlargement.
- Neurologic signs (vestibular signs, Horner's syndrome) may be present secondary to middle ear involvement.
- Signs of pain and discomfort; pain upon opening the mouth.

CAUSES & RISK FACTORS

Chronic inflammation and ceruminous gland hyperplasia/dysplasia appear to play a role in tumor development.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Proliferative chronic otitis externa with ceruminous gland hyperplasia.
- Inflammatory polyps.
- Other tumors including squamous cell carcinoma, basal cell tumor, mast cell tumor, papilloma, sebaceous gland tumor, ceruminous gland adenoma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

- Ear swab cytology for bacteria and yeast.
- Bacterial culture and sensitivity as needed.

IMAGING

- Skull radiography to assess potential involvement of the tympanic bulla, but this is

difficult to interpret due to superimposition of bones in the skull.

- Thoracic radiography to evaluate for pulmonary metastasis.
- CT or MRI is most useful for loco-regional staging and before surgery and radiation therapy, providing greater detail than with radiographs.

DIAGNOSTIC PROCEDURES

- Cytologic examination of aspirate from regional lymph nodes.
- Cytologic examination of fine-needle aspirate from mass.
- Biopsy and histopathology.

PATHOLOGIC FINDINGS

- Cytology from fine-needle aspirate—round to polygonal epithelial cells arranged both singly and in large clusters with deep blue to lavender-gray cytoplasm and a variable quantity of black, intracytoplasmic granular material; unable to differentiate adenocarcinoma from adenoma consistently with cytology.
- Histopathologic characteristics—apocrine type differentiation from ceruminous glands and local invasion into stroma; neoplastic cells show moderate to marked nuclear atypia with frequent mitotic figures.



TREATMENT

- Total ear canal ablation and lateral bulla osteotomy (TECABO) is the preferred surgical approach over lateral ear resection.
- Radiation therapy may be considered for either large (palliative intent) or incompletely excised masses (curative intent).



MEDICATIONS

DRUG(S) OF CHOICE

- Chemotherapy not evaluated, but occasionally considered based on histologic information and clinical staging results.
- Multimodal therapy incorporating corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs) and other analgesics.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

- Physical examination and thoracic radiography at regular intervals following

therapy (every 3–4 months) is recommended for the first year postoperatively.

- Serial CT or MRI to monitor for local tumor regrowth may be recommended.

POSSIBLE COMPLICATIONS

- Permanent or transient Horner's syndrome secondary to surgery.
- Permanent or transient facial paralysis following surgery (more frequent in cats).

EXPECTED COURSE AND PROGNOSIS

- Median survival after lateral ear resection is around 10 months for both dogs and cats.
- Median survival after TECABO is >3 years in both dogs and cats.
- Median survival after radiation therapy is >3 years, but published information is on small numbers only.
- Poor prognosis associated with extensive tumor involvement (advanced stage), preoperative neurologic signs, and conservative therapy (e.g., lateral ear canal ablation alone).



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Otitis externa.
- Peripheral vestibular disease, Horner's syndrome.
- Chronic pain.

ABBREVIATIONS

- NSAID = nonsteroidal anti-inflammatory drug.
- TECABO = total ear canal ablation and bulla osteotomy.

Suggested Reading

Bacon NJ, Gilbert RL, Bostock DE, White RA. Total ear canal ablation in the cat: indications, morbidity and long-term survival. J Small Anim Pract 2003; 44:430–434.

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Acknowledgment The author and book editors acknowledge the prior contribution of Louis-Philippe de Lorimier.

CHAGAS DISEASE (AMERICAN TRYPANOSOMIASIS)

C



BASICS

OVERVIEW

- Caused by hemoflagellate protozoan *Trypanosoma cruzi*.
- Transmission through contact with infected feces of the Reduviid ("kissing") bug, ingestion of bug vector, through blood transfusion, or vertical transmission to offspring.
- After multiplication at entry site (5 days postinfection [PI]), hematogenous spread to heart, brain, and other organs.
- Maximal parasitemia at 14 days PI; associated with acute myocarditis and (less commonly) encephalitis.
- Infection becomes subpatent 30 days PI.
- Dogs then enter long asymptomatic period (months to years); subset develop cardiomyopathy.
- South and Central America—endemic in humans and pets; infected animals are sentinels for human risk.
- United States—in southern states with infected vectors and reservoir hosts (raccoons, opossums, armadillos, mice, rats, squirrels).

SIGNALMENT

- Dogs of any age, breed:
 - Acute infection—more severe in dogs <2 years old.
 - Chronic infection—adults.
 - Sporting breeds and outdoor-housed dogs more likely to be in contact with vectors or reservoir host.
- Cats—more recent evidence of infection and organ pathology.

SIGNS

General Comments

Two syndromes can be difficult to distinguish—acute myocarditis/encephalitis and chronic arrhythmias and myocardial dysfunction.

Historical Findings

- Lethargy, weakness.
- Anorexia.
- Abdominal distension (ascites).
- Cough, dyspnea.
- Syncope, sudden death.
- Ataxia, seizures.

Physical Examination Findings

- Tachy- or bradyarrhythmia.
- Heart murmur.
- Congestive heart failure (tachypnea, dyspnea, ascites).
- Hepatomegaly.
- Generalized lymphadenopathy (acute).
- Neurologic—weakness, ataxia, seizures (acute).

CAUSES & RISK FACTORS

Lives in or travels to endemic area.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cardiomyopathy.
- Congenital heart defect (tricuspid valve dysplasia).
- Myocarditis.
- Distemper, other causes of meningo-encephalitis.

CBC/BIOCHEMISTRY/URINALYSIS

Generally normal.

OTHER LABORATORY TESTS

- Cardiac troponin I—elevation indicates myocardial damage.
- Serology—presence of *T. cruzi* serum antibodies (present by 16 days PI) confirms infection, but not necessarily clinical disease.
- Tests can cross-react with *Leishmania*.
- Cytology—tryomastigote (blood form) occasionally on blood smear, lymph node aspirate, abdominal effusion, or buffy coat during period of high parasitemia.
- Cytology—amastigote (intracellular form) identified on lymph node aspirate or impression.
- PCR—detect parasite DNA in blood or tissue with high specificity; low sensitivity in chronic stage if parasite levels low.

IMAGING

- Thoracic radiography—cardiomegaly, pulmonary edema, pleural effusion.
- Echocardiography—dilation of heart chambers, systolic dysfunction.

DIAGNOSTIC PROCEDURES

ECG

- Supraventricular and ventricular arrhythmias, atrioventricular block (any degree), bundle branch block.
- Ambulatory ECG (Holter) to document abnormalities.

PATHOLOGIC FINDINGS

- Acute—diffuse granulomatous myocarditis, myocardial necrosis, parasitic pseudocysts with intracellular amastigotes.
- Chronic—lymphoplasmacytic inflammation, loss of myocardial fibers, severe interstitial fibrosis.
- *T. cruzi* amastigotes in heart, lymph nodes, liver, spleen, brain.



TREATMENT

- No currently approved treatment for *T. cruzi*.
- Manage heart failure (see Congestive Heart Failure, Left-Sided; Congestive Heart Failure, Right-Sided).
- Tachyarrhythmias—anti-arrhythmic drugs.
- Bradyarrhythmias—pacemaker implantation.

Client Education

- Test housemates/littermates of infected dogs.
- Take measures to eliminate the insect vector—remove brush, pyrethroid insecticide.
- Alert owner to possible zoonotic risk and potential for sudden death.
- Infected female can transfer infection to offspring.
- Cardiology tests (ECG, echocardiography) can identify dogs at risk of developing clinical signs or sudden death.



MEDICATIONS

DRUG(S) OF CHOICE

Limited therapeutic options for treating infection. Variable clinical response to Benznidazole; treated dogs still develop myocardial damage. Other drug protocols under investigation.



FOLLOW-UP

- Monitor positive dogs for clinical disease.
- Prognosis unknown for asymptomatic, positive dogs.
- Dogs with clinical signs or arrhythmias have guarded prognosis.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Public health concern with limited treatment options.
- Risk of human acquiring infection directly from infected dog is low, but infected animal indicates presence of infected vectors or reservoir hosts.

ABBREVIATIONS

- PI = postinfection.

Internet Resources

<https://www.cdc.gov/parasites/chagas>

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Acknowledgment The author and book editors acknowledges the prior contribution of Stephen C. Barr.

CHLAMYDIOSIS—CATS

C



BASICS

DEFINITION

A chronic respiratory infection of cats caused by an intracellular bacterium, characterized by mild to severe conjunctivitis, mild upper respiratory signs, and mild pneumonitis.

PATHOPHYSIOLOGY

- *Chlamydophila felis* (previously *Chlamydia psittaci* var. *felis*)—a Gram-negative, obligate intracellular bacterium spread through close contact, aerosolization, or genital contact during parturition.
- Replicates on the mucosa of the upper and lower respiratory epithelium; produces a persistent commensal flora that causes local irritation, resulting in mild upper and lower respiratory signs and conjunctivitis; can also colonize the mucosa of the gastrointestinal and reproductive tracts.
- Incubation period—7–10 days (longer than that of other common feline respiratory pathogens).

SYSTEMS AFFECTED

- Gastrointestinal—cat: infection without clinical disease; other species: may have clinical gastroenteritis.
- Ophthalmic—acute or chronic conjunctivitis, unilateral often progresses to bilateral.
- Reproductive—infection without clinical disease.
- Respiratory—mild rhinitis, bronchitis, and bronchiolitis.

GENETICS

None

INCIDENCE/PREVALENCE

- Incidence of clinical disease—sporadic; outbreaks of respiratory disease may occur, especially in multicut facilities.
- Prevalence of *C. felis* in the feline population: ~5–10% chronically infected.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

- Cat
- Human

Breed Predilections

None

Mean Age and Range

Usually cats >8 weeks and <1 year of age; any age of cat possible.

Predominant Sex

None

SIGNS

General Comments

- Commonly associated with feline conjunctivitis.

- Infection often subclinical.
- Clinical disease—commonly coinfection with other organisms, such as feline herpesvirus (FHV) and feline coronavirus (FCV).

Historical Findings

- Primarily signs of ocular discharge, blepharospasm.
- Mild upper respiratory infection, with possible sneezing and oculonasal discharge.
- Varying degrees of anorexia, lethargy.
- Lameness possible (uncommon).

Physical Examination Findings

- Conjunctivitis—unilateral or bilateral chemosis, blepharospasm, conjunctival and third eyelid hyperemia; serous to mucopurulent discharge without keratitis.
- Mild nasal discharge.
- Fever.
- Dyspnea and cough extremely unlikely; rales with pneumonitis.

CAUSES & RISK FACTORS

- Concurrent infections with other respiratory pathogens (FHV, FCV, *Bordetella bronchiseptica*, *Mycoplasma felis*).
- Lack of vaccination.
- Multicut facilities, especially adoption shelters and breeding catteries.
- Stress.
- Presence of asymptomatic shedders.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Feline herpesvirus infection—short incubation period (4–5 days), rapid bilateral conjunctivitis, severe sneezing, and ulcerative keratitis.
- Feline calicivirus infection—short incubation period (3–5 days), ulcerative stomatitis, and potentially pneumonia.
- *Mycoplasma felis*.

CBC/BIOCHEMISTRY/URINALYSIS

Leukocytosis possible.

IMAGING

Thoracic radiographs—consolidation of lung tissue with pneumonia.

DIAGNOSTIC PROCEDURES

- PCR—preferred; best sensitivity; submit conjunctival swab in a sterile red top tube with a small amount of sterile saline.
- Culture—obtain conjunctival swab with vigorous exfoliation and submit on ice within 24 hours in special transport media such as 2-sucrose-phosphate (2-SP).
- Conjunctival cytology—characteristic intracytoplasmic basophilic inclusions may be seen with Giemsa staining early in disease.
- Serum antibody titers—limited diagnostic value.
- ELISA kits—variable sensitivity and specificity.

PATHOLOGIC FINDINGS

- Gross—chronic conjunctivitis with mucopurulent ocular discharge; minor rhinitis with nasal discharge; sometimes lung changes indicative of pneumonitis.
- Histopathologic (conjunctiva)—an early intense infiltration of neutrophils; inflammatory response changes to lymphocytes and plasma cells; inclusions detected with special stains (inclusions invisible with routine H&E stains).



TREATMENT

APPROPRIATE HEALTH CARE

Generally outpatient.

NURSING CARE

- Clean eyes and nose as necessary with warm water or saline.
- Provide access to steam, such as in a bathroom, to clear secretions.
- Provide palatable, soft foods; warming food can improve cat's olfaction.
- Generally does not require other supportive therapy (e.g., fluids), unless complicated by concurrent infections.

ACTIVITY

- Quarantine affected cats from contact with other cats.
- Do not allow affected cats to go outside.

DIET

- No restrictions.
- Special diets—to entice anorectic cats to resume eating.

CLIENT EDUCATION

Inform clients of the causative organism, the anticipated chronic course of disease, and the opportunity to vaccinate other cats before exposure.



MEDICATIONS

DRUG(S) OF CHOICE

- Ophthalmic ointments—usually beneficial; oxytetracycline 3–4 times daily for 3 weeks; preparations with polymyxin may be irritating for cats; alternatively erythromycin or fluoroquinolone ointment; resistant to bacitracin, neomycin, gentamicin.
- Systemic antibiotics—tetracyclines are antibiotic of choice; doxycycline (10 mg/kg PO q24h or 5 mg/kg PO q12h for 4 weeks to prevent recrudescence); amoxicillin-clavulanate (20–25 mg/kg PO q12h) as alternative for young kittens.

CONTRAINDICATIONS

Tetracyclines—risk for esophagitis; may affect growing teeth of young kittens.

(CONTINUED)

CHLAMYDIOSIS—CATS

C

PRECAUTIONS

Colonies/shelters/breeding catteries—all cats may have to be treated; treatment should be continued for 4 weeks.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None

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

Monitor for improved health as treatment proceeds.

PREVENTION/AVOIDANCE**Vaccines**

- Both inactivated and modified live vaccines available.
- Vaccines do not prevent infection; rather, they reduce severity and duration of clinical disease.
- American Association of Feline Practitioners—noncore vaccine; for at-risk cats, give a single vaccination at initial visit as early as 9 weeks of age, repeat in 3–4 weeks; revaccinate annually where *C. felis* is endemic.
- Adverse vaccine reactions—mild clinical disease with modified live vaccines in small percentage of vaccinated cats.

Environmental Management

- Quarantine affected cats by >4 ft perimeter.
- Practice appropriate hygiene and beware of fomites.
- C. felis* readily inactivated with common disinfectants.

POSSIBLE COMPLICATIONS

- If kittens are affected <2 weeks of age, eyelids may need to be surgically opened to allow for drainage of purulent material (ophthalmia neonatorum).

- If entire course of antibiotics are not completed, persistently infected cats can become asymptomatic shedders.
- Coinfections increase morbidity.

EXPECTED COURSE AND**PROGNOSIS**

- Without treatment, tends to be chronic, lasting for several weeks or months.
- Prognosis good with appropriate antibiotic therapy.
- Improvement in 1–2 days with therapy; 28 days of treatment needed to clear organism.
- Look for coinfections if not improving as expected.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Affected cats may be concurrently infected with FHV or FCV, especially in multicat and breeding facilities.

AGE-RELATED FACTORS

Primarily a disease of young cats.

ZOONOTIC POTENTIAL

C. felis can infect humans, especially immunocompromised individuals; limited number of reports of mild conjunctivitis in humans transmitted from infected cats.

PREGNANCY/FERTILITY/BREEDING

- Endemic breeding catteries—treat all cats with doxycycline for at least 4 weeks; then vaccinate.
- Role of *C. felis* as a pathogen during pregnancy—unclear; can colonize the reproductive mucosa; severe ophthalmia neonatorum can occur in neonatal kittens infected at or shortly after birth.

SYNOMYS

Feline pneumonitis.

SEE ALSO

- Conjunctivitis—Cats.
- Feline Calicivirus Infection.
- Feline Herpesvirus Infection.
- Feline (Upper) Respiratory Infections.
- Mycoplasmosis.
- Ophthalmia Neonatorum.

ABBREVIATIONS

- 2-SP = 2-sucrose-phosphate.
- FCV = feline calicivirus.
- FHV = feline herpesvirus.

INTERNET RESOURCES

<http://www.abcdcatsvets.org/chlamydia-chlamydophila-felis>

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Fred W. Scott.



**Client Education Handout
available online**

C CHOCOLATE TOXICOSIS



BASICS

DEFINITION

- Chocolate, derived from the seed of the *Theobroma cacao* plant, contains the naturally occurring methylxanthine alkaloids theobromine and caffeine.
- Excessive intake can lead to dose-dependent gastroenteric, cardiac, and neurologic toxicosis.
- Theobromine is the largest fraction of methylxanthines in chocolate products; lower concentration of caffeine is present (Table 1). Other sources of methylxanthines include coffee, tea, diet pills, over-the-counter (OTC) stimulants, and herbal medications.

PATOPHYSIOLOGY

- Variably absorbed orally (caffeine <1 hour; theobromine 10 hours), metabolized by liver, undergo enterohepatic recirculation; metabolites primarily excreted via urine and may be reabsorbed from urinary bladder.
- Estimated theobromine and caffeine half-lives in dogs 17.5 hours and 4.5 hours, respectively.
- Methylxanthines inhibit phosphodiesterase to increase intracellular cyclic adenosine monophosphate (cAMP), stimulate catecholamine release, and increase intracellular calcium, which results in vasoconstriction, increased myocardial and skeletal muscle contractility, and CNS stimulation.
- Toxic dosages:
 - Theobromine—LD₅₀ (dog) 250–500 mg/kg; LD₅₀ (cat) 200 mg/kg. Mild signs (agitation, vomiting, diarrhea): 20 mg theobromine/kg. Moderate signs (tachycardia): 40–50 mg theobromine/kg. Severe signs (seizures): 60 mg theobromine/kg.
 - Caffeine—LD₅₀ (dog) 140 mg/kg; LD₅₀ (cat) 80–150 mg/kg. Clinical signs: >15 mg caffeine/kg. Moderate signs: >25 mg caffeine/kg. Cardiotoxic signs: >50 mg caffeine/kg.
 - Several aids to assess canine risk from chocolate can be found online—see Internet Resources.

SYSTEMS AFFECTED

- Cardiovascular—tachycardia, hypertension, ventricular premature contractions (VPCs), other tachyarrhythmias, bradycardia (rare).
- Gastrointestinal (GI)—vomiting, diarrhea, regurgitation.
- Metabolic—hypokalemia, hyperthermia, dehydration.
- Nervous—agitation, tremors, seizures, ataxia, muscle rigidity, hyperreflexia.
- Renal/urologic—polyuria, polydipsia.
- Respiratory—panting, tachypnea, cyanosis, respiratory failure.

INCIDENCE/PREVALENCE

- Dogs—among 10 most common poisonings reported by small animal practices and animal poison control centers.
- More common at holidays when chocolate products readily available.

GEOGRAPHIC DISTRIBUTION

Indoor dogs at risk owing to closer proximity to chocolate products.

SIGNALMENT

Species

- Dogs most frequently poisoned based on proximity to methylxanthine products and propensity for dietary indiscretion leading to excessive ingestion.
- Cats rarely affected.

Breed Predilections

- Small dogs may be at higher risk due to smaller body weight relative to amount of chocolate consumed.
- Breeds prone to dietary indiscretion, such as Labrador retrievers.

SIGNS

Historical Findings

- History of ingestion.
- Evidence of chewed packaging.
- Vomiting and diarrhea—vomit often contains evidence of chocolate and may be first sign noted.
- Early restlessness and hyperactivity.
- Polydipsia.

Physical Examination Findings

- Physical exam may be normal after recent ingestion (<1–2 hours).
- Vomiting.
- Diarrhea.
- Restlessness and hyperactivity.
- Panting.
- Polyuria/polydipsia.
- Dehydration.
- Tachycardia.
- Cardiac arrhythmias such as VPCs.
- Hypertension.
- Hyperthermia.
- Tremors.
- Hyperreflexia and muscle rigidity.
- Seizures.
- Advanced signs with severe toxicosis—cardiac failure, weakness, cyanosis, coma, and death.
- Death—12–48 hours after ingestion.

CAUSES

Excessive ingestion of chocolate and other methylxanthine products.

RISK FACTORS

- Access to chocolate, which is palatable and attractive to dogs, often readily available, and unprotected in homes and kitchens.
- Dogs with preexisting heart disease may be more sensitive to cardiac effects.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Convulsant or excitatory alkaloids—strychnine, amphetamine, nicotine, 4-aminopyridine.
- Convulsant pesticides such as pyrethroids, organochlorines, bromethalin, zinc phosphide, metaldehyde.
- Tremorgenic mycotoxins.
- Acute psychogenic drugs—LSD, cocaine.
- Medications such as phenylpropanolamine, pseudoephedrine, tricyclic and selective serotonin reuptake inhibitor antidepressants.
- Cardioactive glycosides—*Digitalis* spp., *Nerium oleander*.
- Primary GI, cardiac, or neurologic disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia or hypoglycemia.
- Hypokalemia, especially with caffeine overdose.
- Urine may be dilute due to polydipsia.

OTHER LABORATORY TESTS

- Methylxanthine assay—rarely necessary as history and clinical signs usually sufficient for diagnosis; can be performed on stomach contents, plasma, serum, urine, or liver.

DIAGNOSTIC PROCEDURES

- ECG monitoring—sinus tachycardia, VPCs, and ventricular tachyarrhythmias.
- Blood pressure monitoring.

PATHOLOGIC FINDINGS

- Presence of chocolate in GI tract.
- Nonspecific gastroenteritis.
- No distinctive microscopic lesions.



TREATMENT

APPROPRIATE HEALTH CARE

- Emesis in stable patients considered low risk for aspiration; chocolate is slowly absorbed from a dog's stomach, so emesis may be rewarding up to 6–8 hours after ingestion.
- Gastric lavage with cuffed tube in symptomatic patients with large-volume ingestions once stabilized.
- Activated charcoal may not be necessary with lower-dose exposures or in cases where most of the chocolate was recovered by induction of vomiting or gastric lavage; monitor electrolytes for hypernatremia if giving multiple doses of activated charcoal.
- IV fluid therapy to correct dehydration, promote urinary excretion of methylxanthines, and avoid hypernatremia; SC fluids may suffice with lower-dose exposures; potassium may be supplemented in fluids, if needed.
- Control hyperthermia.
- Urine voiding every 4 hours or urinary catheterization may reduce urinary bladder resorption.
- GI support as needed (see Medications).
- Control hyperactivity and agitation, tremors, seizures (see Medications).
- Treat tachycardia with beta blockers, if sedation not effective; treat arrhythmias with anti-arrhythmic drugs as appropriate (see Medications).

NURSING CARE

Fluid therapy used to correct electrolyte disturbances and dehydration and to enhance excretion of methylxanthines.

ACTIVITY

Avoid stress and limit activity until recovered.

DIET

- No food until vomiting is controlled.
- Convalescence—bland, low-fat diet to aid recovery from gastroenteritis and/or pancreatitis.

CLIENT EDUCATION

Warn owners about toxicologic hazards of chocolate, and advise keeping chocolate out of reach of dogs.



MEDICATIONS

DRUG(S) OF CHOICE

- Induce emesis—only if patient is stable with low risk of aspiration; apomorphine

(CONTINUED)

CHOCOLATE TOXICOSIS

C

Table 1

| Comparative concentrations of caffeine and theobromine | | |
|--------------------------------------------------------|--------------------|-----------------|
| Caffeine Source | Amount (mg/g) | Amount (mg/oz)* |
| Coffee beans | 10–20 | 284–570 |
| Drip coffee | 90–100 mg/6 oz cup | 15–20 |
| Cola drinks | 30–71 mg/12 oz can | 2.5–6 |
| Baking chocolate (unsweetened) | 0.8 | 23 |
| Dark chocolate | 0.43–0.8 | 12–23 |
| Milk chocolate | 0.2 | 6 |
| Cocoa powder (unsweetened) | 2.3 | 70 |
| Guarana | 30–50 | 850–1,400 |
| Caffeine stimulant tablets | 50–200 mg/tablet | _____ |
| OTC migraine pain control | 65 mg/tablet | _____ |
| Theobromine Source | Amount (mg/g) | Amount (mg/oz) |
| Cacao beans | 10–50 | 300–1500 |
| Baking chocolate (unsweetened) | 13–16 | 370–454 |
| Milk chocolate | 1.5–2 | 42–57 |
| Cacao bean hulls | 5–9 | 142–256 |
| Cacao bean mulch | 2–30 | 57–852 |
| Cocoa powder (unsweetened) | 14–29 | 398–832 |

* To convert mg/g to mg/oz, multiply by 28.4.

(0.02–0.04 mg/kg IV); hydrogen peroxide 3% (1–2 mL/kg PO); do not exceed 50 mL in dogs. • Activated charcoal 1–2 g/kg PO with cathartic × 1 dose. With large ingestions, repeat activated charcoal (no cathartic) q8 up to 24h to prevent enterohepatic recirculation. • Hyperactivity—acepromazine (0.02–0.04 mg/kg IV/IM/SC) or butorphanol (0.2–0.5 mg/kg IM/IV), with doses repeated/titrated to effect. • Seizures—diazepam (0.5–1 mg/kg IV) or phenobarbital (2–6 mg/kg IV) as needed to effect. • Tremors—diazepam (0.5–1 mg/kg IV) or methocarbamol (50–220 mg/kg IV slowly, up to daily dose of 330 mg/kg). • Vomiting—maropitant (1 mg/kg SC or IV) q24h as needed. • Persistent ventricular tachycardia—metoprolol (0.04–0.06 mg/kg IV), esmolol (initial loading dose 0.25–0.5 mg/kg IV slowly over 1–2 min, followed by CRI at 10–200 µg/kg/min) or propranolol (0.02–0.06 mg/kg IV); metoprolol or esmolol preferred but may be difficult to obtain. • Ventricular arrhythmias (dogs)—lidocaine (2–4 mg/kg IV followed by 25–100 µg/kg/min IV CRI); lidocaine not recommended in cats. • In rare instance of bradycardia—atropine 0.02–0.04 mg/kg IV/IM/SC; rule out reflex bradycardia from hypertension before use.

CONTRAINDICATIONS

- Do not use epinephrine concurrent with lidocaine. • Avoid erythromycin and corticosteroids, which may reduce excretion of methylxanthines. • Do not use lidocaine in cats due to risk of seizures.

PRECAUTIONS

Keep patient under observation until recovered and treatment no longer needed.

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

Monitor heart rate, blood pressure, ECG, mentation, and temperature closely while hospitalized.

PREVENTION/AVOIDANCE

Warn owners about toxicologic hazards of chocolate and advise keeping chocolate out of reach of dogs.

POSSIBLE COMPLICATIONS

- Aspiration can occur rarely secondary to vomiting. • Pancreatitis can occur in some patients that consume chocolate.

EXPECTED COURSE AND PROGNOSIS

- Expected course—12–36 hours, up to 72 hours in severe cases, depending on dosage and effectiveness of decontamination and treatment.
- Successfully treated patients—usually recover completely. • Prognosis—good if prompt oral decontamination occurs, but guarded with advanced signs of seizures and arrhythmias.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Methylxanthines cross the placenta and are excreted in milk.

SEE ALSO

- Antidepressant Toxicosis—SSRIs and SNRIs.
- Metaldehyde Toxicosis.
- Poisoning (Intoxication) Therapy.

ABBREVIATIONS

- cAMP = cyclic adenosine monophosphate.
- GI = gastrointestinal.
- OTC = over the counter.
- VPC = ventricular premature contraction.

INTERNET RESOURCES

- <https://www.aspca.org/pet-care/animal-poison-control/apcc-mobile-app>
- <https://www.merckvetmanual.com/en-ca/toxicology/food-hazards/chocolate>

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Acknowledgment The author and book editors acknowledge the prior contribution of Gary D. Osweiler.



Client Education Handout
available online

CHRONIC KIDNEY DISEASE

C



BASICS

DEFINITION

Chronic kidney disease (CKD) encompasses functional or structural lesions (in one or both kidneys as detected by blood or urine tests, imaging studies, or kidney biopsy) that have been present for >3 months. This definition includes all cases previously described by the terms renal insufficiency or renal failure, as well as less advanced forms of kidney disease. Patients are categorized into stages along a continuum of progressive CKD (IRIS CKD stages 1–4; www.iris-kidney.com) based on >2 serum creatinine values obtained over several weeks when the patient is fasted and well hydrated. The IRIS system uses the term "kidney" rather than "renal" because it is more universally recognized by pet owners.

PATHOPHYSIOLOGY

More than ~67–75% reduction in renal function results in impaired urine-concentrating ability (leading to polyuria/polydipsia [PU/PD]) and retention of nitrogenous waste products of protein catabolism (azotemia). CKD is progressive; more advanced CKD results in uremia. Decreased renal erythropoietin and calcitriol production results in hypoproliferative anemia and renal secondary hyperparathyroidism, respectively.

SYSTEMS AFFECTED

- Cardiovascular—hypertension; uremic pericarditis.
- Endocrine/metabolic—renal secondary hyperparathyroidism, activation of renin-angiotensin-aldosterone system, erythropoietin deficiency.
- Gastrointestinal—uremic stomatitis and halitosis, nausea, vomiting, anorexia, gastrointestinal bleeding, diarrhea.
- Hemic/lymphatic/immune—anemia; hemorrhagic diathesis.
- Musculoskeletal—renal osteodystrophy; sarcopenia.
- Neuromuscular—seizures and other neurologic signs, muscle tremors, muscle wasting.
- Ophthalmic—retinal detachment, hemorrhage, or edema due to hypertension.
- Reproductive—impaired reproductive capacity.
- Respiratory—uremic pneumonitis.

GENETICS

- Inherited in these breeds (mode of inheritance indicated in parentheses)—Abyssinian cat (dominant with incomplete penetrance); Persian cat (dominant); bull terrier (dominant); Cairn terrier (recessive); German shepherd (dominant); Samoyed

(X-linked dominant); English cocker spaniel (recessive).

- Renal dysplasia—shih tzu, Lhasa apso, golden retriever, Norwegian elkhound, chow chow, standard poodle, soft-coated wheaten terrier, Alaskan Malamute, miniature schnauzer, Dutch kooiker, and many other breeds.

INCIDENCE/PREVALENCE

- 9 cases per 1,000 dogs and 16 cases per 1,000 cats examined.
- Prevalence increases with age—age >15 years, reportedly 57 cases per 1,000 dogs and 153 cases per 1,000 cats examined.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat.

Breed Predilections

See Genetics.

Mean Age and Range

Mean age at diagnosis is 7 years in dogs and 9 years in cats. Animals of any age can be affected; prevalence increases with age.

Predominant Sex

None

SIGNS

General Comments

- Clinical signs related to stage of CKD and complications such as proteinuria and hypertension.
- CKD stages 1 and 2 may be asymptomatic; overt clinical signs typically become apparent in stages 3 and 4.
- Animals with stable CKD (particularly stages 3 and 4) may decompensate, resulting in uremic crisis.

Historical Findings

- PU/PD.
- Anorexia.
- Lethargy.
- Vomiting.
- Weight loss.
- Nocturia.
- Constipation.
- Diarrhea.
- Acute blindness.
- Seizures or coma.
- Cats may have ptalism and muscle weakness with cervical ventroflexion.

Physical Examination Findings

- Kidneys may be small, irregular, enlarged (secondary to polycystic kidney disease or lymphoma), or normal.
- Dehydration.
- Cachexia.
- Weakness.
- Mucous membrane pallor.
- Oral ulceration.

- Uremic halitosis.
- Hypertensive retinopathy.
- Renal osteodystrophy may manifest as bone pain, particularly in skull.
- Reduced body temperature with uremia.

CAUSES

- Unknown in most cases due to late diagnosis.
- Familial and congenital renal disease, nephrotoxins, hypercalcemia, hypokalemic nephropathy, glomerulopathies, amyloidosis, pyelonephritis, polycystic kidney disease, nephroliths, chronic urinary obstruction, drugs, lymphoma, leptospirosis (following acute kidney injury [AKI]), feline infectious peritonitis.

RISK FACTORS

Age, proteinuria, hypercalcemia, hypokalemia, hypertension, urinary tract infection (UTI).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See Polyuria and Polydipsia for differential diagnosis.
- Azotemia—includes causes of prerenal and postrenal azotemia, AKI, and hypoadrenocorticism.
 - Prerenal azotemia—azotemia with urine specific gravity (USG) >1.030 in dogs and >1.035 in cats; rapid reduction in azotemia after correcting hypoperfusion indicates prerenal azotemia; prerenal azotemia commonly occurs concurrent with primary renal azotemia when gastrointestinal signs of uremia are present.
 - Postrenal azotemia—obstruction or rupture of excretory system; rapid correction of azotemia following elimination of obstruction or resolution of leakage from urinary tract supports postrenal azotemia.
 - AKI—differentiated by normal to large renal size, cylindruria, lack of indications of chronicity, and history of recent nephrotoxin exposure or hypotensive episode; AKI can also occur in patients with CKD where rapid developing increase in serum creatinine concentration and uremic signs suggests acute-onset CKD.
 - Hypoadrenocorticism—characterized by hyponatremia and hyperkalemia with hypocortisololemia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypoproliferative anemia.
- High blood urea nitrogen (BUN), creatinine, and symmetric dimethylarginine (SDMA).
- Hyperphosphatemia.
- Metabolic acidosis (normal or high anion gap).
- Hypokalemia or hyperkalemia.
- Hypercalcemia or hypocalcemia.

(CONTINUED)

- USG <1.030 in dogs and <1.035 in cats.
- Proteinuria.

OTHER LABORATORY TESTS

Urinary protein : creatinine ratio to assess proteinuria.

IMAGING

- Abdominal radiographs may demonstrate small kidneys, or large kidneys secondary to polycystic kidney disease or lymphoma.
- Ultrasound demonstrates small kidneys and hyperechoic renal parenchyma with less apparent distinction between cortex and medulla in some animals. Animals with lymphoma often have renomegaly with hypoechoic renal parenchyma.

DIAGNOSTIC PROCEDURES

- Blood pressure measurement to detect hypertension.
- Measurement of glomerular filtration rate may be useful for detection of loss of kidney function before onset of azotemia.
- Renal biopsy may be indicated in proteinuric patients with normal to large kidneys.

PATHOLOGIC FINDINGS

- Gross—small kidneys with irregular surface; fewer glomeruli found on visualizing cut across renal cortex.
- Histopathologic—variable; complete evaluation of biopsy material requires light, immunofluorescent, and electron microscopy; advanced CKD has nonspecific changes including interstitial fibrosis and foci of interstitial mononuclear cells, chronic generalized nephropathy.
- Findings may be specific for diseases causing CKD in some patients with less advanced disease.

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

Patients with compensated CKD may be managed as outpatients; patients in uremic crisis should be managed as inpatients.

NURSING CARE

- Uremic crisis—correct fluid and electrolyte deficits with IV fluids, providing 25% of calculated fluid deficit in first hour; thereafter, serially monitor perfusion, blood pressure, and urine output to assess adequacy of fluid therapy; if perfusion not improved, additional fluid should cautiously be administered. Provide remaining fluid deficit over next 12–24 hours. Overhydration can result in anuria; once patient has been hydrated, only sufficient fluid to sustain hydration should be administered.
- Subcutaneous fluid therapy may benefit patients with moderate to severe CKD. Continue therapy only if clinical improvement noted.

ACTIVITY

Unrestricted

DIET

- Diets designed for CKD delay onset of uremic crisis and extend survival in dogs and cats with CKD stages 2–4; they are standard of care for these patients.
- Important components of renal foods—reduced protein, phosphorus, sodium, and net acid content, supplementation of n-3 fatty acids and antioxidants.
- Free access to fresh water.

CLIENT EDUCATION

- CKD typically progresses to terminal kidney failure over months to years, but may not be progressive in some cats, which may live for years
- Higher levels of proteinuria associated with shorter survival; may be mitigated by anti-proteinuria therapy.
- Heritability of familial renal diseases.

SURGICAL CONSIDERATIONS

- Avoid hypotension during anesthesia.
- Renal transplantation has been successfully performed in cats with CKD.

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

- Antiemetics (maropitant 1 mg/kg q24h; or ondansetron 0.2–1 mg/kg IV q12h) to minimize vomiting and hypoxia due to nausea.
- Potassium chloride in IV fluids or potassium gluconate PO (2–6 mEq/cat/day) as needed to correct hypokalemia.
- Sodium bicarbonate to correct metabolic acidosis (IV to raise blood pH >7.1).

Compensated CKD

- Antiemetic (maropitant) and potassium gluconate as above.
- Mirtazapine (cats, 1.88 mg PO q 24–47h) to promote appetite.
- Intestinal phosphate binders as needed to correct hyperphosphatemia (see Hyperparathyroidism, Renal Secondary).
- Darbepoetin (see Anemia of Chronic Kidney Disease).
- Amlodipine (dogs, 0.1–0.6 mg/kg PO q24h; cats, 0.625–1.25 mg/cat PO q24h) or angiotensin-converting enzyme (ACE) inhibitors (0.5 mg/kg PO q24h) or angiotensin receptor blockers (ARB; e.g., telmisartan 1–3 mg/kg PO q24h) as needed for hypertension; amlodipine and telmisartan are more effective than ACE inhibitors for CKD-induced hypertension; if refractory to monotherapy, consider combination of amlodipine and ACE inhibitor or ARB, with frequent monitoring of blood pressure and electrolytes.
- ACE inhibitor (start at 0.5 mg/kg PO q24h; increase to 1 mg/kg PO q12h) or ARB (telmisartan 1–3 mg/kg PO q24h) for proteinuria.

CHRONIC KIDNEY DISEASE

C

CONTRAINdications

Avoid nephrotoxic drugs (aminoglycosides, cisplatin, amphotericin B) and corticosteroids.

PRECAUTIONS

- Drug dosage or dosing interval may need to be modified for some drugs eliminated by the kidneys.
- Use ACE inhibitors and ARB cautiously; monitor for worsening of azotemia,
- Generally avoid nonsteroidal anti-inflammatory drugs.

POSSIBLE INTERACTIONS

Cimetidine or trimethoprim may cause artifactual increases in serum creatinine concentration by reducing tubular secretion in dogs with CKD.

ALTERNATIVE DRUG(S)

- Metoclopramide (0.2–0.4 mg PO/SC q6–8h) can be used to treat uremic vomiting.
- Hemodialysis and renal transplantation are available at selected referral hospitals.

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

- Monitor at regular intervals; initially weekly for patients receiving erythropoietin; every 1–3 months for stable patients with CKD stages 3 and 4.
- Proteinuric patients—monitor at least every 3–4 months (minimum: serum creatinine and urine protein : creatine ratio).

PREVENTION/AVOIDANCE

- Do not breed animals with familial renal disease.
- Include urinalysis and serum creatinine in yearly examination for older pets; if serum creatinine increases, increase frequency to every 4–6 months.

POSSIBLE COMPLICATIONS

- Systemic hypertension.
- Uremia.
- Anemia.
- UTI.
- Nephrouretrolithiasis.

EXPECTED COURSE AND PROGNOSIS

- Short term—depends on severity.
- Long term—guarded to poor in dogs (CKD tends to be progressive over months to years); poor to good in cats (CKD does not progress in some cats).

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Renal secondary hyperparathyroidism.
- Systemic hypertension.
- Nephrouretrolithiasis.

C CHRONIC KIDNEY DISEASE

(CONTINUED)

C

AGE-RELATED FACTORS

Renal function may decrease with aging.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Patients with mild CKD may maintain pregnancy; those with moderate to severe disease may be infertile or have spontaneous abortions; breeding of females not recommended.

SYNONYMS

- Chronic kidney failure.
- Chronic renal disease or failure.

SEE ALSO

- Acute Kidney Injury.
- Anemia of Chronic Kidney Disease.
- Azotemia and Uremia.
- Congenital and Developmental Renal Diseases.

- Hydronephrosis.
- Hyperparathyroidism, Renal Secondary.
- Hypertension, Systemic Arterial.
- Nephrolithiasis.
- Polycystic Kidney Disease.
- Polyuria and Polydipsia.
- Proteinuria.
- Pyelonephritis.
- Urinary Tract Obstruction.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- AKI = acute kidney injury.
- ARB = angiotensin receptor blocker.
- BUN = blood urea nitrogen.
- CKD = chronic kidney disease.
- PU/PD = polyuria/polydipsia.
- SDMA = symmetric dimethylarginine.
- USG = urine specific gravity.
- UTI = urinary tract infection.

INTERNET RESOURCES

www.iris-kidney.com

Suggested Reading

- Polzin DJ. Chronic kidney disease. In: Ettinger SJ, Feldman EC, eds., *Textbook of Veterinary Internal Medicine*, 7th ed. St. Louis, MO: Elsevier, 2010, pp. 1990–2021.
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Author David J. Polzin

Consulting Editor J.D. Foster



**Client Education Handout
available online**

CHYLOTHORAX

C



BASICS

DEFINITION

- Accumulation of chyle in the pleural space.
- Chyle—triglyceride-rich fluid from the intestinal lymphatics that empties into the venous system (usually cranial cava/jugular vein) in the thorax.
- Pseudochylous effusion—effusion that contains less triglycerides and more cholesterol compared to serum, but appears fatty grossly.
- Thoracic lymphangiectasia—tortuous, dilated lymphatics found in many animals with chylothorax.
- Fibrosing pleuritis—condition in which pleural thickening leads to constriction of lung lobes; when severe, results in marked restriction of ventilation; can be caused by any chronic pleural exudate, but is most commonly associated with chylothorax and pyothorax.

PATOPHYSIOLOGY

- Alteration of flow through thoracic duct (TD) leading to leakage of chyle—can be related to increased pressure or permeability in TD or venous obstruction downstream.
- Can be caused by any disease or process that increases systemic venous pressure at the entrance of the TD to the venous system.
- Cardiac causes—pericardial disease, cardiomyopathy, heartworm disease, other causes of right-sided heart failure; thrombosis around pacing lead wire.
- Noncardiac causes—neoplasia (especially mediastinal lymphoma in cats), lung lobe torsion, diaphragmatic hernia, venous granuloma, venous thrombus.
- Rare TD rupture/trauma—surgical (thoracotomy), nonsurgical (e.g., hit by car).
- Idiopathic considered most common.

SYSTEMS AFFECTED

- Respiratory—due to reduced lung expansion.
- Systemic signs can be present secondary to the respiratory distress (e.g., decreased appetite, weight loss).

GENETICS

Unknown

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Dogs—Afghan hound and Shiba Inu.
- Cats—oriental breeds (e.g., Siamese and Himalayan).

Mean Age and Range

- Any age affected.
- Cats—more common in older cats; could indicate an association with neoplasia.
- Afghan hound—develop

when middle-aged.

- Shiba Inu—develop when young (<1–2 years of age).

Predominant Sex

None identified.

SIGNS

General Comments

- Signs will depend on the rate of fluid accumulation and volume of pleural effusion.
- Usually not exhibited until there is marked impairment of ventilation.
- Many patients appear to have the condition for prolonged periods before diagnosis.

Historical Findings

- Tachypnea and respiratory difficulty.
- Coughing—can be present for months before examination, likely due to lung compression associated with pleural effusion.
- Lethargy.
- Anorexia and weight loss.
- Exercise intolerance.

Physical Examination Findings

- Vary with cause of effusion.
- Muffled heart and lung sounds ventrally.
- Increased bronchovesicular sounds, particularly in dorsal lung fields.
- Pale mucous membranes or cyanosis.
- Arrhythmia.
- Heart murmur.
- Signs of right-sided heart failure (e.g., jugular pulses, ascites, hepatomegaly).
- Decreased compressibility of anterior chest—common in cats with a cranial mediastinal mass.

CAUSES

- Cranial mediastinal masses—lymphoma, thymoma.
- Cardiac disease—heartworm, cardiomyopathy, pericardial disease, congenital diseases.
- Lung lobe torsion.
- Venous obstruction—granuloma, thrombi.
- Congenital abnormality of TD.
- Cardiac or thoracic surgery.
- Idiopathic—most common cause.

RISK FACTORS

Unknown



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of pleural effusion—neoplasia, pyothorax, heart failure, feline infectious peritonitis (FIP).

CBC/BIOCHEMISTRY/URINALYSIS

- Often normal.
- Lymphopenia and hypoalbuminemia—can be found; hyponatremia and hyperkalemia sometimes noted due to fluid shifts with repeat thoracocentesis.

OTHER LABORATORY TESTS

Heartworm testing.

Fluid Analysis

- Classified as an exudate.
- Color will depend on fat content from diet and presence of concurrent hemorrhage—usually milky white and opaque, but can appear serosanguinous

and range from yellow to pink.

- Protein content varies, and high lipid content will make refractive index inaccurate.
- Total nucleated cell count—usually <10,000 cells/ μL .
- Fluid triglycerides—higher compared to serum.
- Fluid cholesterol—lower compared to serum.

Cytology

- Place sample in an EDTA tube to allow cell count to be performed.
- Initially, cytology comprises primarily small lymphocytes, neutrophils, and macrophages containing lipid.
- Chronic effusions contain fewer lymphocytes due to continued loss and more nondegenerate neutrophils due to inflammation from multiple thoracocenteses or irritation of pleural lining by chyle.
- Atypical lymphocytes—suggestive of underlying neoplasia.

IMAGING

Thoracic Radiography

- Two to four views if patient is stable—pleural effusion.
- Dorsoventral view associated with less stress than ventrodorsal view in animal with respiratory difficulty.
- Repeat radiographs after thoracocentesis to assess for underlying causes of effusion or evidence of fibrosing pleuritis; if collapsed lung lobes do not appear to reexpand after pleural fluid is removed or if respiratory distress persists with only minimal fluid present, suspect underlying pulmonary parenchymal or pleural disease (e.g., fibrosing pleuritis).

Ultrasonography/Echocardiography

- Should be performed before thoracocentesis if patient is stable—fluid acts as an acoustic window, enhancing visualization of thoracic structures.
- Assess for underlying causes—detect abnormal cardiac structure and function, pericardial disease, and mediastinal masses.

CT Lymphangiography

- Can quantify TD branches more accurately than standard radiographic lymphangiography.
- In dogs, percutaneously inject 1–2 mL of nonionic contrast material into mesenteric lymph nodes using ultrasound or CT guidance.
- Acquire helical thoracic CT images before and after injection of contrast media.
- Can document location and character of TD and its tributary lymphatics; likely useful for surgical planning.

PATHOLOGIC FINDINGS

- Lymphatics (including TD)—difficult to identify at necropsy.
- Fibrosing pleuritis—lungs appear shrunken; pleural layers (visceral and parietal) are diffusely thickened.
- Fibrosing pleuritis—characterized histologically by diffuse, moderate to marked thickening of the pleura by fibrous connective tissue with moderate infiltrates of lymphocytes, macrophages, and plasma cells.

C CHYLOTHORAX



TREATMENT

APPROPRIATE HEALTH CARE

- Dyspneic animal—immediate thoracocentesis; removal of even small amounts of pleural effusion can markedly improve ventilation.
- Identify and treat the underlying cause, if possible.
- Medical management—usually treated on outpatient basis with intermittent thoracocentesis as needed based on clinical signs (see Medications).
- Chest tubes—place *only* in patients with suspected chylothorax secondary to trauma (very rare), in cases with rapid fluid accumulation, or after surgery.
- Surgery if medical management does not resolve the problem in 2–3 months (see Surgical Considerations); some clinicians believe earlier intervention is better to avoid potential for development of restrictive pleuritis.

NURSING CARE

- Patients undergoing multiple thoracocenteses can rarely develop electrolyte abnormalities (hyponatremia, hyperkalemia) that may need to be corrected with fluid therapy.
- Thoracocentesis—perform under aseptic conditions to reduce risk of iatrogenic infection; antibiotic prophylaxis generally unnecessary if proper technique is used.

ACTIVITY

Patients will usually restrict their own exercise as pleural fluid volume increases or if they develop fibrosing pleuritis.

DIET

- Low fat—potentially decreases the amount of fat in the effusion, which would improve the patient's ability to resorb fluid from the thoracic cavity; not a cure; may help in management by facilitating reabsorption.
- Medium-chain triglycerides are transported via the TD in dogs and are no longer recommended.

CLIENT EDUCATION

- Inform client that no specific treatment will stop the effusion in all patients with the idiopathic form of the disease.
- Inform client that the condition can spontaneously resolve in some patients after several weeks or months.

SURGICAL CONSIDERATIONS

TD Ligation and Pericardectomy

- Recommended in patients that do not respond to medical management.
- The duct usually has multiple branches in the caudal thorax where ligation is performed; failure to occlude all branches results in continued pleural effusion.
- Always

perform in conjunction with lymphangiography; methylene blue injected in the mesenteric lymph node greatly facilitates visualization and complete occlusion of all branches.

- Thickening of the pericardium can prevent formation of lymphaticovenous communications—perform pericardectomy simultaneously with TD ligation; reports of up to 100% success rate when both techniques are performed; second surgery can be necessary if all branches are not occluded.
- Video-assisted thorascopic surgery for thoracic duct ligation and pericardectomy is reported to have similar success rates to thoracotomy (86%).

Other

- Success rates of 83–88% reported for cisterna chyli ablation in combination with TD ligation.
- Salvage procedures for recurrence after TD ligation include cisterna chyli and TD glue embolization, pleuroperitoneal or pleurovenous shunts, or placement of a PleuralPort®.



MEDICATIONS

DRUG(S) OF CHOICE

- Rutin 50–100 mg/kg PO q8h; believed to increase macrophage removal of proteins, which promotes absorption of fluid; complete resolution of effusion appears to occur in some patients; further study is required to determine whether resolution occurs spontaneously or in response to this therapy.
- Somatostatin analog (octreotide)—a naturally occurring substance that inhibits gastric, pancreatic, and biliary secretions and prolongs gastrointestinal transit time, decreases jejunal secretion, and stimulates gastrointestinal water absorption; in traumatic chylothorax, reduction of gastrointestinal secretions may aid healing of the TD by decreasing TD lymphatic flows; resolution of pleural fluid has occurred in dogs and cats with idiopathic chylothorax in which octreotide has been administered, but the mechanism is unknown; octreotide (Sandostatin®; 10 µg/kg SC q8h for 2–3 weeks) is a synthetic analog of somatostatin that has a prolonged half-life and minimal side effects.

CONTRAINDICATIONS

Cardiac disease or neoplasia—treat the underlying disease rather than the effusion (other than heartworm disease in cats where TD ligation may be beneficial while the heartworm infection clears).



FOLLOW-UP

PATIENT MONITORING

- Monitor for signs of recurrence of pleural effusion (tachypnea, labored breathing, respiratory distress)—perform thoracentesis as needed.
- Periodically reevaluate for several years to detect recurrence.

POSSIBLE COMPLICATIONS

- Fibrosing pleuritis.
- Iatrogenic infection with repeated thoracocentesis—important to use aseptic technique.

EXPECTED COURSE AND PROGNOSIS

- Can resolve spontaneously or after surgery.
- Untreated or chronic disease—can result in severe fibrosing pleuritis and persistent dyspnea.
- Euthanasia—frequently performed in patients that do not respond to surgery or medical management.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Diffuse lymphatic abnormalities (e.g., intestinal lymphangiectasia, hepatic lymphangiectasia, pulmonary lymphangiectasia, and chylous ascites)—may be noted; may worsen the prognosis.

AGE-RELATED FACTORS

Young patients may have a better prognosis than old animals because of the association of neoplasia with advanced age.

ABBREVIATIONS

- FIP = feline infectious peritonitis.
- TD = thoracic duct.

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Jill S. Pomrantz.



Client Education Handout
available online

CIRRHOSIS AND FIBROSIS OF THE LIVER



BASICS

DEFINITION

- Hepatic fibrosis—replacement/effacement of hepatic parenchyma, intrasinusoidal, variable zonal, deposition of extracellular matrix (ECM).
- Cirrhosis—regenerative nodules with dissecting fibrotic partitions and regions of parenchymal extinction, deranging hepatic architecture; usually reflects chronic necroinflammatory liver injury.

PATHOPHYSIOLOGY

- Fibrosis—usually reflects injury-associated release of cytokines/mediators stimulating production and accumulation of ECM; exception: ductal plate malformation (DPM), with congenital hepatic fibrosis (CHF) phenotype (severe portal-to-portal bridging fibrosis without chronic inflammation).
- Cirrhosis—consequence of chronic hepatic injury, fibrogenesis, and hepatic regeneration; typified by regenerative nodules, reduced functional hepatic mass, collagen deposition in sinusoids (space of Disse) or portal tracts, compromising parenchymal perfusion.
- Cirrhosis/fibrosis—leads to hepatic dysfunction, capillarization of hepatic sinusoids, collagenization of sinusoids, development of sinusoidal hypertension, intrahepatic shunting through collagenized sinusoids, recanalized vascular pathways in fibrotic partitions between regenerative nodules; these microcirculatory disturbances impair exchanges between blood and hepatocytes.
- Sinusoidal hypertension—leads to hepatofugal portal flow (away from liver); splanchnic hypertension; acquired portosystemic shunt (APSS) formation; episodic hepatic encephalopathy (HE); splanchnic pooling of blood, decreased effective systemic blood volume, stimulation of renal sodium and water retention, with ascites formation; hypertensive splanchnic vasculopathy predisposing to enteric bleeding.

SYSTEMS AFFECTED

- Gastrointestinal (GI)—splanchnic portal hypertension leads to ascites and propensity for enteric bleeding.
- Neurologic—HE.
- Hemic—red blood cell (RBC) microcytosis reflects APSS; bleeding tendencies: failed factor synthesis or activation, thrombocytopenia; reduced anticoagulants increases risk for thrombosis.
- Renal/urologic—ammonium biurate crystalluria; isosthenuria; polyuria/polydipsia (PU/PD); hepatorenal syndrome (rare) may follow therapeutic paracentesis of large-volume ascites (postcentesis hypotension syndrome [PHS]).
- Endocrine/metabolic—hypoglycemia if end-stage liver failure.

- Respiratory—tachypnea if tense ascites or pleural effusion.
- Skin—superficial necrolytic dermatitis, unkempt coat.

GENETICS

Familial predisposition for chronic hepatitis—Doberman pinscher, cocker spaniel, Labrador retriever, Maltese, Bedlington terrier (copper related), West Highland white terrier, others.

INCIDENCE/PREVALENCE

High in dogs with chronic necroinflammatory liver disease, animals with chronic extrahepatic bile duct occlusion (EHBDO), dogs with severe hepatic copper accumulation.

SIGNALMENT

Species

- Cirrhosis—dogs with chronic hepatitis; cats with chronic cholangitis/cholangiohepatitis; dogs and cats with chronic EHBDO.
- Severe fibrosis—dogs and cats with severe DPM-CHF phenotype.

Breed Predilection

- Many breeds and mixed-breed dogs.
- Copper associated hepatopathy (CuAH)—genetics proven only in Bedlington terriers and partially in Labrador retrievers; Doberman pinschers, West Highland white terriers, and Dalmatians appear predisposed; but all breeds at risk for CuAH due to dietary Cu intake.
- DPM-CHF phenotype—boxers may be predisposed, many breeds of dogs and cats; cats with polycystic malformations at risk.

Mean Age and Range

- Cirrhosis (dogs)—any age; more common in middle-aged to older; CuAH any age.
- Biliary cirrhosis (cats)—with chronic cholangiohepatitis often >7 years old.
- Fibrosis—DPM-CHF phenotype (dogs, cats)—ECM accumulates with aging (suspected), genetic cause (see Ductal Plate Malformation).

Predominant Gender

- Cocker spaniels—may be higher in males.
- Doberman pinschers and Labrador retrievers—no sex predilection.
- DPM—no gender predilection.

SIGNS

General Comments

- Initially—vague and nonspecific.
- Later—relate to complications of portal hypertension (e.g., HE, ascites, gastroduodenal bleeding) and impaired hepatic function.

Historical Findings

- Chronic intermittent lethargy, anorexia, reduced body condition.
- GI signs—vomiting, diarrhea or constipation. Melena—late stage or as APSS develop.
- PU/PD.
- Late onset—ascites, bleeding, HE.

- Jaundice—with necroinflammatory disease; DPM usually anicteric.
- Cats—ascites uncommon with acquired necroinflammatory disease, more common with DPM; ptalism, aggression, seizures with HE.

Physical Examination Findings

- Lethargy.
- Poor body condition/coat.
- ± Variable jaundice.
- ± Ascites.
- ± HE.
- Obstructive uropathy—ammonium biurates.
- Anasarca—rare; may develop with overzealous fluid therapy.
- Liver size—dogs: microhepatia; cats: variable.
- Coagulopathy—variable, uncommon in DPM.
- Cutaneous lesions—superficial necrolytic dermatitis.

CAUSES

- Chronic necroinflammatory, oxidant, or immune-mediated liver injury has many causes; may develop subsequent to chronic inflammatory bowel disease (IBD) or pancreatitis.
- CuAH.
- Drug- or toxin-induced liver injury—anti-convulsants; azole antifungals; nonsteroidal anti-inflammatory drug (NSAID) oxibendazole; trimethoprim-sulfamethoxazole; chronic food-borne toxins (aflatoxins), others.
- Infections—leptospirosis, canine adenovirus I, leishmanial, histoplasmosis, protozoal (toxoplasmosis).
- Chronic cholangiohepatitis (cats).
- Chronic EHBDO (>6 weeks, dogs and cats).
- Single episode of massive hepatic necrosis; sago palm (cycad toxicity), xylitol, NSAIDs in dogs with substantial Cu accumulation.

RISK FACTORS

- Breed predisposition.
- Dietary Cu intake >patient tolerance.
- Hepatic iron accumulation—supplementation.
- Chronic hepatobiliary inflammation.
- Chronic EHBDO.
- Chronic phenobarbital administration (dogs).
- NSAIDS—dogs, especially carprofen.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Chronic hepatitis—common in dogs.
- Cholangiohepatitis—common in cats.
- Noncirrhotic portal hypertension—dogs.
- Chronic EHBDO.
- Chronic IBD or pancreatitis.
- Hepatic neoplasia.
- Metastatic neoplasia or carcinomatosis.
- Congenital portosystemic vascular anomaly (shunt).
- Congenital portal atresia— intrahepatic or extrahepatic.
- Right-sided heart failure, pericardial disease.

CIRRHOsis AND FIBROsis OF THE LIVER

(CONTINUED)

C

- Cats—hepatic lipidosis, feline infectious peritonitis, toxoplasmosis.
- Hemolytic anemia (jaundice differential).

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Microcytic RBCs: APSS; mild anemia: small RBCs with normal cell count; anemia of chronic disease; microangiopathic shearing: sinusoidal fibrosis, APSS.
- Mild thrombocytopenia variable.
- Leukogram variable.

Biochemistry

- Bilirubin variable.
- Liver enzyme activities—high (alanine transaminase [ALT] > alkaline phosphatase [ALP]) noted before clinical signs or liver dysfunction; at end-stage enzymes may decline.
- Normal to hypoalbuminemia.
- Normal to hyperglobulinemia.
- Hypocholesterolemia—reflects APSS.
- Low blood urea nitrogen (BUN)—reduced urea cycle activity, APSS, protein-restricted diet, PU/PD.
- Hypoglycemia—rare.
- Hypokalemia—may predispose to HE.
- Hyponatremia—fluid imbalance with ascites.

Urinalysis

- Isosthenuria—with PU/PD.
- Ammonium biurate crystalluria.
- Bilirubinuria, bilirubin crystalluria.

OTHER LABORATORY TESTS

- Ascitic fluid—pure or modified transudate.
- Coagulation tests—inconsistently prolonged prothrombin time (PT), activated partial thromboplastin time, buccal mucosal bleeding time (BMBT).
- Low protein C and antithrombin activity—reflects APSS, synthetic failure, or disseminated intravascular coagulation (DIC).
- Serum bile acids—high; reflects APSS or cholestasis in cirrhosis.
- Hyperammonemia—inferred from ammonium biurate crystalluria.

IMAGING

Radiography

Abdominal—small to normal-sized liver; ascites may obscure details; urate calculi radiolucent unless calcium complexed.

Ultrasonography

- Abdominal—hyperechoic or mixed echogenic liver parenchyma; ± nodularity; often small with cirrhosis; abdominal effusion (ascites); APSS (color-flow Doppler); enlarged portal lymph nodes; no parenchymal change in some cases.
- Doppler interrogation of portal vasculature—may confirm hepatofugal flow or nests of APSS, esp. near left kidney or splenic vessels.

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration cytology—helps rule out neoplasia; rule in bacterial infection; *cannot define fibrosis or nonsuppurative inflammation*.

- Liver biopsy—for definitive diagnosis; accuracy increased by multiple biopsy samples.
- Ultrasound guided—14–16G.
- Laparoscopy/laparotomy—best methods, permits gross visualization, documents APSS, biopsy access to multiple liver lobes and focal lesions.

PATHOLOGIC FINDINGS

Gross

- Fibrosis—small, firm irregular to finely nodular liver; DPM-CHF may not be small; fibrotic liver may display APSS, ± ascites.
- Cirrhosis—firm irregular liver; prominent micro- or macronodules, APSS, ± ascites.

Histopathology

- Immune-mediated hepatitis—periportal, lobular, or centrilobular lymphoplasmacytic infiltrates, hepatic cord disorganization, sinusoidal fibrosis, biliary hyperplasia.
- CuAH—initially centrilobular, may evolve immune-mediated hepatitis; single necrotic hepatocytes; significant fibrotic tissue may falsely decrease quantitative Cu concentration measurements in biopsy samples.
- DPM—bridging partitions with proliferative nonfunctional embryonic bile ducts embedded in ECM interconnecting portal regions.
- Postnecrotic fibrosis—fibrosis marks regenerative repair, disorganized wide hepatic cords; engorged lymphatics reflect sinusoidal hypertension.
- Cirrhosis—diffuse lesion; fibrosis, nodular regeneration distorting lobular architecture, periportal or sinusoidal fibrosis depending on zone of chronic injury, engorged lymphatics; single hepatocyte necrosis if active disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—minimally symptomatic patients.
- Inpatient—diagnostic tests; treatment for dehydration, severe HE, enteric bleeding, tense ascites.

NURSING CARE

- Fluids—avoid lactate if hepatic failure; avoid sodium loading if ascites.
- B complex vitamins (esp. cats)—2 mL/L fluid advised.
- Vitamin K₁—0.5–1.5 mg/kg SC q12h for 3 doses initially; titrate with proteins invoked by vitamin K absence or antagonism (PIVKA; if available) or PT.
- Glucose—if hypoglycemia; 2.5–5% dextrose in polyionic solution; titrate to response.
- Potassium chloride—in fluids, as needed.
- Avoid alkalosis—worsens HE.
- Therapeutic large-volume abdominocentesis if tense ascites nonresponsive to medical treatment; *caution:* PHS—hypotensive crisis and acute renal failure.

ACTIVITY

Limit

DIET

- Withhold oral food in acute severe HE if stupor, coma, or vomiting associated with enteric bleeding or pancreatitis.
- Consider partial parenteral nutrition or total parenteral nutrition.
- If HE—restrict protein intake, use soy or dairy protein sources (dogs) with medical interventions to increase nitrogen tolerance (see Hepatic Encephalopathy).
- Supplement water-soluble vitamins.

CLIENT EDUCATION

- Treatment palliative and symptomatic.
- Fibrosis diminished by control of inflammation and provocative diseases.
- Attenuate factors provoking HE—azotemia, dehydration; infection; catabolism; high-protein meals, hypokalemia; alkalemia; constipation, endoparasitism; enteric bleeding; certain drugs.

SURGICAL CONSIDERATIONS

- Cirrhosis—high anesthetic risk; gas anesthesia preferred: isoflurane or sevoflurane.
- Coagulopathy—predisposes to bleeding; BMBT may better assess risk for bleeding.
- Postoperative intensive care—avoid HE, maintain hydration, euglycemia, electrolytes, acid-base balance (avoid alkalemia).
- Predisposed to enteric bacterial translocation—judiciously administer antibiotics, esp. if surgical procedures involve alimentary canal or biliary structures.



MEDICATIONS

DRUG(S) OF CHOICE

- Treatments for specific etiologies—chelate Cu if CuAH; withdraw potentially hepatotoxic drugs, herbal or natural remedies.
- No clinical trials prove efficacy of specific regimens in animals.

Immune Modulation

- Prednisolone/prednisone—1–2 mg/kg q24h PO; taper to 0.5 mg/kg q48h; do not exceed 40 mg/day/dog.
- Azathioprine—2 mg/kg (or 50 mg/m²) q24h for 14 days, then q48h; contraindicated in cats (toxic); dogs: with prednisone, antioxidants, antifibrinolics, and polyenylphosphatidylcholine (PPC).
- Cyclosporine—5 mg/kg BID tapered to q24h; has been successful as single agent or with corticosteroids.
- Mycophenolate—10–15 mg/kg BID; has been successful as first- or second-line treatment with corticosteroids.

Antifibrinotics

- Immunomodulation, S-adenosylmethionine (SAMe), silybin, vitamin E—considered antifibrinotics as well as hepatoprotectants.

(CONTINUED)

CIRRHOSIS AND FIBROSIS OF THE LIVER

C

- Ursodiol—7.5 mg/kg/day PO q12h with food; use indefinitely.
- Polyunsaturated phosphatidylcholine with dilinolylphosphatidylcholine (PhosChol®)—25 mg/kg/q24h, mix with food.
- Colchicine—0.025–0.03 mg/kg q24–48h; no evidence of chronic benefit; side effects complicate use; no longer recommended.
- Losartan and telmisartan—losartan: 0.5 mg/kg/q24h; telmisartan: 0.5–1 mg/kg q24h initial dose; closely monitor blood pressure, renal function, and potassium, reducing dose if hypotension or hyperkalemia; angiotensin receptor blockers used in humans as antihypertensives and have been shown to be nephroprotective, to protect against some forms of drug-induced hepatotoxicity, and to inconsistently limit hepatic fibrosis.

Antioxidants

- Necroinflammatory disorders.
- SAMe—20 mg/kg q24h PO, *empty stomach*.
- Vitamin E mixed tocopherols—10 U/kg q24h PO with food.

Hepatoprotectants

- Necroinflammatory disorders.
- Ursodeoxycholate, vitamin E, SAMe.
- Silibinin—efficacy unclear, use PPC complexed form (bioavailable), 2–5 mg/kg q24h PO.
- Elemental zinc—1.5–3 mg PO q24h (if low liver zinc confirmed); adjust dose with plasma zinc measurements; avoid $\geq 800 \mu\text{g}/\text{dL}$; contraindicated with concurrent d-penicillamine administration.

Gastroprotectants

- Gastric acid inhibitors—if enteric bleeding (see Hepatitis, Chronic).
- Eliminate endoparasitism.

Ascites

- Restrict activity and sodium intake combined with diuretic therapy.
- Dietary sodium restriction (0.2% dry matter basis or $<0.05 \text{ g}/100 \text{ kcal}$).
- Diuretics (see Hypertension, Portal; Hepatitis, Chronic); slowly mobilize effusion: furosemide (0.5–1 mg/kg IV/SC/PO q12h) with spironolactone (0.5–2 mg/kg PO q12h); adjust dose to response (7–10 day recheck; if no response titrate up q3–5d to max dose 4 mg/kg/day).
- Therapeutic large-volume abdominocentesis if nonresponsive ascites mobilization after 7–14 days of diuretics and sodium restriction.
- Consider vasopressin V₂ antagonists with low-dose diuretics for treatment-resistant ascites (no published data for dogs or cats).

CONTRAINDICATIONS

NSAIDs—avoid; potentiate enteric bleeding; may worsen ascites; potentiate centrilobular hepatic necrosis-hepatotoxic metabolites and CuAH.

PRECAUTIONS

- Diuretics—dehydration, hypokalemia, alkalemia worsen HE.
- Glucocorticoids—increase susceptibility to infection, enteric bleeding, sodium and water retention, ascites, protein catabolism, HE.
- Avoid drugs or reduce dose if first-pass hepatic extraction, if require hepatic conjugation or biotransformation (e.g., metronidazole—reduce conventional dose to 7.5 mg/kg PO q12h, as used for HE).

ALTERNATIVE DRUG(S)

- Dexamethasone—if ascites, replace prednisone/prednisolone to avoid mineralocorticoid effect; divide dose by 7–10, administer q3–4 days; taper dose to efficacy.

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

- Liver enzymes, albumin, BUN, cholesterol, bilirubin—monthly to quarterly.
- Serial monitoring of total serum bile acids—adds no prognostic or diagnostic information.
- Body condition score, weight, muscle mass—reflects nutritional adequacy/nitrogen balance.
- Abdominal girth—reflects ascites volume.
- Azathioprine, mycophenolate, colchicine—monitor for bone marrow toxicity (serial CBCs) and other side effects.

POSSIBLE COMPLICATIONS

HE, septicemia, bleeding—may be life-threatening; DIC—may be terminal event.

EXPECTED COURSE AND PROGNOSIS

- Flare-ups of HE and ascites may require hospitalization to adjust nutritional and medical interventions.
- Sodium restriction and diuretics may require titration to achieve optimal control of ascites.
- Presence of ascites indicates severe disease.
- DPM—survival up to 12 years after diagnosis.
- Cirrhosis—variable: poor long-term prognosis in limited studies, <6 months; however, some can survive years (>5) with careful interventional management depending on whether histologic changes truly “end-stage” or not.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

Dogs with leptospirosis-associated chronic liver disease (rare) may shed organisms.

SEE ALSO

- Coagulopathy of Liver Disease.
- Copper Associated Hepatopathy.
- Ductal Plate Malformation (Congenital Hepatic Fibrosis).
- Hepatic Encephalopathy.
- Hepatitis, Chronic.
- Hypertension, Portal.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALR = alanine transaminase.
- APSS = acquired portosystemic shunt.
- BMBT = buccal mucosal bleeding time.
- BUN = blood urea nitrogen.
- CHF = congenital hepatic fibrosis.
- CuAH = copper associated hepatopathy.
- DIC = disseminated intravascular coagulation.
- DPM = ductal plate malformation.
- ECM = extracellular matrix.
- EHBDO = extrahepatic bile duct occlusion.
- GI = gastrointestinal.
- HE = hepatic encephalopathy.
- IBD = inflammatory bowel disease.
- NSAID = nonsteroidal anti-inflammatory drug.
- PHS = postcentesis hypotension syndrome.
- PIVKA = proteins invoked by vitamin K absence or antagonism.
- PPC = polyenylphosphatidylcholine.
- PT = prothrombin time.
- PU/PD = polyuria/polydipsia.
- RBC = red blood cell.
- SAME = S-adenosylmethionine.

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Acknowledgment The author and book editors acknowledge the prior contribution of Sharon A. Center.



Client Education Handout
available online

CLOSTRIDIAL ENTEROTOXICOSIS



BASICS

DEFINITION

A complex disorder characterized by diarrhea in dogs and cats associated with *Clostridium perfringens* enterotoxins (CPEs).

PATHOPHYSIOLOGY

- *Clostridium perfringens* (CP) is a Gram-positive, spore-forming, strictly anaerobic bacterium.
- CP is a normal commensal organism found in the intestinal tract of humans and animals.
- A strong link between canine acute hemorrhagic diarrhea syndrome (AHDS; formerly hemorrhagic gastroenteritis [HGE]) and the presence of CP has been identified.
- Certain strains of CP (primarily Type A) produce a potent enterotoxin (CPE) as well as pore-forming toxins (NetE and NetF).
- CPE is a cytotoxic enterotoxin that causes tissue destruction; it has been identified in the feces of up to 14% of dogs without diarrhea, thus its role in causing diarrhea is unclear.
- NetF-producing CP isolates have not been found in healthy dogs.
- Not all strains of CP produce CPE or NetF and not all dogs that have CPE in feces are clinical, therefore it is undetermined why some develop diarrhea.
- CPE production is coregulated with sporulation of the organism; conditions that precipitate sporulation in animals include a sudden change in diet, dietary indiscretion, injudicious use of antibiotics causing a severe dysbiosis, and underlying intestinal disease.

SYSTEMS AFFECTED

Gastrointestinal (GI).

INCIDENCE/PREVALENCE

Incidence is unknown; up to 34% of canine diarrhea cases are suspected to be CP related. The infection is far less common in cats.

SIGNALMENT

Species

Dog and cat.

Mean Age and Range

Any age.

SIGNS

General Comments

Can include both large and small bowel diarrhea.

Historical Findings

- Large bowel diarrhea—tenesmus, mucous, frank blood, and increased frequency of defecation.
- Small bowel diarrhea—large volumes of soft to liquid diarrhea.
- Vomiting and abdominal discomfort.
- Severity varies from mild, self-limiting diarrhea to fatal, acute, hemorrhagic diarrhea.

Physical Examination Findings

- Abdominal discomfort.
- Hematochezia.
- Mucoid feces.
- Dehydration if there has

been voluminous diarrhea or vomiting.

- Fever is uncommon.
- Evidence of systemic illness or debilitation is rare.

CAUSES

- In humans, CP-associated diarrhea is usually due to ingestion of enterotoxigenic isolates. In dogs, it is thought to be secondary to disruption of the intestinal microenvironment.
- Anything that disrupts normal enteric microbiota can lead to CP overgrowth and diarrhea.
- CP toxins have been implicated in dogs with AHDS.

RISK FACTORS

- Dietary changes.
- Antibiotic use.
- Stress.
- Primary small intestinal bacterial overgrowth.



DIAGNOSIS

- Diagnostic testing should occur during the acute phase.
- In the absence of sepsis, antibiotic therapy has not been shown to alter resolution of clinical signs, therefore response to antibiotics cannot be used as diagnostic criterion.

DIFFERENTIAL DIAGNOSIS

Any cause of diarrhea can be considered, including, but not limited to, viral, bacterial, or parasitic infection, dietary indiscretion, chronic enteropathy, metabolic disease, neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- If dehydration is present—increased packed cell volume (PCV) from hemoconcentration, increased total plasma protein, increased amylase, and increased blood urea nitrogen (BUN) from prerenal azotemia.
- Dogs with AHDS will often have increased PCV with discordantly low total plasma protein.
- Leukocytosis with neutrophilia and moncytosis.
- Decreased albumin secondary to loss and decreased production.
- Increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities from organ hypoxia secondary to hypovolemia.

OTHER LABORATORY TESTS

There is no gold standard diagnostic test for confirming CP-associated diarrhea.

Microbiology

- Fecal culture alone should not be used to diagnose CP-associated illness because the organism is a normal commensal; CP can be isolated from feces of >80% of healthy dogs and 43–63% of normal cats.
- Fecal endospore cultures are not useful, as sporulation of enterotoxigenic strains of CP occurs in dogs with and without diarrhea.

Enterotoxin Assay

- Fecal ELISA for identification of CPE in patients with diarrhea suspected to be due to CP is the current recommendation; since CPE is present in the feces of 5–14% of clinically normal dogs, this may or may not be clinically useful.
- Fecal ELISA should be run in conjunction with PCR to detect enterotoxigenic strains.
- Real-time polymerase chain reaction (RT-PCR) for detection of the CPE gene and the alpha toxin gene is available; the CPE gene has been found in up to 33.7% of healthy dogs, therefore its presence in a dog with GI disease does not confirm that CP is the cause.

Fecal Cytology

- CP endospores, characterized by “safety-pin” appearance with oval form and dense body at one end of spore wall, can be seen on microscopic evaluation of heat-fixed thin fecal smear stained with Romanowsky-type stain (e.g., Diff-Quik®), Wright's stain, or new methylene blue.
- High numbers of CP endospores on fecal cytology correlates poorly with clinical disease or fecal CPE activity.
- High numbers of fecal endospores can be found in feces of healthy dogs.

DIAGNOSTIC PROCEDURES

- Abdominal ultrasound can help rule out other causes of GI disease.
- Colonoscopy and endoscopy with biopsy can be used to confirm presence of acute mucosal necrosis and neutrophilic infiltration, as well as adherence of rod-shaped bacteria to these necrotic areas, and can rule out other causes of GI disease.

PATHOLOGIC FINDINGS

- Grossly hyperemic or ulcerated mucosa.
- Acute intestinal mucosal destruction and neutrophilic infiltration.
- Immunohistochemical staining of bacterial plaques on necrotic areas may be clostridial antigen positive.



TREATMENT

APPROPRIATE HEALTH CARE

- There are no research-based recommendations for optimal treatment of patients with CP-associated illness.
- If vomiting or diarrhea is not severe, animals may be treated as outpatients with antiemetics and subcutaneous fluids.
- If more severe diarrhea, vomiting, dehydration, or evidence of hypovolemia, hospitalization with IV replacement crystalloids and antiemetics is recommended.

DIET

- Diet change plays a role in treatment and management of cases with chronic recurring disease; diets high in either soluble (fermentable) or insoluble fiber often result in clinical improvement by reducing enteric CP

(CONTINUED)

number, possibly through acidification of the distal intestine, which limits CP sporulation and enterotoxin production.

- Commercial diets can be supplemented with psyllium (1/2–2 tsp/day) as a source of soluble fiber.
- Diets low in fiber should be supplemented with fiber (coarse bran 1–3 tbs/day) as a source of insoluble fiber or psyllium added as a source of soluble fiber.
- Probiotics might help restore the normal intestinal microbiota, thereby reducing risk of recurrent CP-associated diarrhea.

CLIENT EDUCATION

- Acute disease is often self-limiting.
- There have been no documented reports of transmission of CP from animals to humans; however, if there are immunosuppressed members in the household, strict hygiene protocols should be followed.



MEDICATIONS

DRUG(S) OF CHOICE

Antiemetics

- Maropitant—1 mg/kg IV/SC q 24h.
- Ondansetron—0.5–1 mg/kg IV/PO q24h.

Antibiotics

- Antibiotics are unnecessary in animals with mild disease as the infection is typically self-limiting.
- If signs of systemic disease or sepsis are present, antibiotics should be administered.
- Antibiotics that are recommended are ampicillin: 22 mg/kg IV q8h; amoxicillin: 22 mg/kg PO q8h; metronidazole: 10–25 mg/kg IV/PO q12h for 5–7 days; tylosin: 5–10 mg/kg PO q24h.
- Tetracyclines are no longer recommended due to resistance of CP isolates.

ALTERNATIVE DRUGS(S)

- Probiotics (e.g., lactobacillus) may alter the intestinal microbiota, reducing likelihood of recurrences.
- One study reported faster resolution of clinical signs with use of

probiotics than with no treatment.

- Diet change can be instituted following resolution of clinical signs.



FOLLOW-UP

PATIENT MONITORING

- Ensure adequate hydration and intravascular volume, with replacement fluid administration as needed.
- Monitor PCV, total plasma protein, acid-base balance, and electrolyte concentrations.

PREVENTION/AVOIDANCE

- Regular use of high-fiber diets or probiotics.
- Avoiding or anticipating stressful events (e.g., kenneling) and using anxiolytics.

EXPECTED COURSE AND PROGNOSIS

- Overall excellent prognosis; many animals will have resolution of clinical signs without in-hospital treatment.
- Acute hemorrhagic diarrheal events should be addressed with aggressive resuscitation and hospitalization; if the animal responds to therapy, the prognosis is good.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- CP enterotoxicosis can be associated with AHDS.
- The connection to chronic enteropathies is less well understood.

ZOONOTIC POTENTIAL

Unknown

PREGNANCY/FERTILITY/BREEDING

Antibiotic therapy may be contraindicated.

SEE ALSO

- Colitis and Proctitis.
- Small Intestinal Dysbiosis.

ABBREVIATIONS

- AHDS = acute hemorrhagic diarrhea syndrome.

- ALT = alanine aminotransferase.
- AST = aspartate aminotransferase.
- BUN = blood urea nitrogen.
- CP = *Clostridium perfringens*.
- CPE = *Clostridium perfringens* enterotoxin.
- GI = gastrointestinal.
- HGE = hemorrhagic gastroenteritis.
- PCV = packed cell volume.
- RT-PCR = real-time polymerase chain reaction.

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Acknowledgment The author and book editors acknowledge the prior contribution of Stanley L. Marks.



Client Education Handout
available online

CONGESTIVE HEART FAILURE, LEFT-SIDED

C



BASICS

DEFINITION

Failure of the left side of the heart to advance blood at a sufficient rate to meet the metabolic needs of the patient or to prevent blood from pooling within the pulmonary venous circulation.

PATHOPHYSIOLOGY

- Low cardiac output causes lethargy, exercise intolerance, syncope, and prerenal azotemia.
- High hydrostatic pulmonary venous pressure causes leakage of fluid from pulmonary venous circulation into pulmonary interstitium and alveoli; when fluid leakage exceeds ability of lymphatics to drain affected areas, pulmonary edema develops.

SYSTEMS AFFECTED

- All systems can be affected by poor perfusion. • Respiratory—increased rate and effort because of elevated pulmonary venous pressures/edema. • Cardiovascular.

GENETICS

Some congenital heart defects, cardiomyopathies, and valvular heart disease have genetic basis in some breeds.

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

Seen everywhere; prevalence of causes varies with location.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Varies with cause.

Mean Age and Range

Varies with cause.

Predominant Sex

Varies with cause.

SIGNS

General Comments

Signs vary with underlying cause and species.

Historical Findings

- Weakness, lethargy, exercise intolerance.
- Coughing (dogs with large left atria, concurrent tracheobronchial disease, or such severe edema that large airways affected) and dyspnea (increased respiratory rate and effort); respiratory signs often worsen at night and may require assuming standing, sternal, or “elbows abducted” position (orthopnea). • Cats rarely cough from heart failure; coughing should prompt search for primary airway disease.

Physical Examination Findings

- Tachypnea and dyspnea. • Coughing, often soft in conjunction with tachypnea (dogs).
- Pulmonary crackles and wheezes. • Pale/gray/cyanotic mucous membranes.
- Prolonged capillary refill time. • Possible murmur or gallop. • Weak femoral pulses.

CAUSES

Pump (Muscle) Failure of Left Ventricle

- Dilated cardiomyopathy (DCM)/diet-induced DCM. • Trypanosomiasis (rare). • Doxorubicin cardiotoxicity (dogs). • Hypothyroidism (rare).
- Hyperthyroidism (rarely causes pump failure; more commonly causes high output failure).
- Tachycardia-induced cardiomyopathy (caused by persistent pathologic supraventricular or ventricular tachyarrhythmia).

Pressure Overload of Left Heart

- Systemic hypertension (uncommon cause of heart failure in animals). • Subaortic stenosis. • Aortic coarctation (rare; Airedale predisposed). • Left ventricular tumors (rare).

Volume Overload of Left Heart

- Degenerative mitral valve disease (dogs).
- Mitral valve dysplasia (cats and dogs).
- Patent ductus arteriosus (dogs). • Ventricular septal defect, especially if complicated by aortic valve insufficiency. • Aortic valve insufficiency secondary to endocarditis (dogs). • Chronic, severe anemia. • Inadvertent high-volume fluid administration. • Steroid administration (cats, often with previously asymptomatic underlying hypertrophic cardiomyopathy [HCM]).

Impediment to Filling of Left Ventricle

- Restrictive cardiomyopathy (rare in dogs, more common in cats). • Pulmonary vein stenosis (rare). • HCM. • Left atrial masses (e.g., tumor or thrombus). • Mitral stenosis (rare). • Cor triatriatum sinister (cats, rare).

Rhythm Disturbances

- Bradyarrhythmia (high-grade atrioventricular block). • Tachyarrhythmia (e.g., atrial fibrillation, sustained supraventricular tachycardia, ventricular tachycardia).

RISK FACTORS

Conditions causing chronic high cardiac output (e.g., hyperthyroidism and anemia).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Must differentiate from other causes of coughing, dyspnea, and weakness.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually normal; maybe stress leukogram. • Mild to moderate liver enzyme elevation; bilirubin generally normal.
- Prerenal azotemia in some animals.

OTHER LABORATORY TESTS

- Thyroid disorders may be detected.
- Serum NT-proBNP and cardiac troponin I concentrations higher in animals with left-sided congestive heart failure (L-CHF) than in normal animals.

IMAGING

Radiography

- Left heart and pulmonary veins enlarged.
- Pulmonary edema, often hilar, especially

involving right caudal lung lobe in acute edema of dog, but may be patchy, especially in cats; acute pulmonary edema may begin in right caudal lung lobe.

Echocardiography

- Findings vary markedly with cause, but left atrial enlargement relatively consistent finding in cardiogenic pulmonary edema. • Diagnostic test of choice for documenting congenital defects, cardiac masses, and pericardial effusion.

DIAGNOSTIC PROCEDURES

ECG

- Atrial or ventricular arrhythmias.
- Evidence of left cardiomegaly (e.g., wide P waves, tall and wide QRS complexes, and left axis orientation). • May be normal.

PATHOLOGIC FINDINGS

Cardiac findings vary with disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually treat as outpatient unless dyspneic or severely hypotensive. • Identify and correct underlying cause whenever possible.
- Minimize handling of critically dyspneic animals—stress can kill!

NURSING CARE

Oxygen supplementation and postural support in dyspneic patients.

ACTIVITY

Restrict activity when dyspneic or tachypneic.

DIET

Initiate moderately sodium-restricted diet with adequate protein and calories. Severe sodium restriction indicated with advanced disease.

CLIENT EDUCATION

With few exceptions (e.g., animals with thyroid disorders, anemia, arrhythmias, nutritionally responsive heart disease, congenital heart disease), L-CHF is not curable.

SURGICAL CONSIDERATIONS

- Surgical intervention, coil embolization, Amplatz occluder placement, or balloon valvuloplasty may benefit selected patients with some forms of congenital and acquired valvular heart disease; response to these interventions varies. • Pericardiocentesis in animals with pericardial effusion.



MEDICATIONS

DRUG(S) OF CHOICE

Diuretics

- Furosemide (1–2 mg/kg q8–24h) or other loop diuretic is initial diuretic of choice; diuretics indicated to reduce preload and remove pulmonary edema; critically dyspneic animals often require high doses (2–4 mg/kg) IV to

C CONGESTIVE HEART FAILURE, LEFT-SIDED

(CONTINUED)

C

stabilize; dose can be repeated in 1h if animal still severely dyspneic; IV bolus of 0.66 mg/kg followed by CRI of 0.66–1 mg/kg/h for 1–4h causes greater diuresis than equal dose divided into two IV boluses given 4h apart; once edema resolves, taper to lowest effective dose.

- Spironolactone (0.5–2 mg/kg PO q12–24h) increases survival in humans with CHF and is in clinical trials in dogs; use in combination with furosemide. • Thiazide diuretics can be added to furosemide and spironolactone in refractory heart failure cases. • Torsemide (0.2–0.8 mg/kg q24h) may be useful as substitute for furosemide in animals requiring daily furosemide dosing in excess of 12 mg/kg, and it may be more effective than furosemide at delaying death due to cardiac disease in dogs with CHF secondary to degenerative valve disease.

Angiotensin-Converting Enzyme ACE) Inhibitors

- ACE inhibitors such as enalapril (0.5 mg/kg q12–24h) or benazepril (0.25–0.5 mg/kg q12–24h) indicated in most animals with L-CHF. • ACE inhibitors improve survival and quality of life in dogs with L-CHF secondary to degenerative valve disease and DCM.

Positive Inotropes

- Pimobendan (0.25–0.3 mg/kg PO q12h) is a calcium channel sensitizer that dilates arteries and increases myocardial contractility; first-line agent in treating DCM or CHF due to degenerative valve disease efficacy in cats with CHF is not known, but possibly beneficial. • Dobutamine (dogs: 2.5–10 µg/kg/min; cats: 0.5–5 µg/kg/min) is a potent positive inotropic agent that may provide valuable short-term support of a heart failure patient with poor cardiac contractility. • Positive inotropes in general are potentially arrhythmogenic—monitor carefully.

Venodilators

- Nitroglycerin ointment (one-fourth inch/5 kg q6–8h) causes venodilation, lowering left atrial filling pressures. • Used for acute stabilization of patients with severe pulmonary edema and dyspnea, but uncertain benefit.

Antiarrhythmic Agents

Treat arrhythmias if clinically indicated.

CONTRAINDICATIONS

Avoid vasodilators in patients with pericardial effusion or fixed outflow obstruction.

PRECAUTIONS

- ACE inhibitors and arterial dilators must be used with caution in patients with possible outflow obstruction. • Pulmonary hypertension, hypothyroidism, and hypoxia increase risk for digoxin toxicity; hyperthyroidism diminishes effects of digoxin. • ACE inhibitors and digoxin—use cautiously in patients with renal disease. • Dobutamine—use cautiously in cats. • Spironolactone—may cause facial pruritis in cats.

POSSIBLE INTERACTIONS

- Combination of high-dose diuretics and ACE inhibitors may cause azotemia,

especially in animals with severe sodium restriction. • Combination diuretic therapy adds to risk of dehydration and electrolyte disturbances. • Combination vasodilator therapy predisposes animal to hypotension.

ALTERNATIVE DRUG(S)

Arterial Dilators

- Hydralazine (0.5–2 mg/kg PO q12h; 0.5 mg/kg PO to start when added to ACE inhibitor) or amlodipine (0.05–0.2 mg/kg PO q24h) can be substituted for ACE inhibitor in patients that do not tolerate the drug or have advanced renal failure; monitor for hypotension and tachycardia; can be cautiously added to ACE inhibitor in animals with refractory L-CHF. • Nitroprusside (1–10 µg/kg/min) is potent arterial dilator usually reserved for short-term support of patients with life-threatening edema.

Digoxin

- Digoxin (dogs: 0.22 mg/m² q12h; cats: 0.01 mg/kg q48h) is used in animals with atrial fibrillation and myocardial failure (e.g., DCM); commonly used in combination with diltiazem to control rate of atrial fibrillation. • Digoxin is also indicated to treat dogs with refractory heart failure from either myocardial failure or volume loads; however, its use as a primary agent in myocardial failure has been replaced by pimobendan.

Calcium Channel Blockers

Diltiazem (0.5–1.5 mg/kg PO q8h) is frequently used in L-CHF patients for rate control in animals with supraventricular arrhythmias.

Beta Blockers

- Atenolol and metoprolol are sometimes used for rate control in animals with supraventricular tachycardia, hypertrophic cardiomyopathy, and hyperthyroidism. • Used alone or with a class 1 antiarrhythmic drug for control of ventricular arrhythmias; these drugs depress contractility (negative inotropes), so use cautiously in patients with myocardial failure or active signs of CHF.
- On basis of human studies, may enhance survival in animals with idiopathic DCM; treatment is best initiated under guidance of a cardiologist, starting with very low dosage and gradually increasing; carvedilol is sometimes used for this purpose, starting at 0.1 mg/kg q24h and titrating to 0.5 mg/kg q12h.

Nutritional Supplements

- Potassium and magnesium supplementation if deficiency is documented; use potassium supplements cautiously in animals receiving ACE inhibitor or spironolactone. • Taurine supplementation in cats with DCM and dogs with DCM and taurine deficiency (e.g., American cocker spaniels) • L-carnitine supplementation may help some dogs with DCM. • Coenzyme Q₁₀ is of potential value based on results in humans with DCM.
- Ensure animal receiving a nutritionally balanced diet (see Cardiomyopathy, Nutritional).



FOLLOW-UP

PATIENT MONITORING

- Monitor resting respiratory rate and effort, appetite, renal status, electrolytes, hydration, heart rate, bodyweight. • If azotemia develops, reduce diuretic dose; if azotemia persists and animal is also on ACE inhibitor, reduce or discontinue ACE inhibitor; use digoxin with caution if azotemic. • Monitor ECG if arrhythmias suspected. • Check digoxin concentration (0.5–1.5 ng/mL, 8–10 hours post dose).

PREVENTION/AVOIDANCE

- Minimize stress, exercise, and sodium intake in patients with heart disease.
- Pimobendan delays onset of CHF in Doberman pinschers, and in dogs with hemodynamically significant myxomatous mitral valve regurgitation; prescribing an ACE inhibitor with pimobendan early in course of heart disease in patients with DCM may slow progression of heart disease and delay onset of CHF; role of ACE inhibitors in asymptomatic animals with mitral valve disease remains controversial.

POSSIBLE COMPLICATIONS

- Syncope. • Aortic thromboembolism (cats). • Arrhythmias. • Electrolyte imbalances. • Digoxin toxicity. • Azotemia and renal failure.

EXPECTED COURSE AND PROGNOSIS

Prognosis varies with underlying cause; cats and dogs that survive initial episode of pulmonary edema and can be reliably medicated often survive months to more than a year with good quality of life. Animals with reversible causes of L-CHF may recover to normal lives.



MISCELLANEOUS

AGE-RELATED FACTORS

- Congenital causes seen in young animals.
- Degenerative heart conditions and neoplasia generally seen in old animals.

SEE ALSO

Pulmonary Edema, Noncardiogenic.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- DCM = dilated cardiomyopathy.
- HCM = hypertrophic cardiomyopathy.
- L-CHF = left-sided congestive heart failure.

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Client Education Handout
available online

CONGESTIVE HEART FAILURE, RIGHT-SIDED

C



BASICS

DEFINITION

Failure of the right side of the heart to advance blood at a sufficient rate to meet the metabolic needs of the patient or to prevent blood from pooling within the systemic venous circulation.

PATHOPHYSIOLOGY

- High hydrostatic pressure leads to leakage of fluid from venous circulation into the pleural and peritoneal space and potentially into the pericardium and interstitium of peripheral tissue.
- When fluid leakage exceeds ability of lymphatics to drain the affected areas, pleural effusion, ascites, pericardial effusion, and peripheral edema develop.

SYSTEMS AFFECTED

All systems can be affected by either poor delivery of blood or the effects of passive congestion from backup of venous blood.

GENETICS

- Some congenital cardiac defects have a genetic basis in certain breeds.
- Arrhythmogenic right ventricular cardiomyopathy (ARVC) appears to have a genetic basis in boxers and possibly some cats.

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

Syndrome seen everywhere; prevalence of various causes varies with location.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Vary with cause.

Mean Age and Range

Vary with cause.

Predominant Sex

Varies with cause.

SIGNS

General Comments

- Signs vary with underlying cause and between species.
- Pleural effusion without ascites and hepatomegaly is rare in dogs with right-sided congestive heart failure (R-CHF).
- Ascites without pleural effusion is rare in cats with R-CHF.
- Small-volume pericardial effusion without tamponade is relatively common in cats with R-CHF.
- Interstitial peripheral edema is a rare manifestation of R-CHF in both species.

Historical Findings

- Weakness.
- Lethargy.
- Exercise intolerance.
- Abdominal distension.
- Dyspnea, tachypnea.

Physical Examination Findings

- Jugular venous distention.
- Hepatojugular reflux.
- Jugular pulse in some animals.
- Hepatomegaly.
- Ascites common in dogs and rare in cats with R-CHF.
- Possible regurgitant murmur in tricuspid valve region or ejection murmur at left heart base (pulmonic stenosis).
- Muffled heart sounds if animal has pleural or pericardial effusion.
- Weak femoral pulses.
- Rapid, shallow respiration if animal has pleural effusion or severe ascites.
- Peripheral edema (infrequent).

CAUSES

Pump (Myocardial) Failure of Right Ventricle

- Idiopathic dilated cardiomyopathy (DCM).
- ARVC.
- Hypertrrophic cardiomyopathy (cats).
- Restrictive cardiomyopathy (cats).
- Trypanosomiasis.
- Doxorubicin cardiotoxicity.
- Chronic hyperthyroidism.

Volume Overload of Right Ventricle

- Chronic atrioventricular (AV) valve (mitral ± tricuspid) insufficiency due to myxomatous valvular degeneration.
- Tricuspid valve dysplasia.
- Large atrial septal defect.

Pressure Overload of Right Ventricle

- Heartworm disease.
- Chronic obstructive pulmonary disease with pulmonary hypertension.
- Pulmonary thromboembolism.
- Pulmonic stenosis.
- Tetralogy of Fallot.
- Right ventricular tumors.
- Heart base tumors (occasionally, compression of the pulmonary artery).
- Primary pulmonary hypertension.

Impediment to Right Ventricular Filling

- Pericardial effusion (tamponade).
- Constrictive/restrictive pericarditis.
- Right atrial or caval masses.
- Tricuspid stenosis.
- Cor triatriatum dexter.

Rhythm Disturbances

- Bradycardia, generally complete AV block.
- Tachyarrhythmias, generally sustained supraventricular tachycardia.

RISK FACTORS

- No heartworm prophylaxis.
- Offspring of animal with right-sided congenital cardiac defect.
- Conditions that augment demand for cardiac output (e.g., hyperthyroidism, anemia, pregnancy).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must differentiate from other causes of pleural effusion and ascites; generally requires complete diagnostic workup including CBC, biochemistry profile, heartworm test, thoraco- or abdominocentesis with fluid analysis and cytology, and sometimes thoracic and abdominal ultrasound.
- Animals with ascites or pleural

effusion due to heart failure should have jugular venous distension.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC usually normal; animals with heartworm disease may have eosinophilia.
- Mild to moderately high alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase due to passive liver congestion; bilirubin generally normal.
- Prerenal azotemia in some animals.

OTHER LABORATORY TESTS

- Heartworm test may be positive.
- NT-proBNP concentrations higher in animals with cardiac causes of fluid accumulation.

IMAGING

Thoracic Radiography

- Right cardiomegaly in some animals.
- Dilated caudal vena cava (diameter greater than the length of the vertebra directly above the heart).
- Pleural effusion (especially cats).
- Hepatosplenomegaly and possible ascites (especially dogs).

Echocardiography

- Findings vary with underlying cause; especially useful for documenting congenital defect, cardiac mass, and pericardial effusion.
- Abdominal ultrasound reveals hepatomegaly with hepatic vein dilation, flow reversal in the hepatic veins (Doppler), and possibly ascites.

DIAGNOSTIC PROCEDURES

ECG Findings

- Small (<1 mV) QRS complexes in all frontal axis leads if pericardial or pleural effusion.
- Electrical alternans or elevated ST segment with pericardial effusion.
- Evidence of right cardiomegaly (e.g., tall [$>0.4 \text{ mV}$] P waves in lead II, deep S waves in leads I, II, aVF, and right axis deviation).
- Atrial or ventricular arrhythmias.
- ECG may be normal.

Abdominocentesis

Analysis of ascitic fluid in patients with R-CHF generally reveals modified transudate with total protein $>2.5 \text{ mg/dL}$.

Thoracentesis

- Cats with pleural effusion associated with R-CHF may have transudate, modified transudate, or chylous effusion.
- Dogs with pleural effusion and R-CHF may have transudate or modified transudate.

Central Venous Pressure

Central venous pressure is high ($>9 \text{ cmH}_2\text{O}$) or rises dramatically to that level and remains elevated for more than 1h following a fluid bolus (e.g., 5–10 mL/kg IV).

PATHOLOGIC FINDINGS

- Cardiac findings vary with disease.
- Hepatomegaly in animals with centrolobular necrosis (chronic condition).

CONGESTIVE HEART FAILURE, RIGHT-SIDED

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Most animals treated as outpatients unless dyspneic or collapsed (e.g., significant pleural or pericardial effusion).

NURSING CARE

Thoracentesis and abdominocentesis may be required periodically for patients no longer responsive to medical management or those with severe dyspnea due to pleural effusion or ascites.

ACTIVITY

Restrict activity.

DIET

Restrict sodium moderately; severe sodium restriction indicated for animals with advanced disease.

CLIENT EDUCATION

- With few exceptions (e.g., in heartworm disease, arrhythmias, hyperthyroidism, and idiopathic pericardial effusion), R-CHF is not curable.
- Most patients improve with initial treatment but often have recurrent failure.

SURGICAL CONSIDERATIONS

- Surgical intervention or balloon valvuloplasty is indicated to treat certain congenital defects such as pulmonic stenosis or cor triatriatum dexter, and Amplatz occluder placement for morphologically appropriate atrial septal defects.
- Pericardiocentesis or pericardectomy for pericardial effusion.
- Removal of heartworms from the heart via the jugular vein in dogs with caval syndrome.



MEDICATIONS

DRUG(S) OF CHOICE

Drugs should be administered only after a definitive diagnosis is made.

Diuretics

- Furosemide (1–2 mg/kg q8–24h) or another loop diuretic is the initial diuretic of choice; diuretics are indicated to remove excess fluid accumulation.
- Torsemide (0.2–0.8 mg/kg q24h) may be a useful substitute for furosemide in animals requiring a daily furosemide dose in excess of 12 mg/kg.
- Spironolactone (2 mg/kg PO q12–24h) increases survival in humans with heart failure; use in combination with furosemide.

Vasodilators

- Angiotensin-converting enzyme (ACE) inhibitors such as enalapril (0.5 mg/kg q12–24h) or benazepril (0.25–0.5 mg/kg q24h) are helpful when CHF is secondary to DCM or chronic AV valve insufficiency.
- Sildenafil (0.5–1 mg/kg PO q12h up to 2–3 mg/kg q8h) may be beneficial for pulmonary hypertension.

Pimobendan

- Calcium sensitizer that acts as an inodilator, causing arterial vasodilation and increasing myocardial contractility.
- Especially useful in myocardial failure.
- Dose—0.25–0.3 mg/kg PO q12h.

Digoxin

- Digoxin (dogs: 0.22 mg/m² q12h; cats: 0.01 mg/kg q48 h) is used in animals with myocardial failure (e.g., DCM) and atrial fibrillation.
- Digoxin indicated in animals with refractory CHF that have supraventricular arrhythmias.

CONTRAINDICATIONS

- Avoid diuretics in patients with pericardial effusion/tamponade.
- Avoid vasodilators in patients with pericardial effusion or fixed outflow obstructions.

PRECAUTIONS

- ACE inhibitors and arterial dilators must be used with caution in patients with possible outflow obstructions.
- Pulmonary hypertension, hypothyroidism, and hypoxia increase risk for digoxin toxicity; hyperthyroidism diminishes effects of digoxin.
- ACE inhibitors and digoxin—use cautiously with renal disease.
- Dobutamine—use cautiously in cats.
- Spironolactone—may cause facial pruritis in cats.

POSSIBLE INTERACTIONS

- Combination of high-dose diuretics and ACE inhibitors may alter renal perfusion and cause azotemia.
- Combination diuretic therapy promotes risk of dehydration and electrolyte disturbances.

ALTERNATIVE DRUG(S)

- Patients unresponsive to furosemide, spironolactone, vasodilator, pimobendan, and digoxin (if indicated) may benefit from triple diuretic therapy by adding a thiazide diuretic, or substitution of torsemide for furosemide, generally at 0.1–0.2 mg of torsemide for each 1 mg of furosemide previously administered.
- Potassium and magnesium supplementation if deficiency documented; use potassium supplements cautiously in animals receiving ACE inhibitors or spironolactone.
- Treat

arrhythmias if clinically indicated.

- Taurine supplementation in cats with DCM and dogs with DCM and taurine deficiency.
- Carnitine supplementation may help some dogs with DCM (e.g., cocker spaniels and boxers).



FOLLOW-UP

PATIENT MONITORING

- Monitor renal status, electrolytes, hydration, respiratory rate and effort, bodyweight, and abdominal girth (dogs).
- If azotemia develops, reduce diuretic dosage; if azotemia persists and the animal is also on an ACE inhibitor, reduce or discontinue this drug; if azotemia develops, reduce digoxin dosage to avoid toxicity.
- Monitor ECG periodically to detect arrhythmias.
- Monitor digoxin concentrations—normal value 0.5–1.5 ng/mL for serum sample obtained 8–10h after dose is administered.

POSSIBLE COMPLICATIONS

- Pulmonary thromboembolism.
- Arrhythmias.
- Electrolyte imbalances.
- Digoxin toxicity.
- Azotemia and renal failure.

EXPECTED COURSE AND PROGNOSIS

Prognosis varies with underlying cause.



MISCELLANEOUS

AGE-RELATED FACTORS

- Congenital causes seen in young animals.
- Degenerative heart conditions and neoplasia generally seen in old animals.

SEE ALSO

- Ascites.
- Chylothorax.
- Pleural Effusion.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- ARVC = arrhythmogenic right ventricular cardiomyopathy.
- AV = atrioventricular.
- DCM = dilated cardiomyopathy.
- R-CHF = right-sided congestive heart failure.

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CONJUNCTIVITIS—CATS

C



BASICS

DEFINITION

Inflammation of the conjunctiva, the vascularized mucous membrane that covers the anterior sclera (bulbar conjunctiva), lines the eyelids (palpebral conjunctiva), and lines the third eyelid.

PATOPHYSIOLOGY

May be primary or secondary to adnexal or ocular disease.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat

Breed Predilections

Infectious—purebred cats may be predisposed.

Mean Age and Range

Infectious—commonly affects young animals.

Predominant Sex

N/A

SIGNS

- Blepharospasm.
- Conjunctival hyperemia.
- Ocular discharge—serous, mucoid, or mucopurulent.
- Chemosis.
- Conjunctival follicles.
- Upper respiratory infection—possible with infectious etiologies.

CAUSES

Viral

- Feline herpesvirus (FHV)—most common infectious cause; only one that leads to corneal changes (e.g., dendritic or geographic ulcers).
- Calicivirus—may cause conjunctival ulcerations.

Bacterial

- *Chlamydophila felis*—chemosis is common clinical sign.
- *Mycoplasma* spp.—may be overgrowth of normal flora.
- Conjunctivitis neonatorum—accumulation of exudates under closed eyelids prior to natural opening; bacterial or viral component.

Immune-Mediated

- Eosinophilic.
- Lipogranulomatous.
- Allergic.
- Related to systemic immune-mediated disease.

Trauma or Environmental Causes

- Conjunctival foreign body.
- Irritation from dust, smoke, chemicals, or ophthalmic medications.

Secondary to Adnexal Disease

- May develop keratoconjunctivitis sicca (KCS) as a result of scarring.
- Eyelid diseases (e.g., entropion, trichiasis, distichia, or eyelid agenesis)—cause frictional irritation or exposure.
- Dacryocystitis or nasolacrimal system outflow obstruction.

Referred Inflammation from Other Ocular or Periocular Diseases

- Ulcerative keratitis.
- Corneal sequestrum.
- Anterior uveitis.
- Glaucoma.
- Orbital disease.
- Pyoderma.

RISK FACTORS

Stress or immune system compromise (FHV).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must distinguish primary conjunctivitis from secondary conjunctival hyperemia.
- Thorough ophthalmic exam rules out other diseases (e.g., ulcers, uveitis, glaucoma, orbital disease); assess pupil size and symmetry, look for aqueous flare, perform intraocular pressure testing and fluorescein staining.
- Deeper, darker, more linear and immobile blood vessel injection indicates episcleral vasculature congested due to intraocular disease.
- Conjunctival mass biopsy will identify neoplasia (lymphoma and squamous cell carcinoma most common).

CBC/BIOCHEMISTRY/URINALYSIS

Normal, except with systemic disease.

OTHER LABORATORY TESTS

Infectious—serologic testing for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV).

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Thorough adnexal examination—rule out eyelid abnormalities and foreign bodies under eyelids or third eyelid.
- Complete ophthalmic examination—rule out other ocular disease (e.g., uveitis, glaucoma).
- Fluorescein stain—assess for corneal ulceration or dendritic lesions (FHV) and observe nares for stain passage to indicate nasolacrimal system patency.
- Nasolacrimal flush—considered to rule out dacryocystitis or nasolacrimal system obstruction.
- Schirmer tear test—measures aqueous tears to diagnose or rule out KCS; performed before anything is placed in the eye.
- Conjunctival cytology—rarely reveals cause; eosinophils with eosinophilic conjunctivitis; degenerate neutrophils and intracytoplasmic bacteria indicate bacterial infection; intracytoplasmic inclusion bodies indicate chlamydial or mycoplasmal infection; rarely see intranuclear FHV inclusions.
- Conjunctival biopsy—“snip biopsy” may be

useful with mass lesions and immune-mediated disease or chronic disease.

- PCR testing for chlamydia or FHV.
- Virus isolation or immunofluorescence antibody (IFA) testing for FHV; false-positive result if fluorescein staining is done before IFA testing.

- Serologic test for FHV antibodies—not useful (widespread exposure, vaccination).

PATHOLOGIC FINDINGS

- Biopsy—signs of inflammation, possible infectious agents.
- Histopathology of mass lesions may reveal neoplasia (e.g., squamous cell carcinoma and lymphoma).



TREATMENT

APPROPRIATE HEALTH CARE

- Primary—often outpatient.
- Secondary to other diseases (ulcerative keratitis, uveitis, glaucoma)—may need hospitalization to address severe underlying ophthalmic issue.

NURSING CARE

- Irritant-induced conjunctivitis—flush ocular surfaces and remove foreign body if observed.
- Topical hyaluronate-based artificial tear, q8h to benefit tear film.
- Frequent cleaning of eyelid margins and periocular skin to remove ocular discharge.

ACTIVITY

- Generally, no restrictions.
- Suspected contact irritant or acute allergic disease—prevent contact with the offending agent.
- Suspected FHV—minimize stress.
- Do not expose patients with infectious disease to susceptible animals.

DIET

- No change for most patients.
- Suspected underlying skin disease and/or food allergy—food elimination diet.

CLIENT EDUCATION

- When solutions and ointments are prescribed, instruct the client to use solution(s) before ointment(s) and wait at least 5 minutes between treatments.
- If copious discharge is noted, instruct client to clean eyes before giving medication.
- Instruct client to call for instructions if condition fails to improve or worsens.

SURGICAL CONSIDERATIONS

- Lipogranulomatous conjunctivitis—surgical incision and curettage of glandular material and inflammatory infiltrates.
- Entropion, distichia, or other eyelid disease—perform temporary or permanent surgery depending on the findings, signalment, and history.
- Nasolacrimal duct obstruction—difficult; treatment often not recommended (see Epiphora).
- Conjunctival neoplasia—depending on tumor type and extent of involvement, may involve local excision and adjunctive therapy (β-irradiation, cryotherapy), enucleation, or exenteration.
- Symblepharon

CONJUNCTIVITIS—CATS

(CONTINUED)

C

(adhesions between the conjunctiva and cornea)—adhesions may require surgical resection (poor prognosis). • Corneal sequestration—keratectomy often recommended (see Corneal Sequestrum—Cats).



MEDICATIONS

DRUG(S) OF CHOICE

Herpetic

- Condition usually mild and self-limiting.
- Antiviral treatment—indicated for severe intractable conjunctivitis, herpetic keratitis, and before keratectomy for corneal sequestra suspected to be related to FHV; for all antivirals treat 2 weeks past resolution of clinical signs.
- 0.5% cidofovir solution (available from compounding pharmacies)—topical, q12h.
- 0.1% idoxuridine solution or 0.5% ointment (compounding pharmacies)—topical, q4h.
- Vidarabine 3% ointment—topical, q4h.
- Trifluridine 1% solution—topical, q4h; potentially irritating.
- Oral famciclovir is effective and safe; recommended dosage 90 mg/kg PO q12h.
- Lysine 500 mg PO q12h for adult cat (250 mg PO q12h for kitten).
- FortiFlora® probiotic PO q24h may decrease incidence of conjunctivitis associated with FHV.

Chlamydial or Mycoplasmal

- Tetracycline, erythromycin, or chloramphenicol ophthalmic ointment—topically q6–8h; continue for several days past resolution of all clinical signs; recurrence or reinfection common.
- Topical ciprofloxacin ophthalmic solution q6–8h as alternative to ophthalmic ointment.
- Doxycycline 10 mg/kg PO q24h for 3–4 weeks may be superior to or used along with topical treatment.
- Based on bacterial culture and sensitivity results.

Neonatal

Carefully open the eyelid margins (medial to temporal), establish drainage, and treat with topical antibiotic ointment q6–8h and an antiviral for suspected FHV.

Eosinophilic

- Topical corticosteroid—0.1% dexamethasone sodium phosphate q6–8h generally effective; taper gradually to lowest effective dose or transition to cyclosporine.
- Cyclosporine

0.2% ointment 1–2% compounded solution, or tacrolimus 0.03% compounded solution—topical therapy q8–24h.

- Topical 0.5% megestrol acetate solution (available from compounding pharmacies)—q8–12h; safe with concurrent corneal ulceration and/or concurrent FHV ocular disease.
- Oral megestrol acetate—may help resistant condition, but rarely used given possible systemic side effects.

CONTRAINDICATIONS

- Topical corticosteroids—avoid with known or suspected infectious conjunctivitis; may result in FHV recrudescence and predispose to corneal sequestrum formation; never use if corneal ulceration is noted.
- Valacyclovir should never be used in cats.

PRECAUTIONS

- Topical medications may be irritating.
- Monitor all patients treated with topical corticosteroids for signs of corneal ulceration; discontinue agent immediately if corneal ulceration occurs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Other corticosteroids—1% prednisolone acetate.



FOLLOW-UP

PATIENT MONITORING

Recheck shortly after beginning treatment (at 5 days), then in 2 weeks or as needed.

PREVENTION/AVOIDANCE

- Treat any underlying disease that may be exacerbating the conjunctivitis.
- Minimize stress for patients with herpetic disease.
- Isolate patients with infectious conjunctivitis to prevent spread.
- Prevent reexposure to infectious sources.
- Vaccination recommended; infection is still possible if the cat was exposed to an infectious agent before being vaccinated (e.g., FHV infection from an infected queen).

POSSIBLE COMPLICATIONS

- Corneal sequestration (see Corneal Sequestrum—Cats)—usually requires surgical keratectomy.
- Symblepharon—may require surgery.
- KCS—most likely from chronic FHV.

EXPECTED COURSE AND PROGNOSIS

- FHV—most patients become chronic carriers; may see repeated exacerbations, but episodes less common as patient matures; more severe clinical signs at times of stress or immunocompromise.
- Bacterial conjunctivitis—usually resolves with appropriate administration of antibiotic.
- Immune-mediated diseases (e.g., eosinophilic)—control not cure; may require chronic treatment at lowest level possible.
- If underlying disease is found (e.g., KCS, entropion), resolution may depend on appropriate treatment of the disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

FeLV and FIV—may predispose patient to chronic carrier state of FHV conjunctivitis.

AGE-RELATED FACTORS

FHV—tends to be more severe in kittens and in old cats with waning immunity.

ZOONOTIC POTENTIAL

Chlamydophila felis—low.

PREGNANCY/FERTILITY/BREEDING

Use topical and systemic medications with caution, if at all, in pregnant animals.

SEE ALSO

- Corneal Sequestrum—Cats.
- Keratoconjunctivitis Sicca.
- Ophthalmia Neonatorum.
- Red Eye.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FHV = feline herpesvirus.
- FIV = feline immunodeficiency virus.
- IFA = immunofluorescent antibody.
- KCS = keratoconjunctivitis sicca.

Suggested Reading

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CONJUNCTIVITIS—DOGS

C



BASICS

DEFINITION

Inflammation of the conjunctiva, the vascularized mucous membrane that covers the anterior sclera (bulbar conjunctiva), lines the eyelids (palpebral conjunctiva), and lines the third eyelid.

PATHOPHYSIOLOGY

- Primary—allergic, infectious, environmental.
- Secondary to other ocular disease—keratoconjunctivitis sicca (KCS), entropion, distichiasis.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog

Breed Predilection

Breeds predisposed to allergic or immune-mediated skin diseases (e.g., atopy) tend to have more problems with allergic conjunctivitis or KCS.

Mean Age and Range

N/A

Predominant Sex

None

SIGNS

- Blepharospasm. • Conjunctival hyperemia. • Ocular discharge—serous, mucoid, or mucopurulent. • Chemosis. • Follicle formation on posterior third eyelid surface. • Enophthalmos and third eyelid elevation.

CAUSES

Infectious

- Bacterial—rare as primary condition, usually secondary to KCS; conjunctivitis neonatorum involves accumulation of exudates under closed eyelids prior to natural opening. • Viral—canine herpes virus-1, canine distemper virus, or canine adenovirus-2. • Parasitic—*Leishmania*, *Onchocerca*, or *Thelazia*. • Conjunctival manifestation of systemic infectious disease

Immune-Mediated

- Allergic—especially in atopic patients.
- Follicular conjunctivitis—common in dogs <18 months, secondary to chronic antigenic stimulation. • Lymphocytic/plasmacytic conjunctivitis—especially in German shepherd dogs with or without

chronic superficial keratitis (pannus).

- Systemic immune-mediated disease (e.g., pemphigus).

Trauma or Environmental Causes

- Conjunctival foreign body. • Irritation (dust, smoke, ophthalmic medications). • Toxin or chemical contact.

Other

Ligneous conjunctivitis—rare, young female Dobermanns may be predisposed.

Secondary to Adnexal Disease

- Aqueous tear film deficiency (KCS) or qualitative tear deficiency. • Eyelid diseases—entropion, ectropion, medial canthal pocket syndrome, eyelid mass. • Hair or eyelash disorders—trichiasis, distichiasis, ectopic cilia. • Exposure—facial nerve paralysis, lagophthalmos. • Dacryocystitis or nasolacrimal system outflow obstruction (e.g., obstructed duct or imperforate punctum).

Referred Inflammation from Other Ocular or Periocular Diseases

- Ulcerative keratitis. • Nodular episcleritis. • Anterior uveitis. • Glaucoma. • Orbital disease. • Pyoderma.

RISK FACTORS

Atopy, KCS.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Distinguish primary conjunctivitis from secondary conjunctival hyperemia. • Thorough systematic ophthalmic exam identifies other potential diseases (e.g., KCS, ulcers, uveitis, glaucoma, orbital disease); assess pupil size and symmetry, look for aqueous flare, attempt globe retropulsion, perform Schirmer tear test, intraocular pressure measurement, and fluorescein staining. • Deeper, darker, more linear and immobile blood vessel injection indicates congested episcleral vasculature due to episcleritis or intraocular disease. • Mass biopsy will differentiate conjunctival neoplasia (rare: squamous cell carcinoma, melanoma, hemangioma/sarcoma, lymphoma, papilloma, mast cell tumor) or episcleritis.

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless systemic disease.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Adnexal examination—rule out facial nerve paralysis, lagophthalmos, eyelid abnormalities, hair or eyelash disorders, and foreign bodies in cul-de-sacs or under third eyelid. • Schirmer tear test—rule out KCS; perform before anything

else is placed in eye. • Fluorescein stain—no corneal retention rules out ulcerative keratitis; stain flow to nares rules out nasolacrimal disease.

- Tear film breakup time—assesses tear film stability to rule out qualitative tear deficiency.
- Intraocular pressures—rule out glaucoma.
- Globe retropulsion—rule out orbital disease.
- Examine for signs of anterior uveitis (e.g., hypotony, aqueous flare, miosis) or other intraocular disease (e.g., cataracts, lens luxation).
- Consider nasolacrimal duct flush if fluorescein stain did not pass to nares. • Conjunctival cytology—lymphocytes and plasma cells diagnostic for lymphocytic/plasmacytic conjunctivitis; eosinophils in allergic conjunctivitis; degenerate neutrophils and intracellular bacteria with bacterial infection; rarely distemper virus intracytoplasmic inclusions. • Conjunctival biopsy—may be useful with mass lesions and nodular episcleritis or chronic undiagnosed disease. • PCR or viral isolation testing for canine herpesvirus-1.
- Intradermal skin testing—if suspect allergic conjunctivitis.

PATHOLOGIC FINDINGS

- Biopsy—inflammation, may note infectious agents, neoplasia, or nodular episcleritis.
- Ligneous conjunctivitis—thick, amorphous eosinophilic hyaline-like material.



TREATMENT

APPROPRIATE HEALTH CARE

- Primary—outpatient. • Secondary to other disease (e.g., ulcerative keratitis, uveitis, glaucoma, lens luxation)—may require hospitalization to address underlying ophthalmic issue.

NURSING CARE

- Irritant-induced conjunctivitis—flush ocular surfaces and remove foreign body if observed.
- Allergic or follicular conjunctivitis—apply viscous artificial tear gel to both eyes before patient is active outdoors (q8–12h), then flush ocular surface with eye wash when returning indoors to remove “trapped” allergens.
- Secondary to ectropion or medial canthal pocket syndrome—flush ocular surface with eye wash daily to remove dust, dirt, or other matter that collects ventrally. • Warm pack eyelids and periocular skin to soften crusted secretions and improve comfort.

ACTIVITY

- No restriction for most. • Suspected contact irritant or allergic disease—prevent contact with offending agent. • Do not expose patients with infectious viral disease to susceptible animals.

DIET

- No change for most. • Suspected underlying skin disease and/or food allergy—food elimination diet trial.

C CONJUNCTIVITIS—DOGS

(CONTINUED)

C

CLIENT EDUCATION

- When solutions and ointments are prescribed, the client should use solution(s) before ointment(s) and wait 5 minutes between treatments.
- If copious discharge is noted, clean eyes before giving medication.
- Call for instructions if condition fails to improve or worsens.
- An Elizabethan collar should be placed on the patient to prevent self-trauma.

SURGICAL CONSIDERATIONS

- Follicular conjunctivitis—if follicles are unresponsive to medication, consider debridement.
- Entropion, distichia, ectopic cilia, or other eyelid disease—perform temporary or permanent surgery depending on findings, signalment, and history.
- Nasolacrimal duct obstruction—if repeated flushing attempts at weekly intervals along with medical therapy are unsuccessful, consider contrast study and surgery (see Epiphora).
- Conjunctival neoplasia—depending on tumor type and extent of involvement, may involve local excision and adjunctive therapy (β -irradiation, cryotherapy), enucleation, or exenteration.



MEDICATIONS

DRUG(S) OF CHOICE

Bacterial

- Initial treatment—broad-spectrum topical triple antibiotic q6–8h continuing several days past resolution of clinical signs; revise based on bacterial culture and sensitivity results.
- Systemic antibiotic (e.g., cephalosporin)—occasionally indicated, especially for more generalized disease (e.g., pyoderma).

Neonatal

Carefully open eyelid margins (medial to lateral), establish drainage, and treat with topical antibiotic ointment q6–8h.

Herpetic

- Condition usually mild and self-limiting.
- Antiviral treatment—indicated for severe intractable canine herpesvirus-1 conjunctivitis or herpetic keratitis.
- 0.15% ganciclovir gel—topical q4h for 7 days, then q8h.
- 1% trifluridine solution—topical q4h for 2 days, then q6h.
- 0.1% idoxuridine solution (compounding pharmacies)—topical q4h for 2 days, then q6h.
- 0.5% cidofovir solution (compounding pharmacies)—topical q12h; generally avoided: reduces duration of shedding but may worsen clinical disease due to local ocular toxic effects.

Immune-Mediated

- Depends on severity.
- Allergic and follicular conjunctivitis—attempt nursing care first with viscous artificial tear gel lubricants and ocular flushing q8–12h; if nonresponsive consider antihistamine eye drops (e.g., ketotifen) q8–12h, or topical corticosteroid (e.g., dexamethasone) q8–12h.
- Lymphocytic/plasmacytic conjunctivitis—0.1% dexamethasone q8h, then taper gradually to lowest effective dose; could attempt transition to cyclosporine 0.2% ointment, cyclosporine 1–2% compounded solution q12–24h, or tacrolimus 0.03% compounded solution q12–24h.
- Treatment of any underlying disease (e.g., atopy) often improves clinical signs of allergic conjunctivitis.

Tear Deficiencies

- Aqueous tear film deficiency (see Keratoconjunctivitis Sicca).
- Qualitative tear deficiency—cyclosporine 0.2% ointment, cyclosporine 1–2% compounded solution q12h, or tacrolimus 0.03% compounded solution q12–24h, and viscous artificial tear lubricants q6–12h.

CONTRAINdications

Topical corticosteroids—avoid if corneal ulceration is present, patient is at high risk for ulceration (e.g., entropion, lagophthalmos, severe KCS), or with known or suspected infectious conjunctivitis.

PRECAUTIONS

- Topical medications may be irritating.
- Topical corticosteroids—monitor all patients carefully for signs of corneal ulceration; discontinue agent immediately if corneal ulceration occurs.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Other corticosteroids—1% prednisolone acetate, betamethasone, hydrocortisone.



FOLLOW-UP

PATIENT MONITORING

Recheck shortly after beginning treatment (at 5 days), then recheck in 2 weeks or as needed.

PREVENTION/AVOIDANCE

Treat any underlying disease that may be exacerbating the conjunctivitis (e.g., KCS, allergic or immune-mediated skin disease).

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

- Good prognosis when underlying cause identified and treated (e.g., KCS, adnexal disease, eyelash disorder).
- Bacterial—usually resolves with appropriate antibiotics; may depend on control of underlying disease (e.g., KCS).
- Allergic or follicular—nursing care or medical treatment may be needed during peak allergy times.
- Lymphocytic/plasmacytic—tend to be controlled and not cured; may require chronic treatment at lowest level possible.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Atopy.
- Pyoderma.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Use topical and systemic medications with caution, if at all, in pregnant animals.

SEE ALSO

- Epiphora.
- Keratoconjunctivitis Sicca.
- Red Eye.

ABBREVIATIONS

- KCS = keratoconjunctivitis sicca.

Suggested Reading

Hendrix DVH. Diseases and surgery of the canine conjunctiva and nictitating membrane. In: Gelatt KN, Gilger BC, Kern T, eds., Veterinary Ophthalmology, 5th ed. Ames, IA: Wiley-Blackwell, 2013, pp. 945–975.

Maggs DJ, Miller PE, Ofri R. Slatter's Fundamentals of Veterinary Ophthalmology, 6th ed. St. Louis, MO: Elsevier, 2018, pp. 158–177.

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Consulting Editor Katherin E. Myrna



Client Education Handout
available online

CONSTIPATION AND OBSTIPATION



BASICS

DEFINITION

- *Constipation* is defined as infrequent, incomplete, or difficult defecation with passage of hard or dry feces. This does not imply abnormal motility or loss of function.
- *Obstipation* denotes intractable constipation that has failed several consecutive treatments; defecation is impossible in the obstipated patient.

PATHOPHYSIOLOGY

- Constipation can develop with any disease that impairs the passage of feces through the colon. Potential causes include congenital vertebral malformation, spinal cord disease, pelvic canal narrowing (trauma), rectal mass lesions causing obstruction, and perianal disease causing painful defecation. Often in cats no underlying etiology can be identified.
- Delayed fecal transit allows removal of additional salt and water, producing drier feces. Clinical signs are attributable to dehydration and potential toxemia resulting from fecal retention.
- Peristaltic contractions may increase during constipation, but eventually motility diminishes because of smooth muscle degeneration secondary to chronic overdistension.

SYSTEMS AFFECTED

Gastrointestinal.

GENETICS

N/A

INCIDENCE/PREVALENCE

Common clinical problem in older cats; less common in dogs.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

- Dog and cat. • More common in cat.

Breed Predilections

N/A

Mean Age and Range

Any age; most common in older cats.

Predominant Sex

N/A

SIGNS

Historical Findings

- Reduced, absent, or painful defecation.
- Hard, dry feces. • Small amount of liquid, mucoid stool, sometimes with blood present produced after prolonged tenesmus. • Occasional vomiting, inappetence, and/or lethargy.

Physical Examination Findings

- Colon filled with hard feces. Severe impaction may cause abdominal distention.

- Other findings depend on underlying cause. • Rectal examination may reveal mass, stricture, perineal hernia, anal sac disease, foreign body or material, prostatic enlargement, or narrowed pelvic canal.

CAUSES

Dietary

- Bones. • Hair. • Foreign material. • Excessive fiber. • Inadequate water intake.

Environmental

- Lack of exercise. • Change of environment—hospitalization, dirty litter box. • Inability to ambulate.

Drugs

- Anticholinergics. • Antihistamines.
- Opioids. • Barium sulfate. • Sucralfate.
- Antacids. • Kapectolin. • Iron supplements. • Diuretics.

Painful Defecation (Dyschezia)

- Anorectal disease—anal sacculitis, anal sac abscess, perianal fistula, anal stricture, anal spasm, rectal foreign body, rectal prolapse, proctitis. • Trauma—fractured pelvis, fractured limb, dislocated hip, perianal bite wound or laceration, perineal abscess.

Mechanical Obstruction

- Extraluminal—healed pelvic fracture with narrowed pelvic canal, prostatic hypertrophy, prostatitis, prostatic neoplasia, intrapelvic neoplasia, sublumbar lymphadenopathy.
- Intraluminal and intramural—colonic or rectal neoplasia or polyp, rectal stricture, rectal foreign body, rectal diverticulum, perineal hernia, rectal prolapse, congenital defect (atresia ani).

Neuromuscular Disease

- Central nervous system—paraplegia, spinal cord disease, intervertebral disc disease, cerebral disease (lead toxicity, rabies).
- Peripheral nervous system—dysautonomia, sacral nerve disease, sacral nerve trauma (e.g., tail fracture/pull injury). • Colonic smooth muscle dysfunction—idiopathic megacolon in cats.

Metabolic and Endocrine Disease

- Impaired colonic smooth muscle function—hyperparathyroidism, hypothyroidism, hypokalemia (chronic renal failure), hypercalcemia. • Debility—general muscle weakness, dehydration, neoplasia.

RISK FACTORS

- Manx cats may be predisposed due to vertebral (sacral) abnormalities. • Drug therapy—anticholinergics, narcotics, barium sulfate. • Metabolic disease causing dehydration. • Feline dysautonomia. • Intact male—perineal hernia, benign or infectious prostatic disease. • Castrated male—prostatic neoplasia. • Perianal fistula.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Dyschezia and tenesmus (e.g., caused by colitis or proctitis)—unlike constipation, associated with increased frequency of attempts to defecate and frequent production of small amounts of liquid feces containing blood and/or mucus; rectal examination reveals diarrhea and lack of hard stool.
- Stranguria (e.g., caused by cystitis/urethritis)—unlike constipation, can be associated with hematuria and abnormal findings on urinalysis (pyuria, crystalluria, bacteruria).

CBC/BIOCHEMISTRY/URINALYSIS

- Usually unremarkable. • May detect hypokalemia, hypercalcemia. • High packed cell volume (PCV) and total protein in dehydrated patients. • High white blood cell (WBC) count in patients with severe obstipation secondary to bacterial or endotoxin translocation, abscess, perianal fistula, prostatic disease. • Pyuria and hematuria with prostatitis.

OTHER LABORATORY TESTS

- If patient is hypercholesterolemic, consider thyroid panel to rule out hypothyroidism. • If patient is hypercalcemic, consider parathyroid hormone assay.

IMAGING

- Abdominal radiography documents severity of colonic impaction. Other findings may include colonic or rectal foreign body, colonic or rectal mass, prostatic enlargement, fractured pelvis, dislocated hip, or perineal hernias. • Pneumocolon (after enemas to clean colon) may better define intraluminal mass or stricture.
- Ultrasonography may help define extraluminal mass and prostatic disease.

DIAGNOSTIC PROCEDURES

Colonoscopy may be needed to identify a mass, stricture, or other colonic or rectal lesion; rectal/colonic mucosal biopsy specimens should always be obtained.

PATHOLOGIC FINDINGS

Dependent on underlying disease process.



TREATMENT

APPROPRIATE HEALTH CARE

- Remove or ameliorate any underlying cause if possible. • Discontinue any medications that may cause constipation. • May need to treat as inpatient if obstipation and/or dehydration present.

C CONSTIPATION AND OBSTIPATION

(CONTINUED)

C

NURSING CARE

Dehydrated patients should receive IV (preferably) or SC balanced electrolyte solutions (with potassium supplementation if indicated).

ACTIVITY

Encourage activity.

DIET

Dietary supplementation with a bulk-forming agent (bran, methylcellulose, canned pumpkin, psyllium) is often helpful, though they can sometimes worsen colonic fecal distension; in this instance, feed a low-residue diet.

CLIENT EDUCATION

- Feed appropriate diet and encourage activity.
- Survey cat boxes daily to ensure level of defecation activity.

SURGICAL CONSIDERATIONS

• Manual removal of feces through the anus with the animal under general anesthesia (after rehydration) may be required if enemas and medications are unsuccessful. • Subtotal colectomy may be required with recurring obstipation that responds poorly to assertive medical therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Emollient laxatives—docusate sodium or docusate calcium (dogs: 50–100 mg PO q12–24h; cats: 50 mg PO q12–24h).
- Stimulant laxatives—bisacodyl (5 mg/animal PO q8–24h). Ensure that animal is not obstructed prior to use of stimulant laxatives.
- Saline laxatives—isosmotic mixture of polyethylene glycol and poorly absorbed salts; usually administered as a trickle amount via nasoesophageal tube over 6–12h.
- Disaccharide laxative—lactulose (1 mL/4.5 kg PO q8–12h to effect).
- Warm water enemas may be needed; a small amount of mild soap or docusate sodium can be added but is usually not needed; sodium phosphate retention enemas (e.g., Fleet[®]) are contraindicated because of their association with severe hypocalcemia.
- Suppositories can be used as a replacement for enemas; use glycerol, bisacodyl, or docusate sodium products.
- Motility modifiers can be administered—cisapride (dogs: 0.3–0.5 mg/kg PO q8–12h; cats: 2.5–10 mg/cat PO q8–12h) may stimulate colonic motility; indicated with early megacolon.

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CONTRAINDICATIONS

- Lubricants such as mineral oil and white petrolatum are *not* recommended because of the danger of fatal lipid aspiration pneumonia due to their lack of taste.
- Fleet (sodium phosphate) enemas.
- Anticholinergics.
- Diuretics.

PRECAUTIONS

Cisapride and cholinergics—can be used with caution; contraindicated in obstructive processes. Avoid the use of metoclopramide because it does not affect the colon.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Ranitidine causes contraction of colonic smooth muscle in vitro.
- Misoprostol causes contraction of colonic smooth muscle in vitro.
- Newer-generation cisapride-like drugs may be available soon.
- One recent pilot study using multistrain probiotic SLAB51[®] showed clinical improvement in a feline cohort having chronic constipation and idiopathic megacolon.



FOLLOW-UP

PATIENT MONITORING

Monitor frequency of defecation and stool consistency at least twice a week initially, then weekly or biweekly in response to dietary and/or drug therapy.

PREVENTION/AVOIDANCE

Keep pet active and feed appropriate diet. Subcutaneous fluids to ensure hydration can help reduce frequency of constipation, particularly in cats.

POSSIBLE COMPLICATIONS

- Chronic constipation or recurrent obstipation can lead to acquired megacolon.
- Overuse of laxatives and enemas can cause diarrhea.
- Colonic mucosa can be damaged by improper enema technique, repeated rough mechanical breakdown of feces, or ischemic necrosis secondary to pressure of hard feces.
- Perineal irritation

and ulceration can lead to fecal incontinence.

EXPECTED COURSE AND PROGNOSIS

- Fair to good prognosis with early diagnosis and intervention.
- Recurring bouts of constipation/obstipation may occur dependent on underlying cause.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Vomiting—with severe/prolonged obstipation.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Colonic impaction.
- Fecal impaction.

SEE ALSO

Megacolon

ABBREVIATIONS

- PCV = packed cell volume.
- WBC = white blood cell.

Suggested Reading

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Author Albert E. Jergens

Consulting Editor Mark P. Rondeau



Client Education Handout
available online

CONTACT DERMATITIS

C



BASICS

OVERVIEW

- Irritant and allergic contact dermatitis—rare syndromes with similar clinical signs but different pathophysiology; differentiation may be more conceptual.
- Irritant contact dermatitis (ICD)—direct damage to keratinocytes by exposure to particular irritant or sensitizer induces inflammatory response directed at skin without prior sensitization.
- Allergic contact dermatitis (ACD)—type IV (delayed) hypersensitivity: immunologic event requiring sensitization and elicitation; Langerhans cells and keratinocytes interact with environmental haptens to create antigens, leading to sensitization of T-lymphocytes and activation following reexposure with release of cytokines (mainly tumor necrosis factor alpha • [TNF- α], IL1 β GM-CSF).
- Recent reports blur distinction between ICD, ACD, and atopic dermatitis.

SIGNALMENT

- ICD—Any age as direct result of irritation from offending chemical.
- ACD—older dogs; chronic exposure to antigen (months to years); extremely rare in cats, (except exposure to d-limonene-containing insecticides).
- ACD—German shepherd dog, poodle, wirehaired fox terrier, Scottish terrier, West Highland white terrier, Labrador and golden retriever.

SIGNS

Lesions

- Location determined by antigen contact; commonly limited to glabrous skin and regions frequently in direct contact with the environment.
- Extreme erythroderma stops abruptly at hairline.
- Initial erythema, edema, and papules leading to crusts and excoriations; lichenification and hyperpigmentation with chronicity; vesicles uncommon.

Others

- Localized reactions to topical medications.
- Generalized reactions to shampoos or insecticide sprays.
- Pruritus—moderate to severe (most common).
- Seasonal incidence may indicate plant or outdoor antigen.

CAUSES & RISK FACTORS

- Reported offending substances—plants, mulch, cedar chips, fabrics, rugs, carpets, plastics, rubber, leather, nickel, cobalt, concrete, soaps, detergents, floor waxes, epoxy resin, carpet and litter deodorizers, herbicides, fertilizers, insecticides (including topical flea treatments), flea collars, topical preparations (neomycin).
- Increased incidence with atopic disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypersensitivity dermatitis.
- Drug reaction.
- Pelodera dermatitis.
- Hookworm dermatitis.
- Pyoderma.
- *Malassezia* dermatitis.
- Demodicosis.
- Solar dermatitis.
- Thermal injuries.
- Trauma from rough surfaces.

DIAGNOSTIC PROCEDURES

- ACD—closed-patch test (corticosteroids and nonsteroidal anti-inflammatory drugs [NSAIDs] must be discontinued for 3–6 weeks); materials taken from environment or home applied to upper thorax skin under bandage; examine for erythema, edema, pruritus at 48, 72 hours, and 7 days.
- ICD—eliminate exposure to contact irritant or antigen, followed by provocation.
- Open patch test—apply substance to inside pinnae; monitor for mild erythema, edema, pruritus; examine daily for 5–15 days.
- Human patch test kits (TRUE Test®).
- Skin biopsy.

PATHOLOGIC FINDINGS

- Intraepidermal vesiculation and spongiosis; superficial dermal edema with perivascular mononuclear cell infiltrate in ICD and ACD; polymorphonuclear cell infiltrate in ICD; leukocyte exocytosis common.
- Lymphocytic spongiotic or eosinophilic and lymphocytic spongiotic infiltrate with intraepidermal eosinophilic pustules in canine ACD.



TREATMENT

- Eliminate offending substance(s).
- Bathe with hypoallergenic shampoos to remove antigen from skin.
- Create mechanical barriers, if possible—socks, shirts, restriction from environment.



MEDICATIONS

DRUG(S) OF CHOICE

- Prednisolone (1 mg/kg PO q24h for 5–7 days, then q48h for 2 weeks).
- Topical corticosteroids for focal lesions.
- Topical tacrolimus.
- Pentoxyfylline (10–25 mg/kg PO q8–12h initially).
- Cyclosporine (modified, 5 mg/kg q24h).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Pentoxyfylline—do not administer with alkylating agents, cisplatin, or amphotericin B; cimetidine may increase serum levels of pentoxyfylline.



FOLLOW-UP

PREVENTION/AVOIDANCE

Remove offending substances from the environment.

EXPECTED COURSE AND PROGNOSIS

ICD

- Acute condition—may occur after only one exposure; can be manifested within 24 hours of exposure.
- Corticosteroids rarely helpful.
- Lesions resolve 1–2 days after irritant removal.

ACD

- Requires chronic exposure for hypersensitivity to develop.
- Reexposure results in development of clinical signs within 1–5 days; signs may persist for several weeks.
- Responds well to corticosteroids; pruritus returns after discontinuation if antigenic stimulus persists.
- Hypo sensitization not effective.
- Prognosis—good if allergen is identified and removed, otherwise poor: may require lifelong treatment.



MISCELLANEOUS

ABBREVIATIONS

- ACD = allergic contact dermatitis.
- ICD = irritant contact dermatitis.
- NSAID = nonsteroidal anti-inflammatory drug.
- TNF- α = tumor necrosis factor alpha.

Suggested Reading

Ho KK, Campbell KL, Lavergne SN. Contact dermatitis: a comparative and translational review of the literature. *Vet Dermatol* 2015; 26:314–327.

Author Liora Waldman

Consulting Editor Alexander H. Werner Resnick



BASICS

DEFINITION

- A sudden and often repetitively occurring defense reflex that helps clear large airways of excess secretions, irritants, foreign particles, and microbes, or clear foreign material from upper airways.
- The cough reflex consists of three phases: inhalation, forced exhalation against a closed glottis, and violent expulsion of air from the lungs following opening of the glottis, usually accompanied by a sudden noise. Coughing can happen voluntarily as well as involuntarily, although in dogs and cats it is presumed to be essentially involuntary. Coughing should not be confused with other airway sounds (cf differential diagnosis).

PATOPHYSIOLOGY

- A physiologic reflex in healthy animals that protects the lower airways from inhalation of foreign particles and helps clear particles that have been entrapped in the mucus; acts in conjunction with the mucociliary clearance mechanism.
- The cough pathway includes cough receptors, which are made up of sensory nerves in the airways, the vagus nerve, the central cough center, and effector muscles.
- The cough pathway can be stimulated by mechanical or chemical factors; endogenous triggers include airway secretions and inflammation; exogenous triggers include smoke and aspirated foreign material.
- Cough receptors include rapidly adapting stretch receptors (sensitive to mechanical stimuli) that are located within the mucosa of the tracheobronchial tree (especially larynx and trachea), and pulmonary/bronchial C-fibers, which are more sensitive to chemical stimulation; coughing mechanisms and pathways are very complex and are not fully understood, even in humans.

SYSTEMS AFFECTED

- Respiratory—cough of any origin can be an inciting factor for aggravation or precipitation of signs associated with tracheal collapse in susceptible breeds.
- Cardiovascular—enlargement or impaired function of the right ventricle can result from a respiratory disorder causing tissue damage, hypoxic injury, and/or chronic hypoxic pulmonary vasoconstriction (cor pulmonale).

SIGNALMENT

- Dogs and cats of all ages and breeds.
- Much more common clinical sign in dogs than in cats.
- Cough of tracheal origin is less common in cats than in dogs.
- Age, breed, and sex predispositions vary with inciting cause.

SIGNS

- Cough must be differentiated from similar signs such as reverse sneezing, gagging, retching.
- Description of the cough and/or smartphone recording of suspect sounds are helpful in identification of the anatomic

structures involved in dogs (i.e., honking cough is typical of tracheal collapse, harsh sonorous cough followed by terminal retch characterizes cough of tracheal or bronchial origin, faint moist cough is heard in moderate to severe pneumonia). • Cough can be described as dry or moist, productive, honking, short or harsh, faint or sonorous, followed by gagging or retching. • Cough can be elicited by traction on the collar (laryngeal or tracheal origin), aggravated by exercise or excitation (tracheal collapse), or can occur after a period of rest (cough due to heart failure). • Can be accompanied by stertor or stridor (laryngeal, tracheal origin) or dyspnea (many areas).

CAUSES

Upper Respiratory Tract Diseases

- A variety of sinonasal conditions cause extension of inflammation and/or secretions into the pharynx and/or larynx and can lead to the upper airway cough syndrome (UACS), previously referred to as postnasal drip syndrome.
- Laryngeal and/or pharyngeal disease (inflammation, paralysis, tumor, granuloma, collapse).
- Tracheal disease (inflammation, infection, foreign body, collapse, stenosis, tumor).

Lower Respiratory Tract Diseases

(Tracheobronchial or Bronchopulmonary Disease)

- Inflammatory (feline bronchitis syndrome; dogs: chronic bronchitis, eosinophilic bronchopneumopathy).
- Infectious—bacterial, viral (dog: distemper, kennel cough; cat: feline leukemia virus [FeLV], feline immunodeficiency virus [FIV], feline infectious peritonitis [FIP], calicivirus, herpesvirus), parasitic (dog: *Filaroides* spp., *Angiostrongylus vasorum*, *Capillaria aerophila*, *Crenosoma vulpis*; cat: *Aerulostrongylus abstrusus*; dog, cat: *Paragonimus kellicotti*, *Dirofilaria immitis*), protozoal (cat: toxoplasmosis; dog: pneumocystosis), fungal (blastomycosis, histoplasmosis, coccidiomycosis, cryptococcosis, aspergillosis).
- Neoplastic (primary, metastatic, compression due to enlarged lymph nodes).
- Chemical or traumatic (aspiration, near drowning, noxious fumes, foreign body, trauma, hemorrhage).
- Chronic disorders of unknown origin (interstitial pulmonary fibrosis).

Other Diseases

- Cardiovascular diseases (pulmonary edema, left atrial enlargement, heart-base tumor, embolism).
- Gastroesophageal reflux.
- Compression of respiratory structures by adjacent organs (cardiomegaly, megaesophagus, hilar lymph node enlargement).
- Noncardiogenic pulmonary edema (multiple causes).
- Passive smoking inhalation.
- Adverse drug reaction—potassium bromide in cats.

RISK FACTORS

Breed

- Toy and miniature breeds at risk for tracheal collapse.
- Terrier breeds at risk for pulmonary fibrosis.
- Husky, Rottweiler, Labrador, and Jack Russell terrier at risk for eosinophilic bronchopneumopathy.
- Giant breeds at risk for dilated cardiomyopathy.
- Labrador retriever, large breeds at risk for laryngeal paralysis.
- Siamese cats at risk for feline bronchitis syndrome.

Environmental Factors

Longhaired cats that are infrequently groomed will periodically retch, cough, and vomit up mats of hair.

Drugs

Potassium bromide in cats.

Geographic Area (or Travel History)

Certain diseases are common in specific areas (e.g., dirofilariasis, angiostrongylosis).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Similar signs.
- Coughing may be confused with other signs such as sneezing, reverse sneezing, gagging, panting, retching, and vomiting; presence of terminal retch is often misinterpreted as vomiting.
- Honking noise coughing in case of severe tracheal collapse can be described by owners as severe stertor.

CBC/BIOCHEMISTRY/URINALYSIS

Minimum database may suggest acute bacterial infection (leukocytosis with left shift) or eosinophilic airway disease (peripheral eosinophilia).

OTHER LABORATORY TESTS

- Filter test for microfilaria and/or heartworm antigen serology—for heartworm disease.
- Serum antibody titer—toxoplasmosis, FIV, FIP, distemper, *Angiostrongylus vasorum*.
- Coagulation profile—for any patient that presents with cough associated with either epistaxis or hemoptysis.
- Feces examination (Baermann test: identification of *Angiostrongylus* (dogs), *Aerulostrongylus* (cat), or other parasites (*Filarial*, *Crenosoma*)).
- PCR diagnosis available for several microorganisms.
- Tests for evaluation of possible hyperadrenocorticism (potentially causing pulmonary thromboembolism).

IMAGING

- Thoracic radiographs are first step prior to any additional test—provide essential information about intrathoracic airways, lung parenchyma, pleural space, mediastinum, and cardiovascular system.
- Thoracic computed tomography is being more and more often used for identification of respiratory intrathoracic problems.
- Fluoroscopy—helpful to investigate diseases in which dynamic obstruction is

COUGH

C

suspected (tracheal collapse, bronchial collapse, bronchomalacia). • Echocardiography—helpful when heart failure or dysfunction is suspected. • Thoracic ultrasonography—in case of pleural effusion or when a pulmonary or mediastinal mass is suspected.

DIAGNOSTIC PROCEDURES

- Endoscopy allows visualization of both static (tumor, granuloma, abnormal mucosa, excessive secretions) and dynamic (laryngeal paralysis, dynamic airway collapse) airway abnormalities. • When bronchial and/or alveolar infiltrates are present—samples from lower airways can be obtained for diagnostic purpose (cytology, bacterial/mycologic cultures) by bronchoalveolar lavage or tracheal wash.
- Transthoracic (fine-needle aspiration) biopsy or thoracoscopy—allows biopsy sample when interstitial infiltration is prominent.
- Thoracocentesis—allows sampling of pleural fluid, can be performed under ultrasonographic guidance. • Pulse oximetry and blood gas determination. • Pulmonary function tests—require sophisticated material and/or experienced technicians, not readily available in private practice.



TREATMENT

- Usually treated as outpatient. • Most successful management of cough involves treatment and resolution of underlying cause rather than use of medications that suppress signs. • If chronic cough is related to acute or chronic inflammation, anti-inflammatory therapy preferred to cough suppressant therapy.
- Use of cough suppressant therapy must be limited to cases in which the cause of the cough can neither be treated medically nor resolved, and in which excessive coughing leads to exhaustion of the patient or insomnia of the owners, as well as aggravation of the disease.



MEDICATIONS

DRUG(S) OF CHOICE

Antimicrobial Therapy

Indicated for tracheo-broncho-pulmonary disease of bacterial origin. Better selected based in culture and antimicrobial susceptibility testing.

Anti-inflammatory Therapy

- Indicated in feline bronchitis syndrome, canine chronic bronchitis, or canine eosinophilic bronchopneumopathy. • Oral prednisolone 0.5 mg/kg q12h in dogs and cats, then taper the dose progressively to q48h. • Nebulized fluticasone or budesonide 100–200 µg q12h with metered dose inhaler including spacer with face mask and inspiratory valve.

Antitussives

- Hydrocodone (dog only)—0.2–0.3 mg/kg PO q 6–12h. • Butorphanol (dog only)—0.25–1.1 mg/kg every 8–12h. • No antitussive available for cats. • In humans, gabapentin (neuromodulator) recently described to treat refractory chronic cough.
- Gabapentin in dogs, 2–5 mg/kg by mouth every 8h, but unestablished efficacy.

Bronchodilators

Theophylline (for Dogs and Cats)

- Pharmacokinetics are form and species dependent; slow-release formulations exist.
- Beneficial effects of theophylline include relaxation of bronchial smooth muscle, improved diaphragmatic contraction, and probably some anti-inflammatory effects but primary antitussive action not demonstrated. • Side effects are related to inotropic and chronotropic effects, as well as to an increase in blood pressure; can also cause nausea, diarrhea, arrhythmias, and CNS excitation.

Beta-2 Agonists (Cats Only)

- Delivered mostly via a meter dose inhaler (MDI); administered IV in emergency situations. Short-acting (salbutamol, terbutaline, fenoterol) or long-acting (salmeterol, formoterol) drugs. • May be administered temporarily to cause immediate and temporary relief, but not as long-term management; have limited effect. • Side effects include dry mouth, tachycardia, nausea; regular inhalation of racemic and S-albuterol (but not R-albuterol) induces airway inflammation in both healthy and asthmatic cats.

Expectorants

Guafenesin—included in some preparations but benefit not extensively studied or proven.

CONTRAINDICATIONS

Antitussive agents are strictly contraindicated when cough is needed to clean the airways, i.e., in infectious or inflammatory airway disease.

PRECAUTIONS

See side effects of respective drugs.

POSSIBLE INTERACTIONS

Theophylline—clearance may be inhibited by other drugs such as fluoroquinolones, increasing risk of theophylline toxicity.



FOLLOW-UP

PATIENT MONITORING

- Acute cough must be adequately treated in order to avoid chronic cough, leading to possibly irreversible lesions. • Conditions leading to chronic cough sometimes can only be alleviated but not cured; communicate with client to ensure successful management of cough.

POSSIBLE COMPLICATIONS

- Aggravation of tracheal collapse. • Progression toward chronic bronchitis, chronic obstructive pulmonary disease, lung emphysema, irreversible bronchial and parenchymal remodeling, bronchiectasis. • Acute severe cough might lead to syncope, rib fracture, or pneumothorax.
- Right heart dysfunction.



MISCELLANEOUS

AGE-RELATED FACTORS

- In dogs with anatomic disorders of inherited (e.g., primary ciliary dyskinesia) or congenital origin, signs might start early in life. • Puppies and kittens more likely to suffer from infectious disease. • Inflammatory disorders affect middle-aged adults. • Heart failure and tumors more frequent in older animals.

PREGNANCY/FERTILITY/BREEDING

- Dogs affected with primary ciliary dyskinesia. • Possible decreased fertility (in male and female dogs) as cilia from urogenital tract and flagellated cells can be affected.
- Proven hereditary in some breeds (Old English sheepdog; carrier test detection exists).

SEE ALSO

- Asthma, Bronchitis—Cats.
- Bronchitis, Chronic.
- Congestive Heart Failure, Left-Sided.
- Hypoxemia.
- Nasal Discharge.
- Pneumonia, Bacterial.
- Pneumonia, Eosinophilic.
- Respiratory Parasites.
- Sneezing, Reverse Sneezing, Gagging.
- Tracheal Collapse.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIV = feline immunodeficiency virus.
- UACS = upper airway cough syndrome.

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Acknowledgment The author and book editors acknowledge the prior contribution of Dominique Peeters.



**Client Education Handout
available online**

CRUCIATE LIGAMENT DISEASE, CRANIAL

C



BASICS

DEFINITION

The acute or progressive failure of the cranial cruciate ligament (CrCL), which results in partial to complete instability of the stifle joint.

PATHOPHYSIOLOGY

- Function of the CrCL includes passive constraint of the stifle joint by limiting internal rotation of the tibia, hyperextension of the stifle, and cranial displacement of the tibia relative to the femur.
- Two distinct bands—craniomedial band is taut on both flexion and extension of the joint (primary check) and caudolateral band is taut in extension and lax in flexion (secondary check).
- Types of injury:
 - Avulsion—skeletally immature animals in which acute load results in avulsion of the origin or insertion of the ligament.
 - Acute (traumatic) rupture—result of hyperextension, limb overloading, or internal rotation; mid-substance tear of the CrCL; most common cause in cats.
 - Progressive (chronic) degeneration pathogenesis remains elusive; decreases in elasticity, stress/strain energy, failure to maintain collagen fiber organization, and chondroid metaplasia—most common cause in dogs.
- Repetitive subclinical injury may be due to neuromuscular incoordination, aging, conformational abnormalities (excessive tibial plateau angle (TPA), medial luxating patella, narrow intercondylar notch), breed variations, poor muscle tone related to sedentary habits or limb immobilization, and possibly immune-mediated damage.
- Complete and partial tears exist in varying degrees.
- Untreated instability leads to degenerative osteoarthritic changes within a few weeks; severe within a few months.
- Medial meniscal (caudal horn) damage occurs in 33.2–77% of cases—due to shearing force during drawer.

SYSTEMS AFFECTED

Musculoskeletal, ± neurologic.

GENETICS

Suspected

INCIDENCE/PREVALENCE

Most common cause of hind limb lameness in dogs; major cause of degenerative joint disease (DJD) in the stifle joint.

SIGNALMENT

SPECIES

Dog and cat.

Breed Predilections

- All susceptible.
- Rottweiler and Labrador retriever—increased incidence when <4 years

of age.

- West Highland white terrier—overrepresented affected small breed.

Mean Age and Range

- Incidence increases with age >5 years.
- Large- to giant-breed dogs may present earlier in life; approx. 2 years of age.

Predominant Sex

Female—neutered.

SIGNS

General Comments

Severity of lameness—related to degree of rupture (partial vs. complete), mode of rupture (acute vs. chronic), occurrence of meniscal injury, and severity of inflammation and DJD. Condition and therefore lameness may be bilateral.

Historical Findings

- Athletic or traumatic events—generally precede acute injuries.
- Normal activity resulting in acute lameness—suggests degenerative rupture.
- Subtle to marked intermittent lameness (for weeks to months)—consistent with partial tears that are progressing to complete rupture.

Physical Examination Findings

- Varying degrees of lameness and joint effusion, pain, and/or crepitus; affected limb generally held in partial flexion while standing.
- Cranial drawer test—diagnostic for rupture; test in flexion, normal standing angle, and extension.
- Tibial compression test—cranial movement of tibia relative to femur when tightening gastrocnemius by flexing hock.
- Medial periarticular thickening (medial buttress).
- Presence of click or pop—63% accurate in detecting meniscal injury.
- Hind limb muscle atrophy—especially quadriceps muscle group.
- False-negative drawer or compression tests with chronic or partial tears and in painful or anxious patients that are not sedated or anesthetized.
- Earliest sign of partial rupture is pain on hyperextension of stifle.

CAUSES

- Trauma.
- Repetitive microinjury; excessive stifle loading.
- Progressive degeneration.

RISK FACTORS

- Obesity.
- Patella luxation.
- Conformational abnormalities.
- Excessive caudal slope of tibial plateau.
- Narrowed intercondylar notch.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Puppy laxity—positive drawer motion that stops abruptly as CrCL is stretched taut.
- Patella luxation (medial or lateral).
- Collateral ligament injury, long digital extensor tendon

injury.

- Osteochondritis dissecans of femoral condyle.
- Neoplasia (e.g., synovial sarcoma, osteosarcoma, chondrosarcoma).
- Traumatic fractures or avulsions.
- Caudal cruciate ligament rupture—uncommon and generally only seen with significant trauma.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

Radiography

- Verify secondary intra-articular changes such as DJD and rule out other differentials.
- Common findings—joint effusion with capsular distention and effacement of infrapatellar fat pad; periarticular osteophytes; enthesiophytes; CrCL avulsion fractures; calcification of CrCL and/or menisci.
- Cats commonly have mineralized menisci present (incidental finding).
- Necessary for preoperative planning with osteotomy procedures.

Alternative Diagnostic Imaging

Ultrasound and MRI—facility and operator dependent.

DIAGNOSTIC PROCEDURES

- Arthrocentesis—rule out sepsis or immune-mediated disease.
- Arthroscopy—gold standard; direct visualization and magnification of cruciate ligaments, menisci, and other intra-articular structures.

PATHOLOGIC FINDINGS

- Varying degrees of synovitis, cartilage fibrillation, and erosion.
- Periarticular osteophyte formation.
- Meniscal damage.
- Ruptured fibers of CrCL—hyalinization; fibrous tissue invasion; necrosis; loss of parallel orientation of ligament bundles.



TREATMENT

APPROPRIATE HEALTH CARE

- Stabilization surgery—recommended; speeds rate of recovery; reduces degenerative changes; enhances function.
- Conservative management—diet, nonsteroidal anti-inflammatory drugs (NSAIDs), physical rehabilitation, weight loss; approx. 66% of patients have improved function over course of >1 year; DJD is progressive; not generally recommended.

NURSING CARE

Postsurgery—restricted activity with physical rehabilitation (e.g., ice packing, range-of-motion exercises, massage, and muscle electrical stimulation); important for improving mobility and strength.

ACTIVITY

Restricted—duration depends on method of treatment and progress of patient.

(CONTINUED)

CRUCIATE LIGAMENT DISEASE, CRANIAL

C

DIET

- Weight control—important for decreasing load and thus stress on stifle joint.
- Joint-health diets rich in omega-3 fatty acids and chondroprotectants may support overall joint health.

CLIENT EDUCATION

- Regardless of treatment, DJD is common and progressive.
- Return to full athletic function is possible, but requires early surgical intervention and rehabilitation.
- Rupture of contralateral CrCL can occur in 37–48% of patients.

SURGICAL CONSIDERATIONS

- No one technique has proven consistently superior, clinically or radiographically.
- Recent force plate studies show slight differences between common techniques; dogs with tibial plateau leveling osteotomy (TPLO) procedure achieve normal limb loading faster than with extracapsular procedure.

Extra-articular Methods

- Wide variety of techniques that use an implant to mimic CrCL and restore stability; these techniques rely on periarticular fibrosis for long-term stability.
- Alternative method includes fibular head transposition to realign and tension lateral collateral ligament in order to restrict internal rotation and cranial drawer.

Intra-articular Methods

Designed to replace CrCL anatomically with autografts (patellar ligament, fascia), allografts, xenografts, and synthetic materials.

Osteotomy Procedures***Cranial Tibial Closing Wedge Osteotomy***

- Levels TPA by removing cranially based wedge of bone from proximal tibia and eliminates cranial thrust.
- Held in place with bone plate and screws.
- Can potentially shorten tibia and alter stifle biomechanics.

TPLO

- Rotational osteotomy of proximal tibia to level TPA and neutralize cranial tibial thrust.
- Held in place with bone plate and screws.
- Can accomplish correction for angular and torsional deformities.

Tibial Tuberosity Advancement

- Tibial crest osteotomy; crest is held in advanced position with cage and plate; bone graft fills defect.
- Active control of cranial tibial displacement improved, which helps stabilize stifle.
- Can combine technique with lateral transposition of tibial tuberosity to correct concurrent medial luxating patella.

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

NSAIDs—minimize pain; decrease inflammation.

CONTRAINDICATIONS

Avoid concurrent use of corticosteroids with NSAIDs.

PRECAUTIONS

NSAIDs—gastrointestinal irritation or renal/hepatic toxicity may preclude use in some patients.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Chondroprotective drugs (polysulfated glycosaminoglycans, glucosamine, and chondroitin sulfate) may help reduce cartilage damage and improve regeneration.
- Omega-3 fatty acid supplementation to reduce inflammation is recommended.

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

Most techniques require 2–4 months of rehabilitation.

PREVENTION/AVOIDANCE

Avoid breeding animals with conformational abnormalities.

POSSIBLE COMPLICATIONS

- Subsequent meniscal injury can occur in 6–22% of patients.
- Incisional and/or implant-related infection.
- Tibial tuberosity avulsion and/or fractures.
- Patellar luxation.
- Delayed bone healing (osteotomy procedures).
- Pivot shift—unknown clinical significance <2% (self-limiting).

EXPECTED COURSE AND PROGNOSIS

Regardless of surgical technique, success rate better than 85%.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Meniscal damage.

AGE-RELATED FACTORS

See Pathophysiology.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Arthritis (Osteoarthritis).
- Patellar Luxation.

ABBREVIATIONS

- CrCL = cranial cruciate ligament.
- DJD = degenerative joint disease.
- NSAID = nonsteroidal anti-inflammatory drug.
- TPA = tibial plateau angle.
- TPLO = tibial plateau leveling osteotomy.

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**Client Education Handout
available online**

CRYPTOCOCCOSIS



BASICS

DEFINITION

A localized or systemic fungal infection caused by the environmental yeast *Cryptococcus* spp., most commonly *C. neoformans* and *C. gattii*.

PATHOPHYSIOLOGY

- *C. neoformans*—grows in bird droppings and decaying vegetation; soil disturbance increases risk of infection.
- Dogs and cats inhale the yeast and a focus of infection is established, usually in nasal passages; smaller dried, shrunken organisms may reach the terminal airways (uncommon).
- There may be colonization or subclinical infection of nasal passages that spontaneously resolves.
- Stomach and intestinal infections suggest that primary gastrointestinal entry can occur.
- Dissemination—hematogenously spread via macrophages from nasal passages to brain, eyes, lungs, and other tissues; by extension to skin of nose, eyes, retro-orbital tissues, and draining lymph nodes.

SYSTEMS AFFECTED

- Cats—mainly respiratory (nose, nasopharynx, and sinuses), skin (nasal planum), nervous, ophthalmic, and lymphatic.
- Dogs—mainly skin (over nose and sinuses), respiratory (nasal passages, occasionally lungs), nervous (brain), lymphatic, and ophthalmic.

INCIDENCE/PREVALENCE

- Dogs—rare in United States; prevalence 0.00013%.
- Cats—7–10 times more common than in dogs; most common systemic mycoses of cats.

GEOGRAPHIC DISTRIBUTION

- Worldwide.
- Some areas of southern California and Australia have an increased incidence and an outbreak has occurred on Vancouver Island in British Columbia, Canada.
- *C. gattii* grows well around eucalyptus trees.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Dogs—American cocker spaniels (United States), Doberman pinschers and German shepherd dogs (Australia) may be overrepresented.
- Cats—Siamese may be at increased risk.

Mean Age and Range

- Most commonly cats and dogs <6 years of age.
- Can occur at any age.

Predominant Sex

- Dogs—none.
- Cats—males may be overrepresented.

SIGNS

Historical Findings

- Lethargy.
- Varies depending on organ systems involved.
- May have signs/problems for weeks to months.

Dogs

- Neurologic—seizures, ataxia, paresis.
- Ocular signs—periorbital swelling, blindness, uveitis, hyphema.
- Skin ulceration.
- Lymphadenopathy.
- Respiratory—upper respiratory signs, labored breathing, coughing.
- Vomiting, diarrhea, and anorexia.

Cats

- Nasal discharge and ocular signs.
- Neurologic signs—seizures, disorientation, vestibular signs.
- Granulomatous tissue seen at the nares.
- Firm swellings over the bridge of the nose.
- Lymphadenopathy.
- Respiratory abnormalities less commonly noted.

Physical Examination Findings

- Mild fever—<50% of patients.
- Dogs—nasal discharge, multifocal CNS abnormalities, ataxia, anterior uveitis.
- Cats—respiratory noise (stertor), nasofacial swelling, ulcerated crusting skin lesions on the head, lymphadenopathy, neurologic abnormalities (behavior change, circling, vestibular signs, ataxia), ocular abnormalities (blindness, optic neuritis, retinal detachment).

CAUSES

Exposure to cryptococcal organisms and inability of immune system to prevent colonization and tissue invasion.

RISK FACTORS

- Exposure to disrupted soil.
- Infection with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Other causes of focal or diffuse neurologic disease—distemper, inflammatory meningoencephalomyelitis, infectious meningoencephalitis (bacterial, rickettsial, protozoal), neoplasia, fungal diseases (depending on geography).
- Nasal lesions, especially at mucocutaneous junction—immune-mediated, neoplasia (squamous cell carcinoma).
- Lymphadenopathy—lymphoma, fungal disease.
- Chorioretinitis and optic neuritis—fungal infections, distemper, neoplasia.

Cats

- Nasal disease—nasal tumors, chronic rhinitis, chronic sinusitis.
- Ulcerative skin changes—bacterial infection, trauma, neoplasia (squamous cell carcinoma).
- Ocular and neurologic abnormalities—lymphoma, feline

infectious peritonitis (FIP), other infections (fungal, *Toxoplasma*).

CBC/BIOCHEMISTRY/URINALYSIS

- Mild anemia in some cats.
- Eosinophilia occasionally seen.
- Chemistry usually normal.

OTHER LABORATORY TESTS

- Latex agglutination or ELISA—detect cryptococcal capsular antigen in serum or cerebrospinal fluid (CSF); highly sensitive assay; most infected animals have measurable capsular antigen titers; magnitude of titer correlates with extent of infection.
- May be less sensitive in dogs.
- May be positive with colonization alone; antigen titers 1 : 32 or greater seen with fungal invasion.

IMAGING

- Nasal radiographs (cats)—soft tissue density material in nasal passage; bone destruction of nasal dorsum.
- Contrast-enhanced CT or MRI best for identifying brain and nasal lesions.
- Thoracic radiographs—can identify lower respiratory tract disease.

DIAGNOSTIC PROCEDURES

Dogs

Neurologic disease—additional procedures: cytologic examination and culture of CSF, other CSF infectious disease testing, measurement of CSF capsular antigen.

Cats

- Cytology of impression smears or aspirates of mucoid material from nasal passages, or biopsy of granulomatous tissue protruding from nares—characteristic yeast with large negatively-staining (clear) capsule.
- Aspirates of lymph nodes or subcutaneous swellings often high yield.
- Sedated oropharyngeal exam—in patients with upper respiratory obstruction/noise: may identify granuloma in nasopharynx (spay hook or endoscope to expose the mass).
- Biopsy—skin lesions.
- Cultures—confirm diagnosis; determine drug susceptibility.

PATHOLOGIC FINDINGS

- Gross lesions—gray, gelatinous mass produced by polysaccharide capsule; in nose, sinuses, and nasopharynx of cats; skin lesions usually ulcerative.
- Neurologic lesions—more common in dogs; diffuse or focal CNS granulomas.
- Chorioretinitis with or without retinal detachment or optic neuritis.
- Histologic response—usually pyogranulomatous; inflammatory cell infiltrate may be mild as polysaccharide capsule interferes with neutrophil migration; organism characterized by capsule yeast with narrow-neck budding.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient if stable.
- Neurologic signs—may initially require inpatient supportive care.

(CONTINUED)

CRYPTOCOCCOSIS**C****NURSING CARE**

Cats—nasal obstruction influences appetite; encourage to eat by offering warmed, palatable food.

ACTIVITY

N/A

DIET

Patients treated with itraconazole—give medication in fatty food (e.g., canned food) to improve absorption.

CLIENT EDUCATION

- Inform client that this is a chronic disease that requires months of treatment.
- Reassure client that infection is not zoonotic.

SURGICAL CONSIDERATIONS

Remove granulomatous masses in nasopharynx to reduce respiratory difficulties.

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

- Fluconazole—preferred for ocular or CNS disease (water soluble and better penetrates CNS); cats: 50 mg/cat PO q12–24h; dogs: 5 mg/kg PO q12h; most economical drug choice.
- Itraconazole—cats: 10 mg/kg PO q24h; dogs: 5 mg/kg PO q12h; pellets in capsule can be mixed with fatty food; itraconazole liquid has better absorption on empty stomach and compounded itraconazole is not recommended.
- Amphotericin B may have some advantage in severe disease at a dosage of 0.25 mg/kg IV q48h, given slowly over 3–4h, up to a total cumulative dose of 4–16 mg/kg; monitor renal function closely.
- Terbinafine (5 mg/kg PO q12h, 10 mg/kg PO q24h) effective for treatment of cats with resistant infections.
- Flucytosine—25–50 mg/kg PO q6h; synergistic with amphotericin B, may allow lower doses and decrease renal toxicity. Do not use as single agent.

CONTRAINDICATIONS

Caution with concurrent steroid use (immunosuppression).

PRECAUTIONS

- Triazoles—hepatotoxicity; anorexia signals problems; monitor liver enzyme activities monthly initially.
- Itraconazole—ulcerative

dermatitis (differentiate from skin lesions of cryptococcosis); new skin lesions after disease is much improved should be considered a drug reaction.

- Amphotericin B—nephrotoxicity; caution if patient is azotemic, but not absolute contraindication if life-threatening infection.
- Terbinafine—monitor for hepatic toxicity and anorexia.

ALTERNATIVE DRUG(S)

Cryptococcal organisms are prone to becoming resistant to antifungal treatment.

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

- Monitor liver enzyme activities monthly (especially early in treatment) in patients receiving triazole antifungal agent.
- Improvement in clinical signs, resolution of lesions, improvement in wellbeing, and return of appetite measure response to treatment.
- Capsular antigen titers—after 2–3 months of treatment, titers should decrease if treatment is effective; if ineffective, try terbinafine, because organism may become resistant.
- Continue monitoring antigen titers every 1–2 months during treatment and after discontinuing treatment.
- Ideally treat until cryptococcal antigen titers reach zero (may take >2 years).

PREVENTION/AVOIDANCE

The organism is ubiquitous and cannot be avoided.

POSSIBLE COMPLICATIONS

Patients with neurologic disease may have seizures and permanent neurologic deficits.

EXPECTED COURSE AND PROGNOSIS

Treatment—anticipated duration 4 months to ≥1 year; patients with CNS disease may require lifelong maintenance; median time of successful treatment with fluconazole 4 months; median time for itraconazole treatment 8 months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Not considered zoonotic, but possibility of transmission through bite wounds.
- Inform client that organism was acquired from the environment and that he or she could be at increased risk, especially if immunosuppressed.

PREGNANCY/FERTILITY/BREEDING

Azole drugs can be teratogenic and should be used in pregnant animals only if the potential benefit justifies the potential risk to offspring.

ABBREVIATIONS

- CSF = cerebrospinal fluid.
- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIV = feline immunodeficiency virus.

Suggested Reading

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Client Education Handout
available online

CRYPTORCHIDISM

C



BASICS

OVERVIEW

- Incomplete scrotal descent of one or both testes; most common testicular congenital anomaly.
- Abdominal or inguinal location for undescended testis or testes.
- Diagnosis usually made at 2 months of age (i.e., descent to scrotal position should occur before this time), with some exceptions of full descent occurring between 2 and 6 months of age.
- Abdominally retained testicles typically lack spermatozoa and have only Sertoli cells in the seminiferous tubules; estradiol (E2) and testosterone (T) can be present in normal systemic concentrations in affected animals.
- Unilaterally cryptorchid animals are typically fertile.

SIGNALMENT

- Cats—purebred cats have higher incidence.
- Dogs—toy and miniature breeds at 2.7 times greater risk than large breeds of being affected; high rates in miniature schnauzers with persistent Müllerian duct syndrome (PMDS).
- Incidence—rates up to 24.1% in some purebred dogs (compared to 2.1% in overall population) with 50% incidence in dogs with PMDS; in cats observed rates range from 1.3 to 6.2%.
- Unilateral more common than bilateral; right testis retained twice as often in dogs, but with equal frequency in cats.
- Genetics—estimated medium level of heritability with multifactorial genetic basis; females act as genetic carriers for the trait.

SIGNS

- Absence of one, or both, testicles from the scrotum in a patient without history of castration.
- Cats—strong urine odor, tom cat marking behavior, presence of penile spines.
- Abdominal pain, lameness, vomiting—increased risk exists for spermatic cord torsion of neoplastic, retained testes.
- Feminizing paraneoplastic syndrome—estrogen-secreting Sertoli cell tumors produce feminizing signs including gynecomastia, symmetric alopecia of trunk and flanks, hyperpigmentation of inguinal skin, pendulous preputial sheath, prostatic squamous metaplasia.

CAUSES & RISK FACTORS

- Affected males or carriers (i.e., females or nonaffected males of cryptorchid littermates) present in breeding lines.
- Carriers produce increased number of males per litter and increased litter size; efforts to eliminate cryptorchidism difficult in these circumstances.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bilateral—previously castrated patient.
- Unilateral—remaining abdominal or inguinal testis after removal of single scrotal testis.

DIAGNOSTIC PROCEDURES

Transrectal prostate exam—intact males have pronounced prostate; prostate of larger breeds may be beyond reach.

OTHER LABORATORY TESTS

- Human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone (GnRH) stimulation test (differentiate cryptorchidism from castrated)—collect blood sample for baseline T analysis; administer 750 IU hCG IV or 50 µg GnRH IM; repeat sample collection for T analysis in 2–3 hours; twofold increase in T from baseline indicates presence of testicular tissue.
- Canine anti-Müllerian hormone concentration—increased level indicates testicular Sertoli cells present.

IMAGING

Ultrasonography—highly sensitive for identification of inguinal or abdominal testes.



TREATMENT

- Identification and removal of undescended testis or testes.
- Orchiopexy—surgical tacking of retained testis into scrotum; results in misrepresentation of individual's true phenotype and genotype.
- hCG or GnRH—little controlled evidence establishing efficacy or protocol; ethical concerns same as with orchiopexy.
- Failure to remove retained testis—increased risk of testicular neoplasia (13.6 times greater), spermatic cord torsion; 53% of Sertoli cell tumors and 36% of seminomas occur in retained testes.



MEDICATIONS

DRUG(S) OF CHOICE

To possibly induce descent of retained testicle:

- hCG (dogs)—100–1,000 IU IM 4 times in 2-week period before 16 weeks of age.
- GnRH (dogs)—50–750 µg IM 1–6 times between 2 and 4 months of age.
- Buserelin (GnRH analogue; dogs)—10 µg, once weekly, for 3 doses.



FOLLOW-UP

Migration of testes into the scrotum after 4 months is unlikely; rare after 6 months.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Inguinal or umbilical hernia.
- Hip dysplasia.
- Patellar luxation.
- Penile and preputial defects (e.g., hypospadias).

SEE ALSO

- Seminoma.
- Sertoli Cell Tumor.
- Sexual Development Disorders.

ABBREVIATIONS

- E2 = estradiol.
- hCG = human chorionic gonadotropin.
- GnRH = gonadotropin-releasing hormone.
- PMDS = persistent Müllerian duct syndrome.
- T = testosterone.

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Acknowledgment The author and book editors acknowledge the prior contribution of Carlos R.F. Pinto.

CRYPTOSPORIDIOSIS

C



BASICS

OVERVIEW

- *Cryptosporidium* spp.—apicomplexan protozoan causing gastrointestinal disease; ubiquitous in nature with worldwide distribution.
- Infection—sporulated oocysts are ingested, sporozoites are released and penetrate intestinal epithelial cells; after asexual reproduction, merozoites released to infect other cells, sexual reproduction follows, then oocyst shedding.
- Prepatent period—5–10 days (cats).
- Immunocompetent animals—intestinal disease.
- Immunocompromised animals—intestinal, liver, gallbladder, pancreatic, respiratory infection.
- Dogs—prevalence 0.5% worldwide; 2–17% in the United States.
- Cats—prevalence 0–29% worldwide; 2–15% in the United States.

SIGNALMENT

- No sex or breed predilection.
- Dogs—virtually all clinical cases in immunocompromised animals or animals <6 months of age; older dogs can excrete oocysts without clinical signs.
- Cats—more common in immunocompromised cats or kittens <6 months of age.

SIGNS

- Most infections subclinical.
- Principally small bowel diarrhea; large bowel diarrhea reported.

CAUSES & RISK FACTORS

- *C. canis* (dogs), *C. felis* (cats)—ingestion of contaminated water or feces.
- Morphologically, intestinal *Cryptosporidium* species very similar.
- Some species are host specific (*C. canis*, *C. felis*); others (*C. parvum*, *C. muris*) infect multiple species.
- Immunosuppression—major risk factor; common causes feline leukemia virus, canine distemper virus, canine parvovirus, intestinal lymphoma.
- Immunocompetent animals—usually asymptomatic infection with fecal oocyst shedding.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Parasites—giardiasis, trichuriasis.
- Infectious agents—parvovirus, coronavirus, feline infectious peritonitis, *Salmonella*, *Campylobacter*, *Rickettsia*, *Histoplasma*.

- Metabolic—hypoadrenocorticism, hyperthyroidism (cats).
- Infiltrative diseases—e.g., inflammatory bowel disease, intestinal lymphoma.
- Dietary indiscretion or intolerance.
- Toxicities—medications, lead, etc.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal, can reflect underlying disease.

DIAGNOSTIC PROCEDURES

- Sugar and zinc sulfate centrifugal flotation—specific gravity = 1.18–1.3; concentrates fecal oocysts (oocysts are 5 µm, routine salt flotation often fails); oocysts best seen with modified acid-fast stain, may have slight pink color.
- Fecal antigen detection test (ProSpecT *Cryptosporidium* Microtiter Assay, Color-Vue *Cryptosporidium*) available for humans.
- Fluorescent antibody assay—veterinary diagnostic laboratories.
- PCR—commercial laboratories; more sensitive for diagnosis than other techniques.
- Submitting feces to laboratory—laboratory-specific protocols; can mix 1 part 100% formalin with 9 parts feces to inactivate oocysts and decrease health risk to laboratory personnel.

PATHOLOGIC FINDINGS

- Gross lesions—enlarged mesenteric lymph nodes, hyperemic intestinal (especially ileal) mucosa; fix specimens in Bouin's or formalin solution within hours of death; autolysis causes rapid loss of intestinal surface with organisms.
- Microscopic lesions—villous atrophy, reactive lymphoid tissue, inflammatory infiltrates in lamina propria; parasites throughout intestines, most numerous in distal small intestine.



TREATMENT

- Outpatient.
- In immunocompetent animals—diarrhea usually mild and self-limiting; withhold food for 24–48h to control diarrhea; oral glucose-electrolyte solution if mild diarrhea; parenteral fluids (isotonic with potassium added) if severe diarrhea.



MEDICATIONS

DRUG(S) OF CHOICE

- No drugs currently labeled for animal use in United States.
- Paromomycin (Humatin®)—125–165 mg/kg PO q12h for 5 days; aminoglycoside effective in humans with acute intestinal symptoms; may cause nephropathy in young animals with damaged gastrointestinal barrier; monitor urine for casts during therapy.

- Tylosin—11 mg/kg PO q12h for 28 days; reported effective in cat with concurrent lymphocytic diadennitis.
- Nitazoxanide (Alinia®)—25 mg/kg PO q24h for 7–28 days; reduces oocyst shedding in cats; associated with vomiting (responsive to antiemetics); used in limited number of cats.



FOLLOW-UP

- Treatment efficacy based on clinical improvement.
- Monitor oocyst shedding in feces 2 weeks after treatment completion or if signs persist.
- Prognosis excellent if underlying disease treated.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Possible—transmission of infection from dogs and cats to humans possible; in general, transmission from pets to people rare.

Disinfection

- 10% formaldehyde solution or 5% ammonia solution will kill oocysts, but requires 18 hours of exposure; 50% ammonia solution kills oocysts in 30 minutes.
- Resistant to commercial bleach (5.25% sodium hypochlorite) and chlorination of drinking water.
- Moist heat (steam or pasteurization, >55 °C), freezing and thawing or thorough drying also effective.

Suggested Reading

Lucio-Forster A, Griffiths JK, Cama VA, et al. Minimal zoonotic risk of cryptosporidiosis from pet dogs and cats. Trends Parasitol 2010, 26:174–179.

Authors Matt Brewer and Jeba R.J. Jesudoss Chelladurai

Consulting Editor Amie Koenig

DEMODICOSIS



BASICS

D

DEFINITION

An inflammatory parasitic disease of dogs and cats characterized by an increased number of demodectic mites in the hair follicles and on the epidermis.

PATHOPHYSIOLOGY

Dogs

- Three species of mites identified in the dog:
 - Demodex canis*—follicular mite; part of the normal fauna of the skin; typically present in small numbers; resides in the hair follicles and sebaceous glands of the skin, transmitted from the mother to the neonate during the first 2–3 days of nursing.
 - Demodex injai*—large, long-bodied mite found in the pilosebaceous unit, mode of transmission unknown; only associated with adult-onset disease, with highest incidence noted in the terrier breeds often along the dorsal midline (West Highland white terrier and wirehaired fox terrier).
 - Demodex cornei*—lives in the stratum corneum of the epidermis; mode of transmission unknown; most likely a morphologic variant of *D. canis*.
- Proliferation of mites may be the result of immunologic disorder, either genetic or iatrogenic.
- Pruritus occurs when a secondary bacterial infection is present.

Cats

- Two species of mites identified in the cat:
 - Demodex gatoi*—contagious; can be asymptomatic, but most commonly is associated with pruritic dermatitis leading to self-trauma, alopecia, and barbering.
 - Demodex cati*—often associated with immunosuppressive and metabolic disease; these mites cause folliculitis and alopecia, but are rarely pruritic.

SYSTEMS AFFECTED

Skin/exocrine.

GENETICS

Initial proliferation of mites may be the result of a genetic disorder.

INCIDENCE/PREVALENCE

- Dogs—*D. canis* is very common.
- Cats—depending on geographic location, *D. gatoi* may be common or rare; *D. cati* is rare.

SIGNALMENT

Species

Dogs and cats.

Breed Predilections

- D. canis*—American Staffordshire terrier, shar-pei, Boston terrier, English bulldog, and West Highland white terrier.
- D. injai*—West Highland white and wirehaired fox terriers, shih tzu.
- Potential increased incidence in Siamese and Burmese cats.

Mean Age and Range

- Juvenile onset, localized—usually in dogs <1 year of age; median 3–6 months, typically

<5 lesions.

- Generalized—both young and old animals.
- D. cati* may be more common in middle-aged or older cats; *D. gatoi* seems to be more common in younger cats and kittens, but any age can be affected.

SIGNS

Dogs

- Patchy alopecia—most common site is the face, especially around the perioral and periocular areas and forelegs; may also be seen on the trunk and feet.
- Pododemodicosis—lesions localized to the feet.
- Disease can progress to become or begin with a generalized distribution.
- Usually not pruritic unless secondarily infected.
- Hair follicles distended with large numbers of mites, lose hair and develop secondary bacterial folliculitis, followed by rupturing of the follicles (furunculosis).
- With progression, the skin becomes severely inflamed, exudative, and granulomatous.
- D. injai* may be associated with greasy seborrheic dermatitis of the dorsal trunk, comedones, erythema, alopecia, and hyperpigmentation.

Cats

- D. cati*—partial to complete alopecia of the eyelids, periocular region, head, neck, flank, and ventrum.
- D. gatoi*—pruritus with dramatic scaling, erythema, and/or crusting due to inflammation and self-trauma.
- Ceruminous otitis externa has been reported.
- D. cati* often associated with immunosuppressive disease.

CAUSES

- Dog—*D. canis*, *D. injai*, and *D. cornei*.
- Cat—*D. cati* and *D. gatoi*.

RISK FACTORS

Dogs

- Exact immunopathologic mechanism unknown.
- Dogs with generalized demodicosis may have abnormal or depressed T-cell function.
- Development associated with oclacitinib treatment.
- Genetic factors (especially juvenile onset), immunosuppression, and/or metabolic diseases may predispose animal.

Cats

- D. cati*—often associated with metabolic diseases that affect the immune system (e.g., feline immunodeficiency virus [FIV], hyperadrenocorticism, diabetes mellitus).
- D. gatoi*—considered contagious; cats in contact with other cats are at risk.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Dogs

- Bacterial folliculitis/furunculosis.
- Dermatophytosis.
- Any cause of inflammatory alopecia.

Cats

- Allergic dermatitis.
- Dermatophytosis.
- Any cause of alopecia or pruritus.

CBC/BIOCHEMISTRY/URINALYSIS

Normal unless there is an underlying process.

OTHER LABORATORY TESTS

- Feline leukemia virus (FeLV) and FIV serology.
- Fecal samples—rare finding of mites in feces; more common with cats.

DIAGNOSTIC PROCEDURES

- Skin scrapings diagnostic for finding mites in most cases—*D. gatoi* may be difficult to find.
- Hair plucking can be used in areas such as eyelids.
- Skin biopsy—may be needed when lesions are chronic, granulomatous, and fibrotic (especially on the foot); may be needed to diagnose demodicosis in the shar pei breed.



TREATMENT

APPROPRIATE HEALTH CARE

- Localized *D. canis* lesions often (90%) resolve spontaneously.
- Evaluate the health status of patients presenting with generalized lesions of demodicosis.

CLIENT EDUCATION

- Localized—most cases resolve spontaneously.
- Generalized—frequent management problem due to chronicity. Juvenile onset considered to have an inheritable predisposition—breeding of affected animals is not recommended.



MEDICATIONS

DRUG(S) OF CHOICE

Dogs

Isoxazolines antiparasitics

- Treatment of choice—excellent efficacy against demodicosis at label doses for fleas; safe for avermectin-sensitive dogs.
- Side effects uncommon—vomiting, diarrhea, inappetence, or neurologic signs including seizures.

Ivermectin

- 0.3–0.6 mg/kg q24h PO very effective; initiate therapy with a test dose of 0.12 mg/kg q24h for first week to observe for any signs of sensitivity.
- Treat for 30–60 days beyond negative skin scrapings (average 3–8 months).
- Non-FDA-approved usage—do not use in avermectin-sensitive (ABCB-1 mutation) breeds.

Milbemycin Oxime

- 1–2 mg/kg PO q24h cures 50% of cases; 2 mg/kg PO q24h cures 85% of cases.

(CONTINUED)

DEMODICOSIS

D

- ABCB-1 mutation individuals may have neurologic signs with higher doses; tolerate milbemycin better than other drugs in this class.
- Non-FDA-approved usage.

Moxidectin

- 0.3 mg/kg PO q24h or topical application once weekly.
- Non-FDA-approved usage—do not use in avermectin-sensitive (ABCB-1 mutation) breeds.

Amitraz

- Applied in the United States as a 250 ppm (0.025%) dip every 14 days and in Europe as a 500 ppm (0.05%) dip every 7 days. See adverse effects below.
- Clipping the hair coat and bathing with a benzoyl peroxide shampoo before application of the rinse assist response.
- Amitraz-containing collars and spot-ons are not effective.
- Efficacy is proportional to the frequency of administration and the concentration of the rinse.
- Poor compliance limits efficacy.
- 11% and 30% of cases will not be cured; may need to try an alternative therapy or control with maintenance rinse every 2–8 weeks.

DRUG(S) OF CHOICE**Cats*****Isoxazoline antiparasitics***

- Treatment of choice at label doses for fleas.
- Side effects uncommon but include drooling, vomiting, diarrhea, inappetence, or neurologic signs including seizures.

2% lime sulfur

- Can be diluted, sponged over the cat, and allowed to dry without rinsing once weekly for 6 treatments.
- Malodorous, staining, and difficult to apply to the face.
- Patient should be restricted from grooming after application.

Alternatives

Alternative but less effective options for the treatment of *D. gatoi*:

- Milbemycin oxime—1 mg/kg PO q24h.
- Doramectin—0.6 mg/kg SC weekly.
- Ivermectin—0.2–0.3 mg/kg PO q24–48h.

Neurologic side effects such as ataxia are possible with ivermectin.

CONTRAINDICATIONS

Do not use ivermectin in avermectin-sensitive breeds—collies, Shetland sheepdogs, Old English sheepdogs, Australian shepherds, other herding breeds, and crosses with these breeds. Screening for the ABCB-1 mutation is recommended.

PRECAUTIONS***Amitraz***

- Side effects—somnolence, lethargy, depression, anorexia seen in 30% of patients

for 12–36 hours after treatment.

- Rare side effects—vomiting, diarrhea, pruritus, polyuria, mydriasis, bradycardia, hypoventilation, hypotension, hypothermia, ataxia, ileus, bloat, hyperglycemia, convulsions, death.

- Yohimbine at 0.11 mg/kg IV is an antidote, as is atipamezole.
- Incidence and severity of side effects do not appear to be proportional to dose or frequency of use.
- Apply in a well-ventilated area; owners should wear aprons and gloves so they do not come in contact with the dip.
- Human beings can develop dermatitis, headaches, and respiratory difficulty after exposure. Amitraz should not be used by people taking monoamine oxidase (MAO) inhibitors (e.g., some antihistamines, antidepressants, and antihypertensives).
- Can dysregulate blood sugar in diabetics.

Ivermectin and Milbemycin

Signs of toxicity—salivation, vomiting, mydriasis, confusion, ataxia, hypersensitivity to sound, weakness, recumbency, coma, and death.

POSSIBLE INTERACTIONS

- Amitraz—may interact with heterocyclic antidepressants, xylazine, benzodiazepines, and macrocyclic lactones.
- Ivermectin and milbemycin—cause elevated levels of monoamine neurotransmitter metabolites, which could result in adverse drug interactions with amitraz and benzodiazepines.
- Spinosad and other drugs in that class are contraindicated with ivermectin therapy.

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

Repeat skin scrapings and evidence of clinical resolution are used to monitor progress, generally repeated every 2–4 weeks until resolution, and then treatments are continued 1–2 months beyond negative scrapings.

PREVENTION/AVOIDANCE

Do not breed animals with generalized disease.

POSSIBLE COMPLICATIONS

Secondary bacterial folliculitis and furunculosis.

EXPECTED COURSE AND PROGNOSIS

Prognosis is very good for elimination of the demodicosis with isoxazoline treatment. Prognosis depends heavily on compliance, and genetic, immunologic, and underlying diseases. Severe, generalized cases with underlying disease may be refractory to treatments other than isoxazoline.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Adult-onset demodicosis—sudden occurrence is associated with internal disease, malignant neoplasia, and/or immunosuppressive disease; approximately 25% of cases are idiopathic over a follow-up period of 1–2 years.
- *D. cati* associated with FeLV, FIV, toxoplasmosis, iatrogenic immune suppressants, papillomaviral plaques, and systemic lupus erythematosus (SLE).

AGE-RELATED FACTORS

Young dogs are often predisposed to a localized form.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Do not breed animals with the generalized form.

SYNONYMS

- Mange.
- Red mange.

SEE ALSO

Ivermectin and Other Macrocylic Lactones Toxicosis.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- MAO = monoamine oxidase.
- SLE = systemic lupus erythematosus.

Suggested Reading

Sastre N, Ravera I, Villanueva S, et al.

Phylogenetic relationships in three species of canine *Demodex* mite based on partial sequences of mitochondrial 16S rDNA. Vet Derm 2012, 23(6):509–e101.

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Acknowledgment The author and book editors acknowledge the prior contribution of Karen Helton Rhodes.



Client Education Handout available online

DENTAL CARIES



BASICS

D

OVERVIEW

- Caries is the decay of the dental hard tissues (enamel, cementum, and dentin) due to the effects of oral bacteria on fermentable carbohydrates on the tooth surface.
- The word "caries" is Latin for rottenness and is both the singular and plural form.
- Oral bacteria ferment carbohydrates on the tooth surface, resulting in the production of acids leading to demineralization of the hard tissues, thus allowing bacterial and leukocytic digestion of the organic matrix of the tooth.
- Caries has been very common in humans in "westernized" society, where diets rich in highly refined carbohydrates are the norm. Aggressive public education and preventive measures have resulted in a decline in incidence over the past several decades.
- In humans, *Streptococcus mutans* is particularly implicated in the development of caries.
- For various reasons (e.g., diet lower in refined carbohydrates, higher salivary pH, lower salivary amylase, conical crown shape, wider interdental spacing, different indigenous oral flora), caries is not common in the domestic dog, but it does occur and should be looked for.
- A study published in the *Journal of Veterinary Dentistry* in 1998 (see Suggested Reading) reported that 5.3% of dogs 1 year of age or older had one or more caries lesions, with 52% having bilaterally symmetric lesions.
- Caries can affect the crown or roots of the teeth and is classified as pit-and-fissure, smooth-surface, or root caries.

SIGNALMENT

- Caries occurs in dogs.
- Reported in cats; tooth resorption (feline odontoclastic resorptive lesions [FORL]) has sometimes been misnamed feline caries. To the author's knowledge, there are no published reports of true dental caries occurring in the domestic cat, though it is theoretically possible.

- There is no reported breed, age, or gender predilection.
- Anecdotally, the author has observed a higher incidence of pit-and-fissure lesions in the occlusal tables of the maxillary first molar teeth in large-breed dogs such as Labrador retrievers and German shepherds.

SIGNS

- Incipient smooth-surface caries—appears as an area of dull, frosty-white enamel.
- Clinical caries—appears as a structural defect on the surface of the crown or root.
- The defect is frequently filled with or lined by dark, soft necrotic dentin. The defect may also trap and hold food debris.
- Affected dentin will yield to a dental explorer and can be removed with a dental excavator or curette.

CAUSES & RISK FACTORS

- Caries is caused by oral bacteria fermenting carbohydrates on the tooth surface, leading to the production of acids (acetic, lactic, propionic) that demineralize the enamel, cementum, and dentin, followed by digestion of the organic matrix of the tooth by oral bacteria and/or leukocytes.
- There is a constant exchange of minerals between the tooth surfaces (enamel, any exposed dentin or root cementum) and the oral fluids; if there is a net loss of mineral, caries develops.
- Early (incipient) caries may be reversible through remineralization.
- Once the protein matrix collapses, the lesion is irreversible.
- Any factors that allow prolonged retention of fermentable carbohydrates and bacterial plaque on the tooth surface predispose to the development of caries.
- A deep occlusal pit on the maxillary first molar is the most common place for caries to develop.
- Dental surfaces in close contact with an established caries are at risk of developing a lesion by extension.
- Deep occlusal pits and developmental grooves on the crown surface predispose to pit-and-fissure caries.
- Tight interdental contacts predispose to smooth-surface caries.

- Deep periodontal pockets predispose to root caries.
- Animals with poorly mineralized enamel, lower salivary pH, diets high in fermentable carbohydrates, and poor oral hygiene are at risk of developing caries.
- Loss of enamel through any means (hypocalcification at the developmental stage, abrasive wear or attrition, traumatic fracture) that exposes the softer, underlying dentin may increase the risk for the development of caries.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Crown fracture, abrasive wear or attrition with exposed tertiary dentin, or extrinsic staining.
- Enamel hypocalcification with exposed and stained dentin.
- Tooth resorption (FORL) has been misnamed feline caries in the past.
- Tooth resorption can also occur in dogs and may be mistaken for caries.
- Sound dentin is hard and will not yield to a dental explorer, whereas carious dentin is soft and will yield to a sharp instrument.
- Root caries may be confused with external root resorption, though the distinction would often be academic, as either usually indicates the need for extraction.
- The lesion should be staged as to the depth of the pathology.
- Table 1 is adapted from the American Veterinary Dental College approved nomenclature for tooth resorption as published on its website.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

IMAGING

Intraoral Dental Radiography

- Areas of demineralization and tissue loss will appear as lucent areas contrasted against radiodense normal dental tissues.
- If the lesion has penetrated into the pulp chamber, there will be endodontic disease, and periapical disease may be evident if the lesion is sufficiently longstanding.

Table 1

| Stage | Description |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Stage 1 | Defect involves enamel or cementum only. |
| Stage 2 | Defect extends into dentin but not into pulp chamber. |
| Stage 3 | Deep dental hard tissue loss (cementum and/or enamel with loss of dentin that extends to the pulp cavity); most of the tooth retains its integrity. |
| Stage 4 | Extensive dental hard tissue loss (cementum and/or enamel with loss of dentin that extends to the pulp cavity); most of the tooth has lost its integrity. |
| Stage 5 | Majority of crown lost; root remnants remaining. |

(CONTINUED)

DENTAL CARIES

D

- Small lesions may be difficult to demonstrate due to superimposition of normal, radiodense tissues (dental and skeletal).

DIAGNOSTIC PROCEDURES

- Visual examination of the clean, dry tooth surface under good light and with the aid of magnification.
- Exploration with a sharp dental explorer—the explorer will sink into carious dentin and stick, providing the sensation of “tug-back” upon withdrawal.
- Subgingival exploration—reveals irregularities in the root surface.
- Caries detection dyes have been used by human and veterinary dentists to aid in the differentiation between sound and carious dental tissue. However, their use may lead to false-positive results and overtreatment through the removal of excess tissue. Reliance on visual, tactile, and radiographic findings is preferable.

**TREATMENT**

- Focus on prevention—examine the adult dentition of adolescent dogs (6–8 months of age) to identify anatomically compromised areas at risk for the development of caries. Deep pits in the occlusal surface of the maxillary first molar (for example) can be filled with a pit-and-fissure sealant or fluoride-releasing dental bonding agent to prevent caries development if identified prior to the development of any decay.
- Incipient caries—can be arrested and possibly reversed by application of a fluoride varnish or fluoride-releasing dental bonding agent and modification of the risk factors.
- Lesions that result in mild to moderate coronal tissue loss (stage 1 or 2)—remove carious dentin and unsupported enamel using hand instruments and power rotary dental instruments, then restore the coronal anatomy with a bonded, composite restoration or prosthetic restoration.
- Lesions that extend into pulp tissue (stage 3)—endodontic treatment must precede restorative treatment. Alternatively, extraction may be indicated. As the pulp tissue in the roots will be contaminated, complete removal of all root remnants is essential if extraction is performed.

- Lesions that result in extensive coronal tissue loss (stage 4 or 5)—extraction is typically the only treatment option. As the pulp tissue in the roots will be contaminated, complete removal of all root remnants is essential.
- Root caries—if the periodontal disease can be managed and the restoration placed supragingivally, restoration may be possible; however, for most teeth with root caries, extraction will be the treatment of choice.
- If only one root of a multirooted tooth is carious—extraction of the affected root with endodontic treatment of the remaining root(s) is also an option.
- For high-risk patients—application of a pit-and-fissure sealant and/or fluoride-releasing dental bonding agent on remaining teeth with occlusal surfaces may be considered.

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

- Postoperative broad-spectrum antibiotics—may be indicated if there is pulp involvement necessitating endodontic treatment or extraction.
- Postoperative analgesia with nonsteroidal anti-inflammatory drugs and/or narcotics is indicated following endodontic or exodontic treatment or extensive restorative work of vital teeth.

CONTRAINdications/POSSIBLE INTERACTIONS

N/A

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

- Examine and radiograph treated teeth 6 months postoperatively, then annually or as the opportunity presents.
- Evaluate the integrity of the restorations, assess for further decay at the margins or under the restorations, assess for the development of endodontic disease.
- As affected individuals frequently have more than one caries, examine all teeth

carefully (clinically and radiographically) at any opportunity to monitor for the development of new lesions.

PREVENTION/AVOIDANCE

Avoidance of diet and treats high in refined carbohydrates may reduce the risk of the development of further caries.

EXPECTED COURSE AND PROGNOSIS

If a lesion has been properly debrided and restored it should have an excellent prognosis. Appropriate staging and case selection, thorough removal of all carious tissues, and adherence to restorative principles are essential.

**MISCELLANEOUS****SYNONYMS**

- Cavities.
- Dental decay.

ABBREVIATIONS

- FORL = feline odontoclastic resorptive lesions.

INTERNET RESOURCES

- <http://www.toothvet.ca/PDFfiles/DentalCaries.pdf>
- <https://avdc.org/avdc-nomenclature>
- http://www.toothvet.ca/PDFfiles/Tooth_resorption_in_cats.pdf
- http://www.toothvet.ca/PDFfiles/RLs_in_Dogs.pdf

Suggested Reading

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DIABETES INSIPIDUS

D



BASICS

DEFINITION

Diabetes insipidus (DI) is a disorder of water metabolism characterized by polyuria (PU), urine of low specific gravity or osmolality (so-called insipid, or tasteless, urine), and polydipsia (PD).

PATHOPHYSIOLOGY

- Central DI (CDI)—deficiency in the secretion of antidiuretic hormone (ADH).
- Nephrogenic DI (NDI)—renal insensitivity to ADH.

SYSTEMS AFFECTED

- Endocrine/metabolic.
- Renal/urologic.

INCIDENCE/PREVALENCE

- Primary CDI—rare.
- Primary NDI—rare.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

None

Mean Age and Range

- Congenital forms <1 year.
- Acquired forms, any age.

SIGNS

- PU.
- PD.
- Incontinence—occasional.
- Signs of intracranial mass if due to pituitary tumor.
- Dehydration and weakness in animals with uncompensated free water loss.

CAUSES

Inadequate Secretion of ADH

- Congenital defect.
- Idiopathic.
- Trauma.
- Neoplasia.

Renal Insensitivity to ADH

- Congenital—defect in aquaporin (renal tubular channel that allows free water reabsorption).
- Secondary to drugs (e.g., lithium, demeclocycline).
- Secondary to endocrine and metabolic disorders (e.g., hyperadrenocorticism, hyponatremia, hypercalcemia).
- Secondary to renal disease or infection (e.g., pyelonephritis, chronic kidney disease, pyometra).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Polyuric Disorders

- Hyperadrenocorticism.
- Diabetes mellitus.
- Renal disease.
- Hyperthyroidism—cats.
- Hyperadrenocorticism.
- Liver disease—portosystemic shunt.
- Pyometra.
- Pyelonephritis.
- Hypercalcemia.
- Primary PD.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal; hypernatremia in patients with excessive free water loss.
- Urinary specific gravity low (<1.006, hyposthenuria).

OTHER LABORATORY TESTS

Plasma ADH (not commercially available).

IMAGING

- MRI or CT scan if pituitary tumor is suspected.
- Abdominal radiographs or ultrasound may help rule out other polyuric disorders.

DIAGNOSTIC PROCEDURES

- ADH supplementation trial—preferred to water deprivation test; therapeutic trial with synthetic ADH (desmopressin [DDAVP]); positive response (water intake decreases by 50% in 5–7 days).
- Modified water deprivation test (see Appendix II for protocol)—not routinely recommended due to risk of complications.
- Rule out all other causes of PU/PD before considering primary CDI.

PATHOLOGIC FINDINGS

Degeneration and death of neurosecretory neurons in neurohypophysis (primary CDI).



TREATMENT

APPROPRIATE HEALTH CARE

- Patients should be hospitalized for modified water deprivation test; the ADH trial is often performed as an outpatient procedure.
- Animals with NDI should have underlying disease diagnosed and treated.

ACTIVITY

Not restricted.

DIET

Normal, with free access to water.

CLIENT EDUCATION

- Review dosage of DDAVP and administration technique.
- Importance of having water available at all times.

SURGICAL CONSIDERATIONS

Pyometra is a surgical emergency and should be removed as soon as the patient is stabilized.



MEDICATIONS

DRUG(S) OF CHOICE

- CDI—DDAVP (1–2 drops of intranasal preparation in conjunctival sac q12–24h to control PU/PD); alternatively, intranasal preparation may be given SC (2–5 µg, q12–24h). Oral preparation of DDAVP is available in 0.1–0.2 mg tablets, with each 0.1 mg comparable to 1 large drop of intranasal preparation.
- NDI—hydrochlorothiazide (2–4 mg/kg PO q12h), in addition to treatment of any underlying cause.

CONTRAINdicATIONS

None

PRECAUTIONS

Overdose of DDAVP can cause water intoxication.



FOLLOW-UP

PATIENT MONITORING

- Adjust treatment according to patient's signs; ideal dosage and frequency of DDAVP administration based on water intake.
- Laboratory tests such as PCV, total solids, and serum sodium concentration, and patient weight to detect dehydration (inadequate DDAVP replacement).

PREVENTION/AVOIDANCE

Circumstances that might increase water loss.

POSSIBLE COMPLICATIONS

Anticipate complications of primary disease (e.g., pituitary tumor).

EXPECTED COURSE AND PROGNOSIS

- CDI usually permanent, except in patients in which condition was trauma induced.
- NDI usually resolves with treatment of underlying disorder.
- Prognosis generally good, depending on underlying disorder.
- Without treatment, dehydration can lead to stupor, coma, and death.



MISCELLANEOUS

AGE-RELATED FACTORS

- Congenital CDI and NDI usually manifest before 6 months of age.
- CDI related to pituitary tumors usually seen in dogs >5 years old.

DIABETES INSIPIDUS

(CONTINUED)

SYNOMYMS

- Cranial diabetes insipidus.
- ADH-responsive diabetes insipidus.

D**SEE ALSO**

Hyposthenuria

ABBREVIATIONS

- ADH = antidiuretic hormone.
- CDI = central diabetes insipidus.

- DI = diabetes insipidus.
- NDI = nephrogenic diabetes insipidus.
- PD = polydipsia.
- PU = polyuria.

Suggested Reading

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Scott-Moncrieff JCR. Canine and Feline
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Saunders, 2015.

Author Patty A. Lathan**Consulting Editor** Patty A. Lathan**Acknowledgment** The author and book
editors acknowledge the prior contribution
of Rhett Nichols.**Client Education Handout
available online**

DIABETES MELLITUS WITH KETOACIDOSIS



BASICS

DEFINITION

A medical emergency secondary to absolute or relative insulin deficiency, characterized by hyperglycemia, ketonemia, metabolic acidosis, dehydration, and electrolyte depletion.

PATHOPHYSIOLOGY

- Insulin deficiency causes an increase in lipolysis, resulting in excessive ketone body production and metabolic acidosis; an inability to maintain fluid and electrolyte homeostasis causes dehydration, prerenal azotemia, electrolyte disorders, obtundation, and death.
- Many patients with diabetic ketoacidosis (DKA) have underlying conditions such as infection, inflammation, or heart disease that cause stress hormone (e.g., glucagon, cortisol, growth hormone, epinephrine) secretion; this probably contributes to development of insulin resistance and DKA by promoting lipolysis, ketogenesis, gluconeogenesis, and glycogenolysis.
- Dehydration and electrolyte abnormalities result from osmotic diuresis, promoting the loss of total body water and electrolytes.

SYSTEMS AFFECTED

- Endocrine/metabolic.
- Gastrointestinal.
- Hematologic (cats).

GENETICS

None

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Dog—miniature poodle and dachshund.
- Cat—none.

Mean Age and Range

- Dog—mean age 8.4 years.
- Cat—median age 11 years (range: 1–19 years).

Predominant Sex

- Dogs—females 1.5 times more prevalent than males.
- Cats—males 2 times more prevalent than females.

SIGNS

- Shock.
- Dehydration.
- Hypothermia.
- Polyuria.
- Polydipsia or adipsia.
- Anorexia.
- Weakness.
- Vomiting.
- Lethargy.
- Tachypnea.
- Muscle wasting and weight loss.

- Unkempt haircoat.
- Thin body condition.
- Ketone odor on breath.
- Icterus.
- Dandruff.

CAUSES

- Diabetes mellitus.
- Infection (e.g., pyoderma, pneumonia, urinary tract infection, prostatitis, pyelonephritis, pyometra).
- Concurrent disease (e.g., heart failure, pancreatitis, renal insufficiency or failure, asthma, neoplasia, acromegaly).
- Estrus.
- Idiopathic.
- Medication noncompliance.
- Stress.
- Surgery.

RISK FACTORS

- Any condition that leads to absolute or relative insulin deficiency.
- History of corticosteroid or beta blocker administration.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hyperosmolar hyperglycemic state.
- Acute hypoglycemic coma/insulin overdose.
- Uremia/azotemia due to renal disease or postrenal obstruction.
- Other cause of metabolic acidosis (e.g., lactic acidosis, ethylene glycol intoxication, renal tubular acidosis).

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with mature neutrophilia.
- Hyperglycemia—blood glucose concentration usually >250 mg/dL.
- High liver enzyme activity.
- Hypercholesterolemia and lipemia.
- Azotemia.
- Hypochloremia.
- Hypokalemia.
- Hyponatremia.
- Hypophosphatemia.
- Hypomagnesemia.
- High anion gap—anion gap = (sodium + potassium) – (chloride + bicarbonate); normal is 16 ± 4 .
- Glucosuria and ketonuria.
- Variable urinary specific gravity with active or inactive sediment.
- Hyperproteinemia.
- Heinz body anemia (cats).

OTHER LABORATORY TESTS

- Metabolic acidosis— $\text{HCO}_3^- < 15 \text{ mEq/L}$ (total CO_2 estimates HCO_3^-).
- Hyperosmolarity ($> 330 \text{ mOsm/kg}$).
- Bacterial culture of urine and blood.

DIAGNOSTIC PROCEDURES

- Abdominal and thoracic radiography and ultrasound may be necessary to identify comorbid diseases.

- ECG and blood pressure monitoring indicated for patients with shock or electrolyte abnormalities.

PATHOLOGIC FINDINGS

Pancreatic islet cell atrophy.

D



TREATMENT

APPROPRIATE HEALTH CARE

- If the animal is bright, alert, and well hydrated, intensive care and IV fluid administration are not required; start SC administration of insulin (short- or intermediate-acting insulin), offer food, and supply constant access to water; monitor closely for signs of illness (e.g., anorexia, lethargy, vomiting).
- Treatment of animals with DKA that are systemically ill requires intensive inpatient care; goals are to correct depletion of water and electrolytes, reverse ketonemia and acidosis, and increase rate of glucose use by insulin-dependent tissues.

NURSING CARE

- Fluids—necessary to ensure adequate cardiac output and tissue perfusion and to maintain vascular volume; also reduce blood glucose concentration.
- IV administration of isotonic crystalloid supplemented with potassium is initial fluid of choice; volume and rate determined by fluid replacement needs plus maintenance requirements; replace over 24–48h.

ACTIVITY

N/A

DIET

Following stabilization, diet should be adjusted to account for patient's diabetes, concurrent disease, and body condition. High-fiber diets are not recommended in underweight pets.

CLIENT EDUCATION

Serious medical condition requiring lifelong insulin administration in most patients. Confirm that client is prepared to inject twice daily insulin prior to treatment of DKA.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

Insulin

- Regular insulin is the insulin of choice until eating; lispro insulin may also be considered.
- Initial dosage—0.2 U/kg IM (or SC if hydration normal).
- Subsequent dosage 0.1–0.2 U/kg IM given 3–6 h later—may be given hourly if patient is closely monitored; response to previous insulin dosage should be considered when calculating

DIABETES MELLITUS WITH KETOACIDOSIS

(CONTINUED)

D

- subsequent dosages; ideally, glucose concentration should drop by 50–100 mg/dL/h.
- Regular insulin can also be administered as CRI via designated catheter. Dogs: 2.2 units/kg in 250 mL of 0.9% NaCl; Cats: 1.1 units/kg in 250 mL 0.9% NaCl. Then, allow 50 mL of dilute insulin to flow through IV tubing and discard. If blood glucose >250 mg/dL, administer at 10 mL/h; if blood glucose 200–250 mg/dL, administer at 7 mL/h; if blood glucose 150–200 mg/dL, administer at 5 mL/h; if blood glucose 100–150 mg/dL, administer at 5 mL/h and add 2.5% dextrose to IV crystalloid fluids; if blood glucose <100 mg/dL, discontinue IV insulin infusion and continue 2.5–5% dextrose in IV crystalloid infusion.
 - Check blood glucose q1–3h using automated test strip analyzer (Accu-Chek® III, Alpha Trak® II glucometer), corrected for patient's PCV as indicated.
 - Monitor urine or serum ketones daily.
 - Administer longer-acting insulin once patient is eating, drinking, and ketosis is resolved; the dosage is based on that of short-acting insulin given in hospital.

Potassium Supplementation

- Total body potassium is depleted and treatment (e.g., fluids and insulin) will further lower serum potassium.
- If possible, check potassium concentration before initiating insulin therapy to guide supplementation; if extremely low, insulin therapy may need to be delayed (hours) until serum potassium concentration increases.
- Refractory hypokalemia may indicate hypomagnesemia, requiring magnesium replacement at 0.75–1 mEq/kg/24h IV as magnesium chloride or magnesium sulfate.
- Supplementation of potassium should start at 0.2 mEq/kg/h, which can be adjusted to max 0.5 mEq/kg/h. Potassium concentration should be measured q6–8h until stabilized.

Dextrose Supplementation

- Because insulin is required to correct the ketoacidotic state, the supplementation of dextrose allows continuous insulin administration without hypoglycemia.
- Whenever blood glucose <200 mg/dL, 50% dextrose should be added to fluids to produce 2.5% dextrose solution (increase to 5% dextrose if glucose <100 mg/dL). Discontinue dextrose once glucose is maintained above 250 mg/dL.
- Insulin therapy is continued as long as blood glucose >100 mg/dL.

Bicarbonate Supplementation

- Controversial; consider if patient's venous blood pH <7.0 or $\text{HCO}_3^- < 11 \text{ mEq/L}$; of little benefit if pH >7.0.
- Dosage—bodyweight (kg) $\times 0.3 \times$ base deficit (base deficit = normal serum bicarbonate – patient's serum bicarbonate); slowly administer $\frac{1}{4}$ to $\frac{1}{2}$ of dose IV and give remainder in fluids over 3–6h.

- Recheck blood gas or serum total carbon dioxide (TCO_2) before further supplementation.

Phosphorus Supplementation

- Pretreatment serum phosphorus is usually normal; however, treatment of ketoacidosis reduces phosphorus, and serum concentrations should be checked q12–24h once supplementation is initiated.
- Dosage—0.01–0.03 mmol/kg/h for 6–12h in IV fluids (may need to increase dose to 0.06 mmol/kg/h). Remember to account for additional potassium in potassium phosphate if supplemented.

CONTRAINdications

If the patient anuric or oliguric or if blood potassium concentration >5 mEq/L, do not supplement potassium until urine flow is established or potassium concentration decreases.

PRECAUTIONS

- Use bicarbonate with caution in patients without normal ventilation (cannot excrete carbon dioxide created during treatment).
- Acidosis results in falsely elevated blood ionized calcium concentrations; calcium should be rechecked as acidosis resolves and supplemented as necessary.

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Attitude, hydration, cardiopulmonary status, urine output, and bodyweight.
- Blood glucose q1–3h initially; q6h once stable.
- Electrolytes q4–8h initially; q24h once stable.
- Acid-base status q8–12h initially; q24h once stable.

PREVENTION/AVOIDANCE

Appropriate insulin administration.

POSSIBLE COMPLICATIONS

- Hypokalemia.
- Hypoglycemia.
- Hypophosphatemia.
- Cerebral edema.
- Pulmonary edema/heart failure.
- Renal failure.

EXPECTED COURSE AND PROGNOSIS

Guarded



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pancreatitis.
- Hyperadrenocorticism.

- Diestrus.
- Bacterial infection.
- Electrolyte depletion.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- Risk of fetal death may be relatively high.
- Glucose regulation is often difficult in pregnant animals.

SYNONYMS

N/A

SEE ALSO

- Diabetes Mellitus Without Complication—Cats.
- Diabetes Mellitus Without Complication—Dogs.

ABBREVIATIONS

- DKA = diabetic ketoacidosis.
- TCO_2 = total carbon dioxide.

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Deborah S. Greco.



Client Education Handout
available online

DIABETES MELLITUS WITHOUT COMPLICATION—CATS



BASICS

DEFINITION

- Disorder of carbohydrate, fat, and protein metabolism caused by an absolute or relative insulin deficiency, resulting in the hallmark abnormality of persistent hyperglycemia.
- The most common form in cats resembles Type II or non-insulin-dependent diabetes mellitus (DM) of humans.

PATHOPHYSIOLOGY

- Insulin resistance impairs the ability of tissues (especially muscle, adipose tissue, and liver) to use carbohydrates, fats, and proteins.
- Impaired systemic glucose utilization coupled with ongoing hepatic gluconeogenesis causes persistent hyperglycemia, which directly impairs insulin secretion by reducing functional beta cell mass ("glucose toxicity").
- Initial beta cell dysfunction progresses to irreversible failure of insulin production as reactive oxidative species, inflammatory cytokines, and amyloid deposition perpetuate beta cell injury and loss.

SYSTEMS AFFECTED

- Endocrine/metabolic—electrolyte depletion, metabolic acidosis.
- Hepatobiliary—chronic pancreatitis, hepatic lipidosis.
- Neuromuscular—muscle wasting, peripheral neuropathy.
- Renal/urologic—osmotic diuresis with compensatory polydipsia (PD); urinary tract infection.

GENETICS

Genetic susceptibility suspected in certain breeds (e.g., European Burmese cats).

INCIDENCE/PREVALENCE

Reported at between ~1 : 250 (0.4%) to ~1 : 100 (1.2%) cats.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat

Breed Predilections

Breeds with possible increased susceptibility include Burmese (Europe, Australia, and New Zealand), Maine Coon, Russian Blue, Siamese, and Norwegian Forest cats.

Mean Age and Range

Over 80% of cases are 7 years or older at diagnosis; range: 1–19 years.

Predominant Sex

Males are overrepresented, but common in both sexes.

SIGNS

Historical Findings

- Obesity often present prior to diagnosis.

- Polyuria (PU)/PD, polyphagia, weight loss, generalized muscle wasting, poor coat quality.

- Signs suggesting a complication—anorexia, lethargy, depression, vomiting, jaundice.

Physical Exam Findings

Hepatomegaly, dehydration, plantigrade stance (diabetic neuropathy).

CAUSES

- Genetic susceptibility.
- Islet amyloid deposition.
- Pancreatitis.
- Diseases causing insulin resistance (e.g., hyperadrenocorticism and acromegaly).
- Drugs (e.g., glucocorticoids and progestogens).

RISK FACTORS

- Obesity.
- Advanced age.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Stress hyperglycemia—no PU/PD or weight loss; blood glucose concentration normal if sample taken when cat is not stressed; normal fructosamine concentration.
- Renal glucosuria—absence of hyperglycemia; usually does not cause PU/PD or weight loss.

CBC/BIOCHEMISTRY/URINALYSIS

- Mild normocytic, normochromic anemia possible.
- Glucose >150 mg/dL.
- High alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) activities.
- Hypercholesterolemia, hyperbilirubinemia, and hypertriglyceridemia.
- Total CO₂ or HCO₃ low with ketoacidosis or severe dehydration.
- Glucosuria, ketonuria uncommon in uncomplicated DM.
- Isosthenuria, proteinuria.

OTHER LABORATORY TESTS

- Fructosamine >350 μmol/L—confirms persistence of hyperglycemia.
- Feline pancreas-specific lipase >3.50 μg/L—identifies presence of pancreatitis.
- Urine culture—positive in 10–15% of newly diagnosed DM.

IMAGING

- Thoracic and abdominal radiography—to evaluate for concurrent or underlying disease (e.g., neoplasia, cystic or renal calculi, emphysematous cystitis, or cholecystitis).
- Abdominal ultrasonography—in selected patients, particularly those with jaundice, to evaluate for hepatic lipidosis, cholangiohepatitis, and pancreatitis.

DIAGNOSTIC PROCEDURES

Liver fine-needle aspiration—if concern for hepatic lipidosis.

PATHOLOGIC FINDINGS

- Usually no gross necropsy changes; pancreatic weight may be increased.
- Histopathology—normal, more likely to reveal islet amyloidosis, vacuolar or hydropic degeneration of the islets of Langerhans; lymphoplasmacytic pancreatic infiltration rare in cats.



TREATMENT

APPROPRIATE HEALTH CARE

- Compensated cats can be managed as outpatients if they are alert, hydrated, and eating and drinking without vomiting.
- For decompensated patients, see Diabetes Mellitus With Ketoacidosis.

NURSING CARE

Fluid therapy—in decompensated patients.

ACTIVITY

Strenuous activity may lower insulin requirements; consistent daily activity level is helpful.

DIET

Ultra-low-carbohydrate (<12% metabolizable energy) and high protein (>40% metabolizable energy) canned diets may improve glycemic control, and increase the likelihood of diabetic remission in newly diagnosed diabetic cats.

CLIENT EDUCATION

- Discuss maintaining a consistent daily feeding and medication schedule, home glucose monitoring, signs of hypoglycemia and what to do, and when to seek veterinary assistance.
- Clients are encouraged to chart pertinent daily information about the pet, such as any home-obtained glucose readings or patterns of exhibited clinical signs (e.g., PU/PD or appetite).

SURGICAL CONSIDERATIONS

Intact females should have ovariohysterectomy when stable; progesterone secreted during diestrus makes management of DM difficult.



MEDICATIONS

DRUG(S) OF CHOICE

- Insulin is treatment of choice and should be initiated at 1–2 units per cat SC q12h; based on routine monitoring, some cats may eventually be reduced to once-daily dosing.
- Two U-40 insulin formulations are FDA-approved for use in cats—protamine zinc (PZI) and porcine zinc lente insulin suspension.

DIABETES MELLITUS WITHOUT COMPLICATION—CATS

(CONTINUED)

- Most consensus recommendations support the use of PZI or glargine (U-100) as first-choice insulin therapy for cats.

D

PRECAUTIONS

Glucocorticoids, megestrol acetate, and progesterone cause insulin resistance. If steroid therapy is necessary, use oral methylprednisolone. Avoid injectable steroids.

POSSIBLE INTERACTIONS

- Drugs that may increase insulin sensitivity—angiotensin-converting enzyme inhibitors, sulfonamides, tetracycline, beta blockers, monoamine oxidase inhibitors, salicylates.
- Drugs that increase insulin resistance—glucocorticoids, estrogen supplements, furosemide, thiazide diuretics, and calcium channel blockers.
- Always consult a new medication's product insert.

ALTERNATIVE DRUG(S)

- Oral sulfonylureas (e.g., glipizide)—only considered when insulin therapy is not possible (e.g., owner considering euthanasia instead of injections). Initial doses of 2.5 mg PO q12h can be used and monitored similar to insulin. If DM is not controlled after 2 weeks, dose of 5 mg PO q12h may be tried; however, response is seen in <40% of cats and often not sustained long term. Potential side effects are hypoglycemia, hepatic enzyme alterations, icterus, and vomiting.
- Acarbose—an alpha-glucosidase inhibitor used to limit intestinal glucose absorption. Often used in combination with diet and insulin at a starting dose of 12.5 mg PO q12h; diarrhea is most common side effect.
- Drugs warranting further study for utility in managing feline DM include once-weekly injected glucagon-like peptide 1 analogues and oral renal tubular transporter inhibitors.



FOLLOW-UP

PATIENT MONITORING

- Owner-assessed clinical signs (PU/PD, appetite, attitude) and bodyweight—if signs

are normal and weight stable to increasing, disease is likely to be regulated.

- Glucose curves—ideally generated by the owner at home. Perform 5–14 days after starting insulin or after any dose adjustments until controlled, then again at 1 month, and every 3–6 months thereafter.
- Fructosamine—maintain <400 µmol/L. Recheck monthly during initial regulation, then every 3–6 months as part of routine monitoring visits.
- Urinary monitoring—useful for identifying ketones in chronically unregulated patients or persistently negative glucose in cats likely entering remission.
- Flash glucose monitoring system (FreeStyle Libre®)—24-hour glucose monitoring system that measures blood glucose BG every 5 minutes for up to 14 days; use reported in dogs, but not cats. Anecdotal evidence suggests the device is not 100% accurate, but helpful in assessing BG trends in cats in which a BG curve is not possible.

PREVENTION/AVOIDANCE

Prevent or correct obesity; avoid unnecessary use of glucocorticoids or megestrol acetate.

POSSIBLE COMPLICATIONS

- Seizure, blindness, or coma with insulin overdose.
- Diabetic ketoacidosis or hyperglycemic hyperosmolar syndrome.

EXPECTED COURSE AND PROGNOSIS

- Prognosis with treatment and monitoring is good; most animals have a normal lifespan.
- Some cats may recover insulin-secreting ability ("diabetic remission"), typically if glycemic control is achieved within 6 months of diagnosis; however, relapse is common (~30%).
- Reported remission rates vary greatly (0–100%); however, studies surveying general practitioners have suggested ~25–30% is reasonable expectation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Urinary tract infection, chronic pancreatitis.

AGE-RELATED FACTORS

Congenital and juvenile forms of DM are rare (<3% of cases are under 2 years of age) and may be more difficult to manage.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Insulin requirements should be monitored closely during pregnancy as they are expected to fluctuate.
- Severe maternal hypoglycemia can negatively impact fetal viability and neonatal neurologic function, therefore should be avoided during gestation.

SYNONYMS

N/A

SEE ALSO

- Diabetes Mellitus With Ketoacidosis.
- Diabetes Mellitus With Hyperosmolar Hyperglycemic State.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- AST = aspartate aminotransferase.
- BG = blood glucose.
- DM = diabetes mellitus.
- PU/PD = polyuria and polydipsia.
- PZI = protamine zinc insulin.

INTERNET RESOURCES

https://www.aaha.org/guidelines/diabetes_guidelines/default.aspx

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Deborah S. Greco.



Client Education Handout
available online

DIABETES MELLITUS WITHOUT COMPLICATION—DOGS



BASICS

DEFINITION

- Fasting hyperglycemia of sufficient magnitude to result in characteristic clinical signs including weight loss with normal or increased appetite, polydipsia (PD), and polyuria (PU) caused by glucosuria.
- Disorder of carbohydrate, fat, and protein metabolism caused by absolute or relative insulin deficiency. • Generally canine diabetes mellitus (DM) is characterized by loss of insulin-secreting ability through presumed immune-mediated destruction of pancreatic beta cells. • Far less frequently, canine DM may develop as result of combination of relative insulin-deficient state with concurrent peripheral insulin resistance.

PATHOPHYSIOLOGY

- Absolute or relative insulin deficiency results in accelerated tissue catabolism, impaired ability to maintain carbohydrate, lipid, and protein homeostasis, as well as insulin resistance. • Reduced insulin-secreting ability, peripheral insulin resistance, and continued hepatic gluconeogenesis result in persistent hyperglycemia of sufficient severity to overload renal tubular glucose resorption; leading to glucosuria, osmotic diuresis, PU accompanied by compensatory PD. • Loss of insulin-dependent glucose-mediated hypothalamic satiation signaling results in polyphagia. • Decreased insulin-independent utilization of glucose results in catabolic protein breakdown with weight loss and increased lipid mobilization (hyperlipidemia, hepatic lipidosis, production of ketoacids). • Accumulation of large amounts of ketone bodies leads to metabolic acidosis (see Diabetes Mellitus With Ketoacidosis).

SYSTEMS AFFECTED

- Endocrine/metabolic—electrolyte depletion and metabolic acidosis. • Hepatobiliary—hepatic lipidosis. • Ophthalmic—cataracts.
- Renal/urologic—glucosuria resulting in osmotic diuresis and increased likelihood of bacterial urinary tract infections, particularly of upper urinary tract.

GENETICS

Certain breeds dramatically over- and underrepresented, suggesting inherited susceptibility to immune-mediated “isletitis.”

INCIDENCE/PREVALENCE

- Prevalence varies between 1 : 400 and 1 : 500. • Onset has seasonal incidence; more animals diagnosed in autumn and winter.

SIGNALMENT

Species

Dog

Breed Predilections

- Samoyed, Tibetan terrier, Cairn terrier, golden retriever (United States only) overrepresented. • Keeshond, poodle, dachshund, miniature schnauzer, beagle may have increased predisposition. • Boxer, German shepherd, golden retriever (UK only) underrepresented.

Mean Age and Range

Mean ~8 years; range: 4–14 years (excluding rare juvenile form).

Predominant Sex

Female

SIGNS

- PU/PD, polyphagia with weight loss.
- Hepatomegaly. • Cataracts common finding—approximately 80% of dogs with DM for >12 months will have cataracts regardless of level of control. • Lethargy, depression, inappetence, anorexia, and vomiting may occur in animals with ketoacidosis.

CAUSES

- Immune-mediated isletitis. • Disorders that predispose to secondary immune-mediated isletitis—pancreatitis, viral illness.

RISK FACTORS

- Diestrus. • Genetic susceptibility. • Use of glucocorticoids or progestins.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Renal glucosuria—not associated with hyperglycemia, usually no weight loss or polyphagia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram usually normal. • Glucose >200 mg/dL, possible ketonemia. • High serum alkaline phosphatase (ALP) and alanine aminotransferase (ALT) enzyme activities, generally with greater proportionate increase in ALP. • Hypercholesterolemia, lipemia. • Electrolyte alterations vary; hypokalemia and hypophosphatemia may be present. • Total CO₂ or HCO₃ will be low with ketoacidosis or severe dehydration.
- Glucosuria, ketonuria in some dogs.
- Urinary specific gravity variable depending on degree of glucosuria.

OTHER LABORATORY TESTS

- Anion gap—high in patients with ketoacidosis. • Glycated proteins—fructosamine or glycosylated hemoglobin: extent of glycosylation directly related to blood glucose concentration over lifespan of protein in circulation (10–20 days for fructosamine, 4–8 weeks for hemoglobin).
 - Glycated protein concentration modified by changes in albumin or hemoglobin concentrations; accelerated albumin turnover

(e.g., glomerulonephropathy, liver dysfunction, gastrointestinal disease) will lower fructosamine level for given average blood glucose. • Best used for ongoing management of relatively stable diabetic patients; fructosamine concentration in upper third of reference range reflects excellent diabetic control; concentration in lower third is more suggestive of overzealous diabetic control and possible increased risk of hypoglycemia. • Plasma insulin concentrations not particularly helpful—while low insulin concentration suggests insulin deficiency, may be reflection of reversible islet exhaustion (persistent hyperglycemia can impair insulin secretory activity, even if functional beta cells present).

IMAGING

- Radiography—useful to look for comorbidities (e.g., cystic or renal calculi, emphysematous cystitis, cholecystitis, pancreatitis). • Ultrasonography—indicated in selected patients, particularly those with jaundice, to evaluate for presence of obstructive hepatopathy or pancreatitis.

DIAGNOSTIC PROCEDURES

Liver biopsy (percutaneous)—indicated in some jaundiced patients to evaluate other causes for hepatopathy.

PATHOLOGIC FINDINGS

- Necropsy findings—hepatomegaly with significant hepatic lipid accumulation.
- Histopathologic findings generally reveal dramatic reduction in size and number of pancreatic islets with relatively normal exocrine tissue architecture.



TREATMENT

APPROPRIATE HEALTH CARE

- Compensated dogs generally alert, well hydrated, eating and drinking without vomiting, and can be managed as outpatients.
- For management of decompensated patients, see Diabetes Mellitus With Ketoacidosis.

DIET

- Diet should be calorically and constitutionally consistent. • Ideally glucose-lowering effects of insulin should match glucose-raising effects of the meal.
 - Most insulins act maximally 2–4h after SC administration, and most food absorbed within 1h of consumption, so glycemic control almost always improved if dog fed 60–90 min *after* q12h insulin dosing.
 - Animals that “graze” throughout day can be fed dry food ad libitum and given 2 small meals of canned food as above.
 - If insulin can only be administered once daily, feed total daily caloric intake in 2 or 3 meals within first 6–8h after insulin dosing.
 - Feed caloric quantity appropriate for animal’s ideal

DIABETES MELLITUS WITHOUT COMPLICATION—DOGS

(CONTINUED)

D

bodyweight (~60 kcal/kg); food should be something dog will eat reliably and within short period. • Obese diabetic dogs—feed restricted caloric intake to ensure ideal bodyweight achieved within 2–4 months using high-fiber, low-calorie food; while high-fiber diet may improve patient satiety and possibly owner satisfaction, has no role in improving diabetic control. • While snacks should generally be avoided, small treats given at time of injection to positively reinforce owner–patient interaction should be encouraged.

CLIENT EDUCATION

- Most important that insulin and feeding regime are discussed and agreed with owner and they feel comfortable with plan; effective management requires significant owner–patient interaction; flexibility in establishing best management regime is thus paramount and rigid “one size fits all protocols” should be avoided. • Discuss daily feeding and medication schedule, home monitoring, signs of hypoglycemia and what to do, and when to call or visit veterinarian. • Clients encouraged to keep chart of pertinent information about pet, such as daily water consumption, weekly bodyweight, current insulin dose, and amount of food consumed; use of standardized clinical scoring tool should be encouraged to maintain consistency across veterinary and tech teams involved in managing both dog and owner.

SURGICAL CONSIDERATIONS

Intact females should have ovariohysterectomy when stable; progesterone secreted during diestrus makes management of DM more unpredictable.



MEDICATIONS

DRUG(S) OF CHOICE

- Insulin—almost always required • Vetsulin® (porcine-origin lente) 0.75 units/kg SC q12h initial dose; note: U-40 insulin—must use with U-40 insulin syringe; availability may be limited. • Humulin N—intermediate-acting, human insulin; 0.75 units/kg SC q12h initial dose. • Novolin N—intermediate-acting, human insulin; 0.75 units/kg SC q12h initial dose. • PZI Vet® (intermediate- to longer-acting protamine zinc human insulin) rarely used in dogs; note: U-40 insulin—must use with U-40 syringe. • Detemir insulin—longer-acting, synthetic insulin; part of reason for its delayed release is because bound to albumin; unlike insulins mentioned above, starting dose should be considerably lower: 0.1 unit/kg SC q12h initial dose. • Glargine insulin—longer-acting, synthetic insulin; 0.75 units/kg SC q12h initial dose. • Species of origin of insulin may affect pharmacokinetics;

canine and porcine insulin have identical amino acid sequence, hence Vetsulin does not produce significant insulin antibody response, whereas most other commercially available insulins do; however, no evidence the development of insulin antibodies has any clinical significance.

PRECAUTIONS

- Glucocorticoids, megestrol acetate, and progesterone cause insulin resistance.
- Hyperosmotic agents (e.g., mannitol and radiographic contrast agents) should be avoided if patient is already hyperosmolar from hyperglycemia.

ALTERNATIVE DRUG(S)

Oral hypoglycemic agents are generally not recommended.



FOLLOW-UP

PATIENT MONITORING

- Diabetic dogs require regular contact between owner and veterinary team; visits should occur every 3–4 months if animal is stable and clinical signs are controlled, or more frequently if control is poor or variable. Criteria to assess control include:
 - Clinical signs—degree of PU/PD, appetite, and bodyweight; if within acceptable limits, disease likely well regulated; consider using standardized clinical scoring system to consistently evaluate clinical phenotype.
 - Glycated proteins—fructosamine or glycosylated hemoglobin; see above.
 - Glucose curve—provides information on insulin effectiveness, duration of action, nadir (lowest blood glucose level achieved during dosing interval), and potential for rebound hyperglycemia; results subject to influence of stress (hospitalization, multiple blood draws) and “normal” conditions should be mimicked as much as possible; used most effectively when establishing initial control, changing insulin type, dose, or frequency, or problem solving for difficult diabetic; duration of curve ideally matches dosing interval (12 or 24 hours)—identification of nadir (to avoid iatrogenic hypoglycemia) and glucose level at time of dosing are most important aspects of curve; goal is to establish effective insulin dose (decline in blood glucose to 100–200 mg/dL) for appropriate duration (majority of 12- or 24-hour dosing interval) with nadir >80 mg/dL and <150 mg/dL; in dogs average glucose levels for 12-hour period overnight are lower than during daylight period.
 - Home glucose monitoring using serial blood glucose estimations or real-time measures using SC glucose monitoring devices—requires owner commitment, compliance, and competence; most useful as

early indicator of need for reduction in dose in patients with well-controlled clinical signs; should never be used by owner to make independent adjustment of insulin dose; owner-measured urine glucose levels not particularly useful.

PREVENTION/AVOIDANCE

- Neuter females; avoid unnecessary use of megestrol acetate. • No evidence exists to suggest obesity increases risk of DM in neutered dogs.

POSSIBLE COMPLICATIONS

- Cataracts can occur even with good glycemic control. • Weakness, especially with exercise; seizures or coma may occur with insulin overdose.

EXPECTED COURSE AND PROGNOSIS

- Dogs generally have permanent disease unless affected during estrus cycle, where neutering may resolve diabetes for a period.
- Prognosis with twice-daily insulin treatment and feeding aligned with insulin's maximum effects is good.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Urinary tract infection. • Cataracts.

AGE-RELATED FACTORS

Juvenile DM is rare and may be more difficult to manage.

PREGNANCY/FERTILITY/BREEDING

- DM can develop during pregnancy, in which case pregnancy is difficult to maintain.
- Exogenous insulin administration may cause fetal oversize and dystocia. • Insulin resistance develops, making hyperglycemia difficult to control. • Pregnant bitch is prone to ketoacidosis; emergency ovariohysterectomy may be necessary. • Do not breed dogs with DM.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- DM = diabetes mellitus.
- PD = polydipsia.
- PU = polyuria.

Author David B. Church

Consulting Editor Patty A. Lathan



Client Education Handout
available online

DIARRHEA, ANTIBIOTIC RESPONSIVE



BASICS

D

OVERVIEW

- Defined as chronic diarrhea with no identifiable underlying etiology that responds to antibiotic therapy.
- Antibiotic-responsive diarrhea (ARD) was previously termed idiopathic (primary) small intestinal bacterial overgrowth (SIBO); this term is no longer used as it was based on quantitative culture of bacteria in the upper gastrointestinal tract that could not be confirmed by newer PCR-based methods; secondary SIBO is a result of concurrent gastrointestinal diseases (e.g., exocrine pancreatic insufficiency [EPI]).
- Current theories center on the possibility of immune dysregulation, possibly associated with abnormal CD4+ T-cells, immunoglobulin (Ig) A plasma cells, cytokine expression, and, in German shepherd dogs, mutations in pattern recognition receptors.

SIGNALMENT

Species

Dog

Breed Predilections

Increased incidence in German shepherd, boxer, and Chinese Shar-Pei.

Mean Age and Range

More common in young dogs, with median age of 2 years.

Predominant Sex

N/A

SIGNS

Historical Findings

- Small bowel signs—inappetence or anorexia, vomiting, weight loss, large-volume diarrhea.
- Large bowel signs—tenesmus, hematochezia, increased frequency of defecation.

Physical Examination Findings

Weight loss, poor body condition, borborygmus, and flatulence may be detected; hematochezia may be present if there is large bowel involvement.

CAUSES & RISK FACTORS

- Genetic mutations in pattern recognition genes (*TLR4* and *TLR5*) have been associated with the disease.
- Certain enteropathogenic bacteria (*Clostridium perfringens*, *Escherichia coli*, and *Lawsonia intracellularis*) have been suspected but not proven to be etiologic agents.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary SIBO.
- EPI.
- Parasitic infection.
- Inflammatory bowel disease.
- Food-responsive diarrhea.
- Neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- Typically normal.
- Hypoalbuminemia is uncommon finding.

OTHER LABORATORY TESTS

- Fecal examination for parasites should be performed.
- Serum cobalamin levels may be low and folate levels may be increased or decreased.
- Serum trypsin-like immunoreactivity (measured to rule out EPI) is normal.

IMAGING

Routine abdominal imaging (radiographs and ultrasound) should be performed to rule out other causes for diarrhea. These tests are unremarkable in cases of ARD.

DIAGNOSTIC PROCEDURES

Diagnosis depends upon ruling out all other causes for chronic diarrhea (especially food-responsive diarrhea) and a clinical response to an appropriate course of antibiotic therapy.



TREATMENT

- Hospitalization generally not indicated; treated on outpatient basis.
- Role of diet in ARD is unknown; current recommendations are to feed low-fat, highly digestible food or elimination or hydrolyzed diet.



MEDICATIONS

DRUG(S) OF CHOICE

- Several options for antibiotics available—tylosin (5–10 mg/kg PO q24h); metronidazole (10–15 mg/kg PO q12h); oxytetracycline (10–20 mg/kg PO q8h).
- In some cases, combination therapy may be necessary.
- Antibiotic therapy administered for 4–6 weeks and then discontinued.
- If serum cobalamin levels decreased, cobalamin supplementation should be pursued; dogs: 50 µg/kg up to max dose of 1,500 µg parenteral cobalamin; doses given as SC injections once weekly for 6 weeks, then once every other week for 6 weeks; serum cobalamin levels should be reassessed at end of therapy; oral cobalamin supplementation is effective at dosage of 0.25–1.0 mg PO daily.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Oxytetracycline may cause staining of tooth enamel; doses should be decreased in animals with hepatic or renal insufficiency; oxytetracycline has been associated with high incidence of bacterial transfer of resistance genes.
- Metronidazole undergoes extensive hepatic metabolism; dosages should be reduced in animals with hepatic insufficiency.

- Long-term administration of both tylosin and metronidazole has been found to induce long-term dysbiosis in ARD dogs, which is very difficult to correct; this dysbiosis is associated with changes in bile acid metabolism and serum metabolome, and persists for over 6 months after discontinuing treatment.



FOLLOW-UP

- Clinical resolution of diarrhea is most important criterion.
- Weight gain may also be seen; hypoalbuminemia (if present) should resolve.
- Relapses usually occur when antibiotics are discontinued; some dogs can be maintained on very low doses of antibiotics long term, however the development of antimicrobial resistance in these dogs is a concern.
- Recent studies suggest ARD dogs have poor long-term prognosis, possibly due to induction of dysbiosis; many dogs eventually will become steroid resistant or will be euthanized because of treatment resistance.



MISCELLANEOUS

SEE ALSO

Small Intestinal Dysbiosis.

ABBREVIATIONS

- ARD = antibiotic-responsive diarrhea.
- EPI = exocrine pancreatic insufficiency.
- Ig = immunoglobulin.
- SIBO = small intestinal bacterial overgrowth.

Suggested Reading

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Author Karin Allenspach

Consulting Editor Mark P. Rondeau

DIARRHEA, CHRONIC—CATS

D



BASICS

DEFINITION

- A change in the frequency, consistency, and volume of feces for more than 3 weeks or with a pattern of episodic recurrence.
- Can be either small bowel, large bowel, or mixed in origin.

PATHOPHYSIOLOGY

- High solute and fluid secretion—secretory diarrhea.
- Low solute and fluid absorption—osmotic diarrhea.
- High intestinal permeability.
- Abnormal gastrointestinal (GI) motility.
- Many cases involve various combinations of these four basic pathophysiologic mechanisms.

SYSTEMS AFFECTED

- Endocrine/metabolic—fluid, electrolyte, and acid-base.
- Exocrine.
- GI.
- Lymphatic.

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Breed Predilections

None

Mean Age and Range

Any age.

Predominant Sex

None

SIGNS

General Comments

- Underlying disease process determines extent of clinical signs.
- 2–3% increase of water content of stool results in gross description of diarrhea.
- Classification of small, large, and mixed bowel types of diarrhea may have overlap of descriptive findings.

Historical Findings

- Small bowel diarrhea can include—normal to increased volume; normal to moderately increased (2–4 times/day) defecation frequency; weight loss; polyphagia; melena; flatulence and borborygmus; vomiting; variable.
- Large bowel diarrhea can include—smaller volume; frequency of defecation is increased (>4 times/day); often hematochezia and mucus; tenesmus; urgency; dyschezia; flatulence and borborygmus; variable; vomiting; variable.

*Physical Examination Findings**Small Bowel*

- Poor body condition associated with malabsorption, maldigestion, and protein-losing enteropathy (PLE).
- Variable dehydration.
- Abdominal palpation may reveal segmental or diffusely thickened small bowel loops associated with infiltrative disease, abdominal effusion, foreign body, neoplastic mass, intussusception,

or enlarged mesenteric lymph nodes.

- Rectal palpation typically unremarkable.

Large Bowel

- Body condition typically unremarkable.
- Dehydration—uncommon.
- Abdominal palpation may reveal thickened large bowel, foreign body, neoplastic mass, intussusception, or enlarged mesocolic lymph nodes.
- Rectal palpation may reveal irregularity of rectal mucosa, intraluminal or extraluminal rectal masses, rectal stricture, or sublumbar lymphadenopathy.

CAUSES

*Small and Large Intestinal Diseases**Primary Disease*

- Inflammatory bowel disease (IBD)—e.g., lymphoplasmacytic enteritis, eosinophilic enteritis, granulomatous enteritis.
- Neoplasia—e.g., lymphoma, including large cell (B-cell lymphoma) and small cell alimentary lymphoma (T-cell), adenocarcinoma, mast cell neoplasia.
- Bacterial—e.g., *Salmonella* spp., enterotoxic *Escherichia coli*, other enterobacteriaceae species, *Clostridia* spp.: usually acute diarrhea.
- Viral—e.g., enteric coronavirus (usually acute diarrhea unless combined with other viral infections or co-factors), feline infectious peritonitis, feline leukemia virus (FeLV) associated, feline immunodeficiency virus (FIV) associated.
- Mycotic—e.g., histoplasmosis.
- Algal—e.g., protothecosis, pythiosis.
- Parasites—e.g., *Giardia*, *Toxocara* spp., *Ancylostoma*, *Toxascaris leonina*, *Cryptosporidium* spp., *Cystoisospora* spp., *Tritrichomonas foetus*.
- Partial obstruction—e.g., foreign body, intussusception, neoplasia.
- Secondary lymphangiectasia—very rare in cats.
- Intestinal microbial dysbiosis—cause vs. effect.
- Short bowel syndrome.
- GI ulceration—rare in cats.

Maldigestion

- Hepatobiliary disease—lack of bile salts needed for intraluminal digestion.
- Exocrine pancreatic insufficiency (EPI).

Dietary

- Dietary intolerance (food-responsive diarrhea).
- Food allergy.

Metabolic Disorders

- Hyperthyroidism.
- Cobalamin deficiency—typically secondary to underlying IBD or lymphoma.
- Renal disease.
- Hepatobiliary disease.
- Adverse drug reactions.

Congenital Anomalies

- Short colon.
- Portosystemic shunt.
- Persistent pancreaticomesojejunal ligament.

RISK FACTORS

Dietary changes, feeding poorly digestible or high-fat diets.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

First localize the origin of the diarrhea to the small or large bowel (or both) on the basis of historical signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia in some cats with parasitism, eosinophilic enterocolitis, hypereosinophilic syndrome, or neoplasia.
- Macrocytosis in some cats with hyperthyroidism or FeLV infection.
- Anemia that is variably regenerative and may show microcytosis suggests chronic GI bleeding and iron deficiency.
- Leukopenia in some cats with FeLV or FIV infection.

- Panhypoproteinemia caused by PLE is uncommon in cats with intestinal disease, but can occur; hypoalbuminemia can be seen.
- Biochemical profiles and urinalysis abnormalities may suggest renal disease, hypoproteinemia, hepatobiliary disease, or endocrinopathy.

OTHER LABORATORY TESTS

Fecal and/or Rectal Scraping Exam

- Direct wet prep, routine centrifugation fecal flotation, fecal ELISA testing may indicate GI parasites.
- Cytologic examination of rectal scrapings may reveal specific organisms, such as *Histoplasma*, *Prototrichomonas*, or *Tritrichomonas*.
- PCR fecal testing should be interpreted with caution, because positive results for toxin genes or infectious agents may or may not correlate with clinical disease; interpret PCR results in light of patient signalment, history, clinical presentation, vaccination history, and other laboratory data.
- PCR for *Tritrichomonas*—most sensitive test; be certain to send fresh fecal sample, colonic lavage fluid, or loop scraping for testing.
- Culture feces if *Salmonella* is suspected—special media required.

Thyroid Function Tests

- High total T₄ or free T₄ concentration indicates hyperthyroidism.
- If hyperthyroidism is suspected but T₄ is normal, perform a T₃ suppression test, repeat the T₄ a few months later, or perform a technetium scan of the thyroid glands.

Serologic Testing

Test for FeLV and FIV—especially if hematologic abnormalities are present.

Test for Exocrine Pancreatic Function

Feline-specific trypsin-like immunoreactivity—test of choice for diagnosis of EPI.

IMAGING

- Survey abdominal radiography may indicate abnormal intestinal pattern, organomegaly, mass, foreign body, pancreatic disease, hepatobiliary disease, urinary disease, or abdominal effusion; low yield in most cats with chronic diarrhea.
- Contrast radiography (upper GI series or barium enema) may indicate bowel wall thickening, intestinal ulcers, mucosal irregularities, mass, radiolucent foreign body, or stricture; procedure performed infrequently in cats in light of advantages of abdominal ultrasonography.
- Abdominal ultrasonography may demonstrate bowel wall thickening, abnormal bowel wall layering, GI or extra-GI masses, intussusception, foreign body, ileus, abdominal effusion, hepatobiliary

DIARRHEA, CHRONIC—CATS

(CONTINUED)

disease, pancreatitis, renal disease, or mesenteric or mesocolic lymphadenopathy.

D

DIAGNOSTIC PROCEDURES

If maldigestive (EPI), metabolic, parasitic, dietary, and infectious causes have been excluded, consider empiric dietary therapy, utilizing an elimination diet for 2 weeks before performing endoscopy and biopsy or a laparotomy for definitive diagnosis.

Endoscopy/Laparoscopy

- Upper GI flexible endoscopy allows examination and biopsy of gastric and duodenal mucosa; always obtain multiple (8–10) mucosal specimens from each segment/area.
- Flexible colonoscopy allows examination of entire rectum, colon, cecum, and ileum; always obtain multiple mucosal specimens (8–10) from each segment.
- Visual impressions of GI mucosal detail may not reflect histopathologic changes; always take biopsies.
- Endoscopic biopsies rely upon infiltrative and inflammatory diseases being represented in first two layers of the intestinal wall, and segments biopsied being representative of disease process.
- Full-thickness biopsies can be obtained via laparoscopy from one or more segments of small intestine (not large intestine) via exteriorization of the segment(s), but are not typically necessary as most diseases can be diagnosed endoscopically.

Surgical Biopsy

Surgical approach beneficial if biopsies of multiple organs (small intestine, lymph nodes, stomach, pancreas, liver) are desired.

Ultrasound-Guided GI Aspiration or Biopsy

- Can perform ultrasound-guided fine-needle aspiration on some GI mass lesions, but cytologic interpretation accuracy is subject to sample quality, expertise, and limitations of technique; small cell alimentary lymphoma cannot be diagnosed by cytology, as cells will be small lymphocytes.
- Paracentesis of peritoneal fluid for fluid analysis, culture, and cytology is recommended.
- Concern has been expressed for risk of translocation of cancer cells or infective organisms with these procedures.

PATHOLOGIC FINDINGS

Vary with underlying disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical management most common.
- Treat underlying cause.

NURSING CARE

- Give fluid therapy with balanced electrolyte solution as needed.
- Correct electrolyte and acid-base imbalances.

ACTIVITY

No restriction.

DIET

- Feeding elimination diet (intact novel protein source or hydrolyzed protein) will resolve diarrhea in 40–60% of cats with chronic enteropathy; response should be detected within 2–3 weeks following dietary implementation.
- Repeated changes of diet made in order to maintain a symptom-free situation suggest that further testing needed.

CLIENT EDUCATION

Complete resolution of signs is not always possible in cats with IBD, neoplasia, or fungal disease despite proper treatment.

SURGICAL CONSIDERATIONS

Pursue exploratory laparotomy and surgical biopsy if evidence of obstruction, intestinal mass, or mid-small bowel disease unreachable via endoscopic procedure.



MEDICATIONS

DRUG(S) OF CHOICE

- Disease specific.
- Prednisolone (1–2 mg/kg BID) for management of IBD; chlorambucil (2 mg/cat q48–72h) should be considered together with prednisolone in severe IBD cases that are refractory to steroids alone or for management of small cell intestinal lymphoma.
- Supplementation with cyanocobalamin at 250 µg SC per cat on a weekly basis for 6 consecutive weeks, followed by every 3 weeks for the indefinite future.
- Probiotics can be beneficial in some patients with chronic nonspecific diarrhea.

CONTRAINDICATIONS

Anticholinergics exacerbate most types of chronic diarrhea and should not be used for empirical treatment.

PRECAUTIONS

Opiate antidiarrheals such as diphenoxylate and loperamide can cause hyperactivity and respiratory depression in cats and should not be used for more than 3 days.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Assess changes in frequency and severity of diarrhea and bodyweight.
- Resolution usually occurs within 2–3 weeks following successful implementation of dietary therapy; consider reevaluating diagnosis if diarrhea does not resolve.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Dehydration.
- Lowered body condition.
- Abdominal effusions as related to specific cause of chronic diarrhea.

EXPECTED COURSE AND PROGNOSIS

Vary with underlying disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Toxoplasmosis.
- Giardiasis (low zoonotic potential).
- Cryptosporidiosis.
- Salmonellosis.
- *Campylobacter jejuni*.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

None

SEE ALSO

- Cobalamin Deficiency.
- Diarrhea, Antibiotic Responsive.
- Exocrine Pancreatic Insufficiency.
- Food Reactions (Gastrointestinal), Adverse.
- Inflammatory Bowel Disease.
- Small Intestinal Dysbiosis.

ABBREVIATIONS

- EPI = exocrine pancreatic insufficiency.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- GI = gastrointestinal.
- IBD = inflammatory bowel disease.
- PLE = protein-losing enteropathy.

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Mark E. Hitt.



Client Education Handout
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DIARRHEA, CHRONIC—DOGS

D



BASICS

DEFINITION

- A change in the frequency, consistency, and volume of feces for more than 3 weeks.
- Can be small bowel, large bowel, or mixed.

PATHOPHYSIOLOGY

- Secretory diarrhea.
- Osmotic diarrhea.
- Increased permeability.
- Abnormal gastrointestinal (GI) motility.
- Many cases involve combinations of these pathophysiological mechanisms.

SYSTEMS AFFECTED

- Endocrine/metabolic.
- Exocrine.
- Cardiovascular (fluid balance).
- GI.
- Lymphatic.

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Pythiosis occurs often in young, large-breed dogs living in rural areas, with a higher incidence in states bordering the Gulf of Mexico.

SIGNALMENT

Species

Dog

Breed Predilections

- Yorkshire terrier, West Highland white terrier, Rottweiler, soft-coated wheaten terrier—lymphangiectasia secondary to inflammatory bowel disease (IBD).
- Boxer and French bulldog—granulomatous colitis.

Mean Age and Range

Any age.

Predominant Sex

None

SIGNS

General Comments

- Disease processes determine extent of clinical signs.
- 2–3% increase of water content of stool results in gross description of diarrhea.
- Classification of small, large, and mixed bowel types of diarrhea may have overlap of descriptive findings.

Historical Findings

- Small bowel diarrhea can include—normal to increased volume; normal to moderately increased (2–4 times/day) defecation frequency; weight loss; polyphagia; melena; flatulence and borborygmus; vomiting—variable.
- Large bowel diarrhea can include—smaller volume; frequency of defecation increased (>4 times/day); often hematochezia and mucus; tenesmus; urgency, dyschezia; flatulence and borborygmus—variable; vomiting—variable.

Physical Examination Findings

Small Bowel

- Poor body condition associated with malabsorption, maldigestion, and protein-losing

enteropathy (PLE). • Variable dehydration.

- Abdominal palpation may reveal thickened small bowel loops (diffuse or segmental) associated with infiltrative disease, abdominal effusion, foreign body, neoplastic mass, intussusception, or enlarged mesenteric lymph nodes.
- Rectal palpation typically unremarkable.

Large Bowel

- Body condition more typically normal.
- Dehydration—uncommon.
- Abdominal palpation may reveal thickened large bowel, foreign body, neoplastic mass, intussusception, or enlarged mesocolic lymph nodes.
- Rectal palpation may reveal irregularity of colorectal mucosa, intraluminal or extraluminal rectal masses, rectal stricture, or sublumbar lymphadenopathy.

CAUSES

Small Bowel

Primary Small Intestinal Disease

- Inflammatory bowel disease (e.g., lymphoplasmacytic enteritis, eosinophilic enteritis, granulomatous enteritis, immunoproliferative enteropathy of Basenjis).
- Primary or secondary lymphangiectasia.
- Neoplasia.
- Bacterial (*Campylobacter jejuni*, *Salmonella* spp., invasive adherent or enterotoxic *Escherichia coli*, other enterobacteriaceae species).
- Mycotic (e.g., histoplasmosis).
- Algal (e.g., protothecosis, pythiosis).
- Parasites (e.g., *Giardia*, *Toxocara* spp., *Ancylostoma*, *Toxascaris leonina*, *Cryptosporidium* spp., *Cystoisospora* spp.).
- Partial obstruction (e.g., foreign body, intussusception, neoplasia).
- Antibiotic-responsive diarrhea (ARD; intestinal microbial dysbiosis).
- Short bowel syndrome.

Maldigestion

- Exocrine pancreatic insufficiency (EPI).
- Hepatobiliary disease—lack of intraluminal bile.

Dietary

- Food-responsive enteropathy.
- Food allergy.

Metabolic Disorders

- Hepatobiliary disease.
- Hypoadrenocorticism.
- Uremic gastroenteritis.
- Toxins—enterotoxins, aflatoxins, exotoxins, food poisoning.
- Adverse drug reactions.

Large Bowel

Primary Large Intestinal Disease

- Inflammatory bowel disease (e.g., lymphoplasmacytic colitis, eosinophilic colitis, granulomatous colitis).
- Neoplasia.
- Infection (e.g., histoplasmosis, adherent invasive *E. coli* [granulomatous colitis], *Prototheca*, pythiosis).
- Parasites (e.g., *Trichuris vulpis*, *Giardia intestinalis*, *Entamoeba histolytica*, *Balantidium coli*).
- Ileocolic intussusception and cecal inversion.

Dietary

- Diet—dietary indiscretion, diet changes, food-responsive enteropathy, foreign material (e.g., bones, plastic, wood, hair).
- Fiber-responsive large bowel diarrhea.

Miscellaneous

Irritable bowel syndrome.

RISK FACTORS

Small Bowel

- Large-breed, younger, and less severely affected dogs have higher risk of food-responsive diarrhea.
- Yorkshire terrier, West Highland white terrier, Rottweiler, soft-coated wheaten terrier predisposed to lymphangiectasia secondary to IBD.

Large Bowel

- Dietary changes or indiscretion, stress, and psychological factors may play a role.
- Granulomatous colitis (invasive adherent *E. coli*-associated)—boxer, French bulldog <3 years old.
- Pythiosis more common in large-breed dogs that spend more time outside (roaming, hunting).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

First localize the origin to the small or large bowel (or both).

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia may be associated with parasitism, eosinophilic enterocolitis, hypoadrenocorticism, paraneoplastic causes, or pythiosis.
- Lymphopenia and hypocholesterolemia may be associated with lymphangiectasia.
- Anemia and microcytosis suggest chronic GI bleeding and iron deficiency.
- Panhypoproteinemia resulting from PLE associated with infiltrative small bowel disorders and lymphangiectasia.
- Biochemical profiles and urinalysis abnormalities may suggest renal disease, hepatobiliary disease, or endocrinopathy.

OTHER LABORATORY TESTS

Fecal and/or Rectal Scraping Exam

- Direct wet-prep examination, fecal ELISA testing, and zinc sulfate centrifugation (for *Giardia*) may indicate GI parasites; multiple samples may be required for whipworm infestations.
- Cytologic examination of rectal scrapings may reveal specific organisms, such as *Histoplasma* or *Prototheca*.
- PCR fecal testing can be helpful when screening for uncommon or difficult to diagnose infections; interpret with caution as many of the microorganisms can be found in healthy, nondiarrheic animals (e.g., viral enteritis, cryptosporidiosis, *Giardia*, *Salmonella*, *C. perfringens* enterotoxin gene, *C. difficile*, *Campylobacter jejuni*); PCR testing should be interpreted in light of patient signalment, history, clinical presentation, vaccination history, and other laboratory data.
- Culture feces if *Campylobacter* or *Salmonella* suspected—special media required; check with laboratory prior to submission.

Tests of Exocrine Pancreatic Function

Canine-specific trypsin-like immunoreactivity (TLI)—test of choice for confirming EPI.

Tests for Malabsorption

- Serum folate—low serum folate may be associated with proximal small intestinal malabsorption.
- Cobalamin—low serum

DIARRHEA, CHRONIC—DOGS

(CONTINUED)

D

cobalamin may be associated with EPI or ileal malabsorption; primary cobalamin deficiency syndromes are rare (border collie, giant schnauzer).

Tests for Metabolic Disease

- Resting cortisol—value <2.0 µg/dL should be followed up with adrenocorticotrophic hormone stimulation test to evaluate for hypoadrenocorticism.
- Fasting and 2-hour postprandial serum bile acids—test if hepatobiliary disease suspected; significantly increased values suggest hepatic dysfunction or portosystemic shunting.

IMAGING

- Survey abdominal radiography may indicate abnormal intestinal pattern, organomegaly, mass, foreign body, pancreatic disease, hepatobiliary disease, urinary disease, or abdominal effusion.
- Contrast radiography (upper GI series or barium enema) may indicate bowel wall thickening, intestinal ulcers, mucosal irregularities, mass, radiolucent foreign body, or stricture; utility of contrast radiography has been replaced with ultrasound in most patients.
- Abdominal ultrasonography may demonstrate bowel wall thickening, abnormal bowel wall layering, GI or extra-GI masses, intussusception, foreign body, ileus, abdominal effusion, hepatobiliary disease, or mesenteric or mesocolic lymphadenopathy.

DIAGNOSTIC PROCEDURES

If maldigestive (EPI), metabolic, parasitic, dietary, and infectious causes have been excluded, then consider dietary trial using elimination diet (novel, single protein source) or hydrolyzed diet for 2 weeks in stable dogs prior to performing advanced diagnostics (endoscopy or laparotomy and biopsy). Up to 75% of dogs in referral practices have been shown to be diet responsive.

Endoscopy/Laparoscopy

- Upper GI flexible endoscopy allows examination and biopsy of gastric and duodenal mucosa; always obtain multiple (8–10) mucosal specimens from each segment.
- Flexible colonoscopy allows examination of rectum, colon, cecum, and ileum; always obtain multiple mucosal specimens (8–10) from each segment.
- Gross appearance of mucosa does not always correlate with histopathology; always take biopsies.
- Endoscopic biopsies rely upon diseases being represented in first two layers of intestinal wall and segments biopsied being representative of others not reached.
- Full-thickness biopsies not indicated as most diseases can be diagnosed endoscopically.
- Surgical approach can be advantageous if biopsies of multiple organs (e.g., small intestine, lymph nodes, stomach, pancreas, liver) are desired.

Ultrasound-Guided GI Aspirates

- Ultrasound-guided fine-needle aspiration of GI mass lesions can be helpful for diagnosing mast cell tumors, carcinomas, and large-cell lymphoma.
- Seeding of neoplastic cells is a concern.

Capsule Endoscopy

Capsule endoscopy procedures can help identify location of bleeding ulcers in the jejunum.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical management most common.
- Treat underlying cause.

NURSING CARE

- Fluid therapy with balanced electrolyte solutions as needed.
- Correct electrolyte and acid-base imbalances.

ACTIVITY

No restrictions.

DIET

- Therapy with elimination diets or hydrolyzed diets can be beneficial in up to 75% of dogs with uncomplicated chronic enteropathies.
- Feeding lower-fat, novel (for the patient) protein source, highly digestible, or fiber-supplemented diets for 3–4 weeks may resolve diarrhea due to dietary intolerance or allergy; repeated changes of diet to maintain symptom-free situation suggests further testing needed.

CLIENT EDUCATION

Complete resolution of signs is not always possible in dogs with severe IBD, lymphangiectasia, intestinal neoplasia, and pythiosis.

SURGICAL CONSIDERATIONS

Pursue laparotomy and biopsy if evidence of obstruction, intestinal mass, or mid-small bowel disease unreachable via ultrasound-guided procedure, or if diagnosis based on endoscopic biopsy or ultrasound-guided procedure is questioned because of poor response to therapy.



MEDICATIONS

DRUG(S) OF CHOICE

- Disease-specific.
- Prednisone (2 mg/kg BID for 2 weeks, with slow tapering over 6 weeks) for IBD.
- Cyclosporine has shown to rescue dogs with steroid-refractory IBD.
- Need for cyanocobalamin supplementation must be assessed in all dogs with chronic enteropathy.
- Probiotics beneficial in some dogs with chronic enteropathy.

CONTRAINDICATIONS

Anticholinergics can exacerbate the situation with many causes of chronic diarrhea; they are sometimes used to relieve cramping associated with irritable bowel syndrome.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

N/A



FOLLOW-UP

PATIENT MONITORING

- Frequency and consistency of stool, appetite, and bodyweight.
- In dogs with

PLE—serum proteins, cholesterol, and clinical signs (ascites, subcutaneous edema, pleural effusion).

- Resolution of diarrhea usually gradual with treatment; if does not resolve, reevaluate diagnosis.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Dehydration.
- Lowered body condition.
- Abdominal effusions as related to specific cause of chronic diarrhea.
- Ascites, subcutaneous edema, and/or pleural effusion with hypoalbuminemia from PLE.

EXPECTED COURSE AND PROGNOSIS

Vary with underlying disease.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

- Giardiasis (low risk of transmission).
- Salmonellosis.
- Campylobacter jejuni*.
- Ascaridiasis.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

N/A

SEE ALSO

- Colitis, Histiocytic Ulcerative.
- Diarrhea, Antibiotic Responsive.
- Fiber-Responsive Large Bowel Diarrhea.
- Food Reactions (Gastrointestinal), Adverse.
- Inflammatory Bowel Disease.
- Lymphangiectasia.
- Protein-Losing Enteropathy.
- Small Intestinal Dysbiosis.

ABBREVIATIONS

- ARD = antibiotic-responsive diarrhea.
- EPI = exocrine pancreatic insufficiency.
- GI = gastrointestinal.
- IBD = inflammatory bowel disease.
- PLE = protein-losing enteropathy.
- TLI = trypsin-like immunoreactivity.

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Acknowledgment The author and book editors acknowledge the prior contribution of Mark E. Hitt.



Client Education Handout
available online

DISSEMINATED INTRAVASCULAR COAGULATION



BASICS

DEFINITION

An acquired complex hemostatic defect arising from a variety of inciting causes that leads to intravascular activation of coagulation and consumption of clotting factors. It results in widespread formation of microthrombi with clinical manifestations of thrombosis and/or hemorrhage. Non-overt disseminated intravascular coagulation (DIC) is the early, compensated form of DIC that features consumption of coagulation factors and generation of microthrombi without clear clinical signs. Overt (decompensated) DIC refers to the classic phenotype associated with hemorrhage, thrombosis, and organ failure.

PATHOPHYSIOLOGY

- DIC represents a complication of a variety of primary conditions. It begins with a hypercoagulable state that leads to production or embolization of microthrombi in small vessels.
- The primary conditions act through increased exposure/production of tissue factor (TF) that activates the extrinsic coagulation pathway.
- TF is normally restricted from intravascular exposure. Increased TF exposure occurs through widespread endothelial injury and/or inflammation.
- Inflammation activates endothelial cells, platelets, and monocytes leading to membrane expression of TF. Inflammatory cytokines also induce vesiculation of these membranes, releasing large quantities of microparticles into circulation that are enriched with both TF and phosphatidylserine (PS) and facilitate initiation of coagulation. Some neoplastic cells constitutively produce membrane TF and also release microparticles.
- Microparticles provide a suitable membrane surface for amplifying intrinsic and common pathway coagulation, potentially leading to uncontrolled production of thrombin that overwhelms endogenous coagulation inhibitors. Fibrin clots generated by thrombin can cause vascular occlusion and lead to organ dysfunction.
- Widespread microthrombus formation consumes coagulation factors and platelets while initiating fibrinolysis. By-products of fibrinolysis (fibrin degradation products [FDPs]) have anticoagulant properties and inhibit platelet function. Hemorrhage at a variety of sites can follow.
- Uncontrolled progression leads to widespread tissue hypoxia, multiorgan dysfunction, and death.

SYSTEMS AFFECTED

Multisystemic syndrome.

INCIDENCE/PREVALENCE

Associated with severe systemic inflammatory disease.

SIGNALMENT

Species

Dogs and cats; diagnosed more in dogs.

Breed Predilections

None

Mean Age and Range

Depends on the primary disease.

Predominant Sex

None

SIGNS

- Vary with the primary disease and with DIC-associated organ dysfunction.
- Petechiae.
- Bleeding from venipuncture sites, mucosa, or into body cavities.
- Bleeding is infrequent in cats, possibly leading to underdiagnosis.

CAUSES

- Gastric dilatation-volvulus.
- Heart failure.
- Heartworm disease.
- Heat stroke.
- Hemolysis, especially immune mediated.
- Hemorrhagic gastroenteritis.
- Infectious diseases, systemic (especially endotoxemia).
- Inflammation, severe—regardless of underlying cause.
- Liver disease, severe.
- Malignancies, especially hemangiosarcoma, mammary carcinoma, and pulmonary adenocarcinoma in dogs and lymphoma in cats.
- Pancreatitis.
- Protein-losing nephropathy.
- Shock, hypoxia, acidosis.
- Thrombocytopenia, especially immune-mediated.
- Transfusion incompatibility.
- Trauma.
- Envenomation.

RISK FACTORS

Vary with cause.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Key differentials—immune-mediated thrombocytopenia, anticoagulant toxicity, coagulation factor deficiency, paraproteinemia.
- Highly variable diagnostic pattern includes thrombocytopenia, prolonged clotting times (prothrombin time [PT], activated partial thromboplastin time [APTT]), decreased fibrinogen, decreased antithrombin (AT), and increased products of fibrinolysis (FDPs, D-dimers).

- Suspect DIC any time thrombocytopenia and prolonged clotting tests are seen together.

- Patients showing predisposing conditions should have laboratory monitoring every 24–48 hours. A sudden drop in platelet count and a 20–30% prolongation in APTT is suspicious for non-overt DIC. This is a critical stage for intervention to prevent progression to overt DIC.
- Hepatic insufficiency may mimic DIC. Decreased production of clotting factors is common. Decreased clearance of normal fibrin(ogen)olytic by-products may increase FDP values. Mild idiopathic thrombocytopenia may also be seen. Spontaneous bleeding is uncommon unless DIC is present.

CBC/BIOCHEMISTRY/URINALYSIS

- Inflammatory leukogram, often with a stress component.
- Mild to moderate thrombocytopenia ($40-100 \times 10^3/\mu\text{L}$); less reliable in cats.
- Anemia is possible. Red blood cell (RBC) fragmentation is a supportive finding.
- Biochemical changes reflect affected organs; acute kidney injury may result in isosthenuria, oligo-anuria, or the identification of casts in urine sediment.

OTHER LABORATORY TESTS

- Prolonged clotting tests (PT, APTT); APTT is prolonged first, PT becomes prolonged with transition to overt DIC.
- Hypofibrinogenemia, although inflammatory increase may mask consumption.
- Increased FDPs and D-dimers. D-dimers are very sensitive and specific. DIC is unlikely if D-dimers are low/negative. Neither test is specific enough alone to diagnose DIC.
- Decreased AT; may be a positive acute phase reactant in cats, masking consumption.
- Thromboelastography may provide evidence of hypocoagulability or fibrinolysis.

DIAGNOSTIC PROCEDURES

Diagnostic procedures should be focused on identifying the inciting cause of inflammation, and may include imaging, tissue biopsy, or surgery as dictated by clinical signs.

PATHOLOGIC FINDINGS

- Usually related to the primary disease or DIC-affected organs.
- Petechiae common.



TREATMENT

APPROPRIATE HEALTH CARE

- Requires intensive inpatient treatment.
- Aggressive treatment of the primary disease is essential (e.g., antimicrobials for sepsis).

DISSEMINATED INTRAVASCULAR COAGULATION

(CONTINUED)

NURSING CARE

- Maintain tissue perfusion and oxygenation using fluids, transfusions, and oxygen therapy.
- Restore depleted factors by blood/plasma transfusions. Use fresh frozen plasma (10–20 mL/kg) to correct bleeding due to factor deficiency.

ACTIVITY

Limited by disease severity.

DIET

Maintain nutritional support as appropriate for the clinical condition of the patient.

CLIENT EDUCATION

Inform the owner that the condition is life-threatening with a guarded to poor prognosis.

SURGICAL CONSIDERATIONS

Related to primary disease. Plasma or whole blood transfusion to restore clotting factors is a presurgical consideration. Surgery may be contraindicated with uncontrolled bleeding.



MEDICATIONS

DRUG(S) OF CHOICE

- There is no specific pharmacologic therapy for DIC per se.
- Heparin may be used in patients that have overt thrombosis or in those at high risk of thrombosis with normal coagulation times. Unfractionated heparin is preferred to low molecular weight heparin in human patients with DIC.
- Heparin binds to and potentiates the action of AT. Plasma or blood transfusions may be needed to replenish AT for heparin to be an effective anticoagulant.
- Starting doses for unfractionated heparin are 150–200 U/kg SC q8h. It may also be given as a CRI starting at 20–30 U/kg/h IV (i.e., same total daily dosage). Therapy should be monitored using serial measurements of APTT or anti-Xa activity.

CONTRAINDICATIONS

- Heparin therapy should be avoided in patients with coagulopathy.

- Inhibitors of fibrinolysis should not be used.
- The use of antiplatelet medications in thrombocytopenic patients is not indicated.
- Corticosteroids impair function of mononuclear phagocytes and do not have a clear indication for DIC unless important for therapy of the underlying disease (e.g., lymphoma).

PRECAUTIONS

- Heparin may cause hemorrhage, and therapy should be monitored.
- Volume overload may occur in cases with renal or pulmonary compromise.

POSSIBLE INTERACTIONS

None



FOLLOW-UP

PATIENT MONITORING

- Clinical improvement and the arrest of bleeding are key positive findings.
- Daily lab testing (e.g., coagulation tests, fibrinogen, platelet counts) is warranted in severe cases to identify positive or negative trends. Less frequent testing may suffice in milder cases.
- Coagulation times and fibrinogen often normalize more rapidly than FDPs and platelet counts.

PREVENTION/AVOIDANCE

Early detection of non-overt DIC can allow therapy before disease progresses to overt DIC.

POSSIBLE COMPLICATIONS

Aside from the primary disease, affected organs may have permanent dysfunction or marginal reserve capacity.

EXPECTED COURSE AND PROGNOSIS

For overt DIC, mortality rates for dogs range from 50% to 77%. For cats, rates may be >90%.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Unlike in humans, obstetric complications are not a common cause in dogs and cats.

SYNOMYS

- Consumptive coagulopathy.
- Disseminated intravascular coagulopathy.

SEE ALSO

- Coagulation Factor Deficiency.
- Thrombocytopenia.

ABBREVIATIONS

- APTT = activated partial thromboplastin time.
- AT = antithrombin.
- DIC = disseminated intravascular coagulation.
- FDP = fibrin degradation product.
- PS = phosphatidylserine.
- PT = prothrombin time.
- RBC = red blood cell.
- TF = tissue factor.

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Client Education Handout
available online

DYSPNEA AND RESPIRATORY DISTRESS



BASICS

DEFINITION

Dyspnea—a subjective term that in human medicine means “an uncomfortable sensation in breathing” or a sensation of air hunger; in veterinary medicine, it is used to indicate difficulty breathing or respiratory distress.

PATHOPHYSIOLOGY

Dyspnea and respiratory distress are believed to occur when the CNS notes a difference between the afferent feedback from a given efferent motor drive signal (ventilation demanded) and what the brain had anticipated would be the appropriate afferent response (ventilation achieved).

SYSTEMS AFFECTED

Respiratory

SIGNALMENT

Dogs and cats; age, breed, and sex predisposition vary with inciting cause.

SIGNS

Historical Findings

- Acute or chronic onset.
- Often associated with tachypnea, coughing, exercise intolerance, lethargy, inappetence.

Physical Examination Findings

- General signs of respiratory distress—tachypnea, increased abdominal effort, nasal flaring, open-mouth breathing, cyanosis, orthopnea (neck extension, elbow abduction), altered mentation; other signs depend on underlying cause.
- Nasal disease—stertor, nasal discharge, lack of airflow through nostrils; dyspnea improves with open-mouth breathing.
- Upper airway/laryngeal disease—stridor, panting, cough, hyperthermia, dysphonia, respiratory effort and noise on inspiration, fixed obstruction such as a mass or foreign body in a large airway: dyspnea on inspiration and expiration.
- Tracheal collapse—honking cough, tracheal sensitivity, respiratory effort and noise: inspiratory effort if cervical tracheal collapse, expiratory effort if intrathoracic tracheal collapse.
- Lower airway disease—cough, expiratory wheezes on auscultation, abdominal effort.
- Pulmonary parenchymal disease—may have crackles, harsh or moist lung sounds on auscultation.
- Pneumonia—fever, may have tracheal sensitivity.
- Cardiogenic pulmonary edema—heart murmur, arrhythmia, hypothermia, pale mucous membranes, prolonged capillary refill time.
- Pleural space disease—diminished breath sounds: ventrally—fluid; dorsally—air; unilaterally—space-occupying lesions or

pyothorax/chylothorax. Paradoxical respiratory pattern (inward movement of the abdominal wall during inspiration).

- Thoracic wall disease—can have paradoxical respiratory pattern, visible or palpable trauma (open pneumothorax, flail chest).
- Pulmonary thromboembolism (PTE)—may have clinical signs of underlying disease predisposing to thrombosis, e.g., hyperadrenocorticism, immune-mediated hemolytic anemia (IMHA), systemic inflammatory response syndrome (SIRS)/sepsis, protein-losing nephropathy (PLN), protein-losing enteropathy (PLE), neoplasia.
- Other signs will pertain to the underlying disease, e.g., shock, trauma.

CAUSES & RISK FACTORS

Upper Airway Disease

- Nasal obstruction—stenotic nares, nasopharyngeal polyp or stenosis, infection, inflammation, neoplasia, trauma, foreign body, coagulopathy.
- Pharynx—elongated soft palate, foreign body, neoplasia, granuloma, stenosis.
- Larynx—laryngeal paralysis, everted laryngeal saccules, edema, collapse, foreign body, neoplasia, inflammation, trauma, webbing.
- Trachea—collapse, stenosis, trauma, foreign body, neoplasia, parasites, extraluminal compression (lymphadenopathy, enlarged left atrium, heart-base tumors).

Lower Airway Disease

Allergic disease, inflammatory, infectious (*Mycoplasma*), parasitic, neoplastic (bronchogenic carcinoma).

Pulmonary Parenchymal Disease

- Edema—cardiogenic or noncardiogenic.
- Pneumonia—infectious; parasitic; aspiration; eosinophilic; interstitial.
- Neoplasia (primary or metastatic).
- Inflammatory—acute respiratory distress syndrome (ARDS); uremic pneumonitis; smoke inhalation.
- Hemorrhage—trauma; coagulopathy.
- PTE—IMHA; PLN, PLE; heartworm disease; hyperadrenocorticism; neoplasia.
- Others—lung lobe torsion, atelectasis.

Pleural Space Disease

- Pneumothorax—traumatic; iatrogenic; secondary to pulmonary parenchymal disease; ruptured bulla; migrating foreign body; primary spontaneous (no underlying cause).
- Pleural effusion—transudates, exudates; hemothorax; chylothorax.
- Soft tissue—neoplasia; diaphragmatic hernia.
- Fibrosing pleuritis.

Thoracic Wall Disease

- Open pneumothorax—trauma.
- Flail segment—trauma.
- Neoplasia.
- Paralysis due to cervical spinal disease, botulism, polyradiculoneuritis, tick bite

paralysis, myasthenia gravis, elapid snake envenomation, hypokalemia.

Diaphragmatic Disease

- Trauma—rupture; hernia.
- Phrenic nerve disease.
- Neoplasia.
- Fibrosis.

Abdominal Distention

Organomegaly—hyperplasia; neoplasia, pregnancy; obesity; ascites; gastric dilatation, torsion.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Inspiratory dyspnea—suggests extrathoracic upper airway disease.
- Expiratory dyspnea—suggests intrathoracic airway disease.
- Dyspnea on inspiration and expiration can occur with fixed upper airway obstructions and severe intrathoracic disease.
- Congestive heart failure—murmur, arrhythmia, tachycardia, poor pulse quality, jugular pulses, hypothermia, crackles on auscultation, fluid dripping from nose.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—can cause nonrespiratory dyspnea.
- Polycythemia—chronic hypoxia.
- Inflammatory leukogram—pneumonia, pneumonitis, pyothorax.
- Eosinophilia—hypersensitivity or parasitic airway disease.
- Thrombocytosis—hyperadrenocorticism predisposes to PTE.
- Sodium : potassium ratio <27—can be seen with pleural or abdominal effusions.
- Azotemia—if severe may lead to uremic pneumonitis.
- Proteinuria—can predispose to PTE.
- Multiple organ dysfunction—ARDS.
- Hypoproteinemia—may suggest protein-losing disease that can predispose to PTE or pleural effusion.

OTHER LABORATORY TESTS

- Pleural fluid analysis.
- Fecal examination for parasites if indicated
- Serum antigen or antibody titers—heartworm, toxoplasmosis, distemper, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV).
- Increased urine protein : creatinine ratio with PLN could indicate loss of antithrombin and hypercoagulability resulting in PTE.
- PaO_2 —partial pressure of oxygen dissolved in arterial blood; normoxemia: PaO_2 80–120 mmHg (room air, sea level); hypoxemia: PaO_2 <80 mmHg; FIO_2 —fraction of inspired oxygen ranges from 0.21 (room air) to 1.0; $\text{PaO}_2/\text{FIO}_2$ ratio—measure

DYSPNEA AND RESPIRATORY DISTRESS

(CONTINUED)

D

of lung efficiency during oxygen therapy; $\text{PaO}_2/\text{FIO}_2 \geq 400$ —normal lung efficiency; 300–400—mild insufficiency; 200–300—moderate insufficiency; <200—severe insufficiency. Reduction in lung efficiency can be due to venous admixture, hypoventilation, low inspired oxygen.

- PaCO_2 or PvCO_2 —partial pressure of CO_2 dissolved in arterial or venous blood; measure of ventilation; normal 30 mmHg $<\text{PCO}_2 < 40$ mmHg. $\text{PCO}_2 > 45$ mmHg = hypercapnia = hypoventilation = decreased alveolar minute ventilation (MV).
- Coagulation testing—if suspect hemothorax and/or pulmonary hemorrhage.
- Plasma NT-proBNP and cardiac troponin-I (cTNI) concentrations may aid in differentiation of cardiac and noncardiac causes of dyspnea.

IMAGING

• Cervical and thoracic radiography—upper airway disease: soft palate elongation, large airway narrowing, lymphadenopathy, intraluminal abnormalities. Lower airway disease: bronchial thickening, middle lung lobe consolidation (cats), atelectasis, hyperinflation, and diaphragmatic flattening (primarily cats). Pneumonia: alveolar infiltrates; aspiration pneumonia usually cranioventral distribution or middle lobe affected. Cardiogenic pulmonary edema: enlarged cardiac silhouette, pulmonary venous distention, enlarged left atrium with perihilar pulmonary infiltrates in dogs; infiltrates can be of any distribution in cats. Noncardiogenic pulmonary edema: usually caudodorsal distribution. ARDS: diffuse, symmetric alveolar infiltrates. Pulmonary vascular abnormalities: PTE, heartworm disease. Pleural space disease: pneumothorax, pleural effusion, mass lesions, diaphragmatic hernias. Thoracic wall disease: rib fractures, neoplasia.

- Thoracic ultrasonography—evaluation of distribution of pleural effusion, pneumothorax (absence of “glide sign”), and parenchymal disease (presence of “comet tail” artifact). Pulmonary mass identification: guide fine-needle aspiration; mediastinal evaluation.
- Echocardiography—evaluate cardiac function and chamber size if cardiogenic pulmonary edema or pleural effusion suspected; elevated pulmonary artery pressure, right ventricular overload with ventricular septal flattening can support diagnosis of PTE; visualize heart-based masses.
- Abdominal radiography or ultrasound—evaluation of abdominal distension.
- Fluoroscopy—evaluate tracheal and bronchial collapse; evaluate diaphragmatic function.
- CT—airway, pulmonary parenchymal, and pleural space disease can be evaluated; can detect lesions not clearly defined on radiographs.

- Pulmonary vascular angiography—gold standard for diagnosis of PTE.
- Ventilation perfusion scintigraphy—abnormal perfusion scan is considered supportive of PTE.

DIAGNOSTIC PROCEDURES

- Pulse oximetry— SpO_2 ; peripheral capillary hemoglobin oxygen saturation. The relationship between PaO_2 and SpO_2 is defined by the oxygen hemoglobin dissociation curve: PaO_2 of 60 mmHg = SpO_2 of 90%; PaO_2 of 80 mmHg = SpO_2 of 95%; PaO_2 of >100 mmHg = SpO_2 of 100%. Below 95%, small changes in SpO_2 signify large changes in PaO_2 . SpO_2 measurements in animals on high inspired oxygen lack sensitivity.
- Thoracentesis—fluid analysis and culture.
- Laryngoscopy/nasopharyngoscopy/tracheoscopy—evaluate upper airway; laryngeal paralysis, tracheal collapse, foreign bodies, masses.
- Bronchoscopy—evaluate upper and lower airways; perform bronchoalveolar lavage for cytology and culture. Requires anesthesia, perform only when stabilized.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient care until the cause is identified and treated or determined not to be life-threatening; therapy dependent on underlying cause.
- Always administer oxygen and keep patient in sternal recumbency until ability to oxygenate is determined.
- May require intubation and positive-pressure ventilation in patients with severe respiratory distress refractory to oxygen therapy.
- Upper airway disease—use sedation to reduce respiratory effort. Check body temperature and actively cool patients as needed.
- Lower airway disease—bronchodilators; systemic corticosteroids may be required to stabilize cats with acute bronchoconstriction.
- Pulmonary parenchymal disease—antibiotics if pneumonia; treat coagulation disorders; cardiogenic edema requires furosemide ± vasodilators. Noncardiogenic edema requires oxygen therapy, may require positive-pressure ventilation.
- Pleural space disease—thoracocentesis for air and fluid. Place a chest tube if repeated thoracocentesis is necessary to keep patient stable.
- Thoracic wall disease—surgery as indicated, particularly if open chest wound is present; flail chest may require surgery if medical management fails or there is a severe displacement of fractures. Thoracic wall paralysis/muscle fatigue: positive-pressure ventilation if severely hypercapnic.

- Abdominal distension—drain ascites as needed; relieve gastric distension.

NURSING CARE

- Oxygen therapy via cage, nasal cannula, Elizabethan collar covered in plastic wrap, mask, or flow-by. Humidify oxygen source if giving oxygen therapy for more than a few hours.
- Maintain in sternal recumbency and turn hips every 3–4 hours if patient cannot tolerate lateral recumbency.
- Monitor temperature regularly, as excess work of breathing results in hyperthermia, which augments respiratory distress.

DIET

Weight-reducing diet if obesity is a contributing cause.

SURGICAL CONSIDERATIONS

- Anesthesia must be carefully tailored to the patient. Securing an airway is essential and rapid intravenous induction is important. The ability to positive-pressure ventilate patients is often required.
- Animals with upper airway obstruction are fragile and can rapidly decompensate. Have multiple-sized endotracheal tubes available.
- Dyspnea associated with a laryngeal mass can respond to debulking surgery, but edema and hemorrhage can lead to worsened obstruction. Warn owners of increased likelihood of aspiration pneumonia complications in animals with laryngeal disease.
- Avoid positive-pressure ventilation in patients with a closed pneumothorax. Must monitor oxygenation status of anesthetized patients with pulse oximetry and when possible arterial blood gases.



MEDICATIONS

DRUG(S) OF CHOICE

Varies with underlying cause (see Appropriate Health Care).



FOLLOW-UP

PATIENT MONITORING

- Patients receiving oxygen therapy can be monitored by assessing the degree of respiratory effort. As the animal stabilizes, perform a room air trial and reevaluate the level of respiratory difficulty. Arterial and venous blood gases can be a useful assessment.
- Pulse oximetry is an effective and noninvasive tool for monitoring patients on room air.
- Repeat radiographs are often indicated in assessing pulmonary parenchymal disease and pleural space disease.

(CONTINUED)

DYSPNEA AND RESPIRATORY DISTRESS

D

**MISCELLANEOUS****SEE ALSO**

- Acute Respiratory Distress Syndrome.
- Asthma, Bronchitis—Cats.
- Brachycephalic Airway Syndrome.
- Congestive Heart Failure, Left-Sided.
- Congestive Heart Failure, Right-Sided.
- Laryngeal Diseases.
- Panting and Tachypnea.
- Pneumonia, Aspiration.
- Pneumothorax.
- Pulmonary Edema, Noncardiogenic.

ABBREVIATIONS

- ARDS = acute respiratory distress syndrome.
- cTNI = cardiac troponin-I.
- FeLV = feline leukemia virus.

- FIO₂ = fraction of inspired oxygen.
- FIV = feline immunodeficiency virus.
- IMHA = immune-mediated hemolytic anemia.
- MV = minute ventilation.
- PaCO₂ = partial pressure of carbon dioxide.
- PaO₂ = partial pressure of oxygen.
- PLE = protein-losing enteropathy.
- PLN = protein-losing nephropathy.
- PTE = pulmonary thromboembolism.
- SIRS = systemic inflammatory response syndrome.
- SpO₂ = oxygen saturation.

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Acknowledgement The author and book editors acknowledge the prior contribution of Kate Hopper.



**Client Education Handout
available online**

DYSTOCIA



BASICS

D

DEFINITION

Difficult birth.

PATHOPHYSIOLOGY

- Dystocia may occur due to maternal or fetal factors and may occur during any stage of labor.
- May be caused by abnormal fetal presentation, posture, or position.
- Normal stages of labor:

Stage 1

- Onset of uterine contractions and relaxation of cervix; ends with rupture of first chorioallantoic sac—averages 6–12h (up to 36h in primiparous bitch).
- Bitch—may be restless, nervous, shiver, pant, pace, and nest.
- Queen—tend to vocalize initially; purr and socialize as Stage 1 progresses.

Stage 2

- Delivery of fetuses.
- Bitch—obvious abdominal contractions; beginning of stage 2 to delivery of first offspring usually <4h; average time to delivery of subsequent fetus 20–60 min (may be as long as 2–3h).
- Queen—average length of parturition 16h, with range of 4–42h (up to 3 days in some cases); important to consider this variability when intervening.
- Number of fetuses present may significantly affect length of stages 2 and 3.

Stage 3

- Delivery of fetal membranes.
- May alternate between stage 2 and 3 with multiple fetuses.

INCIDENCE/PREVALENCE

- Dog—incidence unknown due to breed variability and breeder intervention.
- Cat—3.3–5.8% of parturitions; mixed-breed cats 0.4%, higher in pedigree cats, to 18.2% in Devon Rex.

SIGNALMENT

Breed Predilections

Dogs

- Higher incidence with miniature and small breeds (small litter size, concurrent large fetal size); may occur in large breeds with large or singleton litters.
- Brachycephalic breeds—broad head and narrow pelvis.
- Large fetal head : maternal pelvis ratio—Sealyham terrier, Scottish terrier.
- Uterine inertia—Scottish terrier, dachshund, border terrier, Aberdeen terrier, Labrador retriever.
- Other breeds with increased incidence of dystocia—chihuahua, dachshund, Pekingese, Yorkshire terrier, miniature poodle, Pomeranian.

Cats

Brachycephalic (Persian, Himalayan) or dolichocephalic (Devon Rex) breeds.

SIGNS

Historical Findings

- More than 30 min of persistent, strong, abdominal contractions without fetal delivery.
- More than 4h from onset of stage 2 to delivery of first fetus (bitch).
- More than 2h between delivery of fetuses (bitch).
- Failure to commence stage 1 labor within 24h of rectal temperature drop below 37.2 °C (99 °F) or within 36h of serum progesterone concentration <2 ng/mL (bitch).
- Female cries, displays signs of pain, and constantly licks vulvar area when contracting.
- Prolonged gestation—more than 72 days from day of first mating (bitch); more than 59 days from first day of cytologic diestrus (bitch); more than 66 days from luteinizing hormone (LH) peak (bitch); more than 68 days from last day of mating (queen).

Physical Examination Findings

- Presence of greenish-black discharge (uteroverdin) preceding birth of first fetus by more than 2h or increasing amounts before delivery of first fetus.
- Bloody discharge prior to delivery of first fetus.
- Diminished or absent Ferguson's reflex (stimulation or pressure to dorsal vaginal wall to elicit abdominal straining; "feathering") indicates uterine inertia.

CAUSES

Fetal

- Oversize; fetal monsters, fetal anasarca, fetal hydrocephalus, prolonged gestation due to inability of singleton fetus to initiate labor.
- Abnormal presentation, position, or posture of fetus in birth canal.
- Fetal death.

Maternal

- Inadequate uterine contractions (primary or secondary uterine inertia)—myometrial defect, hypocalcemia electrolyte imbalance, psychogenic disturbance, exhaustion.
- Ineffective abdominal press—pain, fear, debility (exhaustion), diaphragmatic hernia, age.
- Placentitis, metritis, endometritis.
- Pregnancy toxemia, gestational diabetes.
- Abnormal pelvic canal—previous pelvic injury, abnormal conformation, pelvic immaturity.
- Congenitally small pelvis—Welsh corgis, brachycephalic breeds.
- Inguinal hernia.
- Abnormality of vaginal vault—stricture, septae, vaginal hyperplasia, hypoplastic vagina, intra- or extraluminal cysts, neoplasia.
- Abnormal vulvar opening—stricture, fibrosis from trauma, neoplasia.
- Insufficient cervical dilation.
- Lack of adequate lubrication.
- Uterine torsion.

- Uterine rupture.

- Uterine neoplasia, cysts, or adhesions.

RISK FACTORS

- Age.
- Brachycephalic and toy breeds.
- Persian, Himalayan, and Devon Rex breeds.
- Obesity.
- Abrupt changes in peripartum environment.
- Previous history of dystocia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Uterine inertia—hypocalcemia versus hypoglycemia.

Physical Examination

- Complete physical examination—careful abdominal palpation to confirm presence of fetuses.
- Digital vaginal examination—fetus or fetal membranes in vaginal canal, assess maternal pelvic canal, Ferguson's reflex.
- Bitch unresponsive to oxytocin or lacking Ferguson's reflex—uterine inertia more likely than obstructive dystocia unless obstructed for several hours.

CBC/BIOCHEMISTRY/URINALYSIS

Minimum database—packed cell volume (PCV), total protein, serum glucose, urea nitrogen, and calcium (ionized preferable to total concentration corrected for albumin) concentrations. Pregnant females have mild anemia.

OTHER LABORATORY TESTS

Serum progesterone concentration.

IMAGING

- Radiography—determine pelvic conformation, number and position of fetuses, evidence of fetal obstruction, oversize, or death.
- Fetal death—collapse of fetal skeletons, abnormal association of fetal bones to axial skeleton, presence of air/gas surrounding fetus, fetal balling.
- Ultrasonography—recommended for monitoring fetal viability, heart rate (fetal heart rate <180 bpm indicates fetal stress, >260 bpm indicates need for close monitoring), placental separation, and character of fetal fluids (presence of meconium or blood in amniotic fluid).



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—until delivery of all fetuses and dam is stable.
- Treat hypoglycemia and hypocalcemia.
- Uterine inertia—medical treatment if no evidence of fetal stress.

(CONTINUED)

DYSTOCIA

D

- Ecbolic agents contraindicated with possible obstructive dystocia—may accelerate placental separation and fetal death or cause uterine rupture.
- WhelpWise® tocodynamometer monitors fetal heart rates and uterine contraction patterns; useful for bitches with large litters or history of uterine inertia to determine need for intervention.

Manual Delivery

Fetus lodged in vaginal vault:

- Lubricate liberally.
- Digital manipulation—least amount of damage to fetus and dam. Apply traction in postero-ventral direction.
- Instrument delivery not recommended due to inadequate space—may mutilate fetus or lacerate dam.
- Never apply traction to distal extremities or tail of a live fetus.
- Failure to deliver fetus located in vaginal canal within 30 min—Cesarean section (C-section) indicated.

SURGICAL CONSIDERATIONS

- Indications for C-section—uterine inertia unresponsive to oxytocin or uterine inertia with more than four fetuses remaining in utero (maximizes fetal survivability), pelvic or vaginal obstruction, inability to correct fetal malposition, fetal oversize, fetal stress, in utero fetal death.
- Elective C-section—breeds prone to dystocia, bitches with a history of dystocia, bitches with singleton or large litter size, performed to maximize fetal survivability.

General Comments

- Provide fluid therapy with balanced electrolyte solution before, during, and after surgery.
- Gravid uterus can compress great vessels and place pressure on diaphragm, compromising venous return and tidal volume.
- Preoxygenation of patient before anesthesia is indicated.
- Anesthetic protocol for C-section:
 - Premedication can include glycopyrrolate (bitches, queens: 0.01 mg/kg IV/IM) if fetal heart rates are normal; or atropine (bitches, queens: 0.04 mg/kg IM) if fetal bradycardia present.
 - Alpha-2 agonist agents (xylazine, dexmedetomidine) are contraindicated.
 - Rapidly acting induction agents include propofol or alfaxalone; ketamine may cause dose-dependent neonatal respiratory and neurologic depression; severely depressed or exhausted patients may be induced with combination of opioid and benzodiazepine

with supplemental propofol or alfaxalone for intubation, if needed.

- Maintenance may include inhalant anesthetics or propofol IV CRI.
- Use of a midline lidocaine line block (1–2 mg/kg SC) can decrease inhalant anesthetic requirement.
- Epidural—0.5% bupivacaine (0.2 mg/kg) and preservative-free morphine (0.1 mg/kg) or 2% lidocaine (2–4 mg/kg).
- Postoperative analgesia may be provided with opioids, although they are excreted in the milk to varying degrees.
- Reversal agents—repeated dosing may be necessary until neonate has processed all anesthetic drugs:
 - Opioids used during anesthesia can be reversed in neonate with naloxone (0.04 mg/kg IV/IM/SC/sublingual/intranasal).
 - Benzodiazepines used during anesthesia can be reversed in neonate with flumazenil (0.01 mg/kg IV/IM/SC/sublingual/intranasal).

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

- Hypoglycemia—treat prior to hypocalcemia:
 - Bolus 0.5 g/kg IV (diluted 1 : 3).
 - Add 5% dextrose to balanced electrolyte solution and infuse IV at 60–80 mL/kg/day.
- Hypocalcemia:
 - Bitch—10% calcium gluconate 0.2 mL/kg IV over 10 min; monitor for bradycardia. Repeat q4–6h as needed.
 - May also be given SC at a dose of 0.5 mL/4.5 kg diluted 1:1 with sterile saline. If using 23% solution, dilute at least 1:3 prior to administration.
 - Queen—10% calcium gluconate 0.5–1.0 mL/cat IV over 10 min—use with caution; risk of uterine rupture increased due to strong uterine contractions following calcium.
- Oxytocin—once calcium and glucose deficits are treated; microdose at 0.5–3.0 IU IM/SC depending on size of bitch and response to treatment. May repeat q30 min as long as delivery progresses. Consider C-section if more than three doses of oxytocin per fetus are required or more than four fetuses remain.

CONTRAINDICATIONS

Oxytocin—contraindicated with obstructive dystocia, fetal stress, longstanding in utero fetal death, uterine rupture, uterine torsion.

**FOLLOW-UP****PREVENTION/AVOIDANCE**

- Schedule elective C-section for bitches with abnormal pelvic canal, anatomic abnormalities, predisposition to dystocia, previous history of uterine inertia.
- Scheduling surgery—extremely important that D1 diestrus, LH peak, or ovulation is identified during breeding to ensure acceptable fetal survivability. If ovulation timing is not available, ultrasonographic gestational aging and maturation assessment is necessary.

EXPECTED COURSE AND PROGNOSIS

- If dystocia is identified promptly and intervention is successful—good to fair for survival of dam; fair for fetuses.
- If dystocia unrecognized or untreated for 24–48h—poor to guarded for life of dam; fetal survival unlikely.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Dystocia may or may not impact future fertility, but may recur depending on cause. Resolution of dystocia by C-section does not preclude natural whelping for future deliveries.

SEE ALSO

- Breeding, Timing.
- Uterine Inertia.
- Vaginal Malformations and Acquired Lesions.

ABBREVIATIONS

- C-section = Cesarean section.
- LH = luteinizing hormone.
- PCV = packed cell volume.

Suggested Reading

Johnston SD, Root Kustritz MV, Olson PNS. Canine parturition; Feline parturition. In: Canine and Feline Theriogenology. Philadelphia, PA: Saunders, 2001, pp. 105–128, 431–437.

Author Cheryl Lopate

Consulting Editor Erin E. Runcan



Client Education Handout
available online

EAR MITES



BASICS

E

OVERVIEW

Otodectes cynotis mites infest primarily the external ear canal and cause variable degrees of otic discharge and pruritus.

SIGNALMENT

- Common in young dogs and cats, although it may occur at any age.
- No breed or sex predilection.

SIGNS

- Pruritus is usually present, but can be minimal.
- Pruritus primarily located around the ears, head, and neck; occasionally generalized.
- Thick, red-brown, or black otic exudate ("coffee grounds" appearance)—usually seen in the outer ear.
- Otic exudate and pruritus demonstrate individual variability.
- Crusting and scales may occur on the neck, rump, and tail (dogs).
- Excoriations on the convex surface of the pinnae often occur, owing to the intense pruritus.

CAUSES & RISK FACTORS

Otodectes cynotis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pediculosis.
- *Pelodera* dermatitis.
- Sarcoptic mange.
- Notoedric mange.
- Chiggers.
- Otitis externa secondary to allergy/hypersensitivity.
- Flea bite hypersensitivity.

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

N/A

DIAGNOSTIC PROCEDURES

- Ear swabs placed in mineral oil—usually effective means of identification.
- Skin scrapings—may identify mites if signs are generalized.
- Mites may be visualized in external ear canal.
- Diagnosis may be made by response to treatment.



TREATMENT

- Outpatient.

- Diet and activity—no alteration necessary.
- Very contagious—all animals in contact with the affected animal must be treated.
- Thoroughly clean and treat the environment.



MEDICATIONS

DRUG(S) OF CHOICE

- Ears should be thoroughly cleaned with a commercial ear cleaner.
- Otic parasiticides should be used for 7–10 days to eradicate mites and eggs; effective topical commercial products contain pyrethrins, thiabendazole, ivermectin, and milbemycin; treat during alternative weeks for two to three treatment cycles recommended to prevent reinfection from eggs.
- Selamectin—per label instructions or repeated at 2 weeks.
- Imidacloprid/moxidectin (Advantage Multi/Advocate)—per label instructions.
- Ivermectin—200–300 µg/kg PO (three treatments) or SC (two treatments) at 14-day intervals; non-FDA-approved usage.
- Isoxazolines—per label instructions; non-FDA-approved usage.
- Flea treatments should be applied to animal for elimination of ectopic mites.
- Mites may persist in the environment; environmental treatment may be helpful.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Ivermectin and moxidectin—sensitivity in ABCB-1 mutant dogs; do not use orally or by injection in collies, shelties, their crosses, or other herding breeds; use only if absolutely necessary in animals <6 months of age; an increasing number of toxic reactions have been reported in kittens.
- Ivermectin and milbemycin—cause elevated levels of monoamine neurotransmitter metabolites, which could result in adverse drug interactions with amitraz and benzodiazepines.
- Isoxazolines—use with caution in pets with previous history of seizures.



FOLLOW-UP

- Ear swab and physical examination should be done 1 month after therapy commences.
- Prognosis is good.
- If signs persist after treatment, an additional, underlying cause may be present.
- Repeat infestation indicates an uncontrolled source of mites.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Transient papular dermatitis in human beings.

Suggested Reading

Helton Rhodes KA, Werner A. Blackwell's Five-Minute Veterinary Consult Clinical Companion: Small Animal Dermatology, 3rd ed. Hoboken, NJ: Wiley-Blackwell, 2018.

Thomas RC. Treatment of ectoparasites. In: Bonagura JD, Twedt DC, eds. Current Veterinary Therapy XV. St. Louis, MO: Elsevier Saunders, 2014, pp. 428–432.

Author Karen A. Kuhl

Consulting Editor Alexander H. Werner Resnick

ECLAMPSIA



BASICS

OVERVIEW

- Postparturient hypocalcemia.
- Usually develops 1–4 weeks postpartum; may occur at term, prepartum, or during late lactation.
- Hypocalcemia alters cell membrane potentials, causing spontaneous discharge of nerve fibers and tonic-clonic contraction of skeletal muscles.
- Life-threatening tetany and convulsions, leading to hyperthermia.
- Cerebral edema possible.

SIGNALMENT

- Dog—postpartum bitch; most common in toy breeds; higher incidence with first litter.
- Most common prior to day 40 postpartum; occasionally occurs prepartum.
- Breeds at increased risk—chihuahua, miniature pinscher, shih tzu, miniature poodle, Xoloitzcuintli, Pomeranian.
- Cat—rare.

SIGNS

Historical Findings

- Poor mothering.
- Restlessness, nervousness.
- Panting, whining.
- Vomiting, diarrhea.
- Ataxia, stiff gait, limb pain.
- Facial pruritis.
- Muscle tremors, tetany, convulsions.
- Recumbency, extensor rigidity—usually seen 8–12 hours after onset of signs.

Physical Examination Findings

- Hyperthermia.
- Rapid respiratory rate.
- Dilated pupils, sluggish pupillary light responses.
- Muscle tremors, muscular rigidity, convulsions.

CAUSES & RISK FACTORS

- Calcium supplementation during gestation, including dairy products.
- Inappropriate Ca : P ratio in gestational diet.
- Low bodyweight : litter size ratio.
- Poor prenatal nutrition.
- First litter.
- Large litter size.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypoglycemia—may be concurrent; hypoglycemia alone does not cause muscular rigidity.

- Toxicosis—distinguished by signalment and history.
- Epilepsy or other neurologic disorder—differentiated by signalment; calcium concentration diagnostic.

CBC/BIOCHEMISTRY/URINALYSIS

- Total serum calcium <9 mg/dL in bitches; <8 mg/dL in queens.
- Although ionized calcium (<2.4–3.2 mg/dL) is the form important for normal neuromuscular function, measurement of total serum calcium is usually sufficient for diagnosis.
- Hypoglycemia—may be concurrent.
- Hypomagnesemia has been reported in 44% of affected bitches; may promote tetany.
- Serum potassium elevated in 56% of cases, due to metabolic acidosis or respiratory alkalosis.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

ECG may show prolonged QT interval, bradycardia, tachycardia, or ventricular premature complexes.



TREATMENT

- Emergency inpatient.
- Hyperthermia—cool by wetting haircoat and exposing to breeze from fan.
- Puppies—remove from dam onto a foster dam or hand-raise; if not possible or undesirable due to behavioral need for contact with dam, remove pups from dam for 24 hours, or until serum calcium is stabilized, and provide supplemental calcium for remainder of lactation; continue to monitor serum calcium level.



MEDICATIONS

DRUG(S) OF CHOICE

- Calcium gluconate—10% solution 0.22–0.44 mL/kg IV given slowly to effect over 5 min; monitor heart rate or ECG during administration; corresponds to dosage of 50–150 mg/kg.
- Correct hypoglycemia—50% dextrose: 0.5 g/kg diluted 1 : 3 with saline IV; can supplement maintenance IV fluids to 2.5% or 5% dextrose for longer-term treatment.
- Diazepam—0.5 mg/kg IV; for unresponsive seizures.
- Cerebral edema—if present, can treat with mannitol: 0.25–0.5 g/kg IV over 20 min, or

7.2% hypertonic saline 1–3 mL/kg IV over 15–20 min.

- Long-term therapy—calcium carbonate or calcium gluconate 10–30 mg/kg PO q8h until lactation ends (calcium carbonate 500 mg tablets supply 200 mg calcium).
- Magnesium supplementation may be helpful in hypomagnesemic bitches.
- Start puppies/kittens on solid food at 3–4 weeks of age.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Corticosteroids—avoid; cause decreased intestinal absorption and increased renal excretion of calcium.



FOLLOW-UP

PATIENT MONITORING

- Serum calcium concentration—monitor until stabilized in the normal range.
- Avoid calcium supplementation during gestation.
- Diet—maternal: ensure calcium : phosphorus ratio of 1.1 : 1 or 1.2 : 1; avoid high-phytate foods (e.g., soybeans); puppies: supplement feeding for large litters.

POSSIBLE COMPLICATIONS

- Cerebral edema.
- Death.
- Hand-raising of puppies.

EXPECTED COURSE AND PROGNOSIS

- Probably will recur with subsequent litters; calcium supplementation can be started after parturition for bitches with history of eclampsia in prior litters.
- Prognosis—good with immediate treatment; poor with delayed treatment.



MISCELLANEOUS

Suggested Reading

Davidson AP. Reproductive causes of hypocalcemia. Topics Compan Anim Med 2012, 27:165–166.

Drobatz KJ, Casey KK. Eclampsia in dogs: 31 cases (1995–1998). J Am Vet Med Assoc 2000, 217(2):216–219.

Gonzalez, K. Periparturient diseases in the dam. Vet Clin North Am Small Anim Pract 2018, 48(4):663–681.

Author Joni L. Freshman

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ECTROPION**BASICS****OVERVIEW**

- Eversion or rolling out of the eyelid margin, resulting in exposure of the palpebral conjunctiva.
- Can be conformational/congenital (primary) or acquired (secondary).
- Exposure and poor tear retention/distribution may predispose patient to irritation, recurrent infections, and sight-threatening corneal disease.

SIGNALMENT

- Dogs, seldom cats.
- Breeds with higher than average prevalence—sporting breeds (e.g., spaniels, hounds, and retrievers); giant breeds (e.g., Saint Bernard, mastiff); any breed with loose facial skin (especially bloodhounds).
- Primary—genetic predisposition in listed breeds; may occur in dogs <1 year old.
- Acquired—noted in other breeds; occurs late in life secondary to age-related loss of facial muscle tone and skin laxity.
- Intermittent—caused by fatigue; may be observed after strenuous exercise or when drowsy.

SIGNS

- Eversion of the lower eyelid with lack of contact of the lower lid to the globe and exposure of the palpebral conjunctiva and third eyelid.
 - Often excessively long palpebral fissure (macroblepharon).
 - Conjunctivitis and history of mucoid to mucopurulent discharge caused by chronic exposure to air and debris. Debris generally located between lid and globe in inferior conjunctival cul-de-sac.
 - Tear staining of periocular skin caused by poor tear drainage.
- History of bacterial conjunctivitis.

CAUSES & RISK FACTORS

- Primary disease—most common due to breed-associated facial conformation and alterations in eyelid support.
- Acquired disease—from marked weight loss or muscle mass loss about the head and orbits, tragic facial expression in hypothyroid dogs, and cicatricial ectropion from scarring of the eyelids secondary to injury or from surgical overcorrection of entropion.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Usually clinically obvious.
- Look for any underlying disorder in nonpredisposed breeds and dogs with late-age onset.

- Loss of orbital or periorbital mass—may occur in patients with masticatory myositis.
- Facial nerve paralysis—associated with lack of muscle tone of orbicularis oculi muscles.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

- Possible masticatory myositis—test for auto-antibodies against type 2M muscle fibers.
- Palpebral nerve paralysis or tragic facial expression—consider testing for hypothyroidism.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Palpebral nerve paralysis—full neurologic evaluation; potential for hypothyroidism.
- Secondary conjunctivitis—flush fornix and examine for follicles.
- Fluorescein or rose Bengal staining of cornea and conjunctiva—to identify corneal ulcerations; may reveal severity of exposure problem.

**TREATMENT**

- Supportive care (topical lubricant, rinsing eyes with eyewash after being outside to remove debris) and good ocular and facial hygiene—sufficient for most mild disease.
- Surgical treatment—eyelid shortening or radical facelift; necessary for severely affected patients that have chronic ocular irritation.
- Intermittent, fatigue-induced condition—do not treat surgically.

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

- Topical broad-spectrum ophthalmic antibiotics—bacterial conjunctivitis or corneal ulceration. Neomycin/polymyxin B/bacitracin (or based on culture and sensitivity) q6–8h.
- Lubricant ointments (e.g., Puralube®)—reduce conjunctival and corneal desiccation secondary to exposure.
- Hypothyroid and masticatory myositis-induced conditions—may respond well to appropriate medical treatment of underlying disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A

**FOLLOW-UP**

- May become more severe as patient ages.

- Nonsurgically treated patient—monitor for signs of infectious conjunctivitis, exposure keratopathy, corneal ulceration, and facial dermatitis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hypothyroidism.
- Masticatory myositis, extraocular myositis.

AGE-RELATED FACTORS

Old animals more likely to have ectropion secondary to loss of facial muscle tone.

SEE ALSO

- Hypothyroidism.
- Myopathy – Masticatory and Extraocular Myositis.

Suggested Reading

Stades FC, van der Woerdt A. Diseases and surgery of the canine eyelid. In: Gelatt KN, Gilger BC, Kern TJ, eds., Veterinary Ophthalmology, 5th ed. Ames, IA: Wiley-Blackwell, 2013, pp. 853–864.

Author Sarah L. Czerwinski**Consulting Editor** Kathern E. Myrna

Acknowledgment The author and book editor acknowledge the prior contribution of J. Phillip Pickett.

ENTROPION



BASICS

OVERVIEW

- Inversion or rolling in of eyelid margin, resulting in frictional irritation of cornea and/or conjunctiva from contact with outer surface of eyelid.
- May result in keratitis, corneal ulceration, or corneal perforation.
- Can be conformational/congenital (primary) or acquired (secondary).
- Severe corneal disease may threaten vision.

SIGNALMENT

- Common in dogs—seen in chow chow, Chinese Shar-Pei, Norwegian elkhound, sporting breeds (e.g., spaniel, retriever), brachycephalic breeds, toy breeds, and giant breeds; age—puppies as early as 2–6 weeks old; usually identified in dogs <1 year old.
- Cats—usually in brachycephalic breeds, in young cats due to chronic ocular surface disease, and older animals due to retrobulbar fat loss.

SIGNS

- Mild, medial—chronic epiphora and medial pigmentary keratitis (toy dogs and brachycephalic dogs and cats).
- Mild, lateral—chronic mucoid to mucopurulent ocular discharge (giant-breed dogs).
- Upper lid, lower lid, or lateral canthal—severe blepharospasm, purulent discharge, pigmentary or ulcerative keratitis, potential cornea rupture (chow chow, shar-pei, bloodhound, sporting breeds).
- Cats—often have associated keratoconjunctivitis, corneal ulceration, or corneal sequestrum (brown-black corneal opacity).

CAUSES & RISK FACTORS

- Genetic predisposition—based on facial conformation and eyelid support.
- Brachycephalic breeds (dogs and cats)—excessive tension on ligamentous structures of medial canthus plus nasal folds and facial conformation results in rolling inward of medial aspects of upper and lower eyelids at the medial canthus.
- Giant breeds and breeds with excessive eyelid length (macroblepharon), heavy/loose facial skin, or excessive facial folds—laxity of lateral canthus allows entropion of upper and lower eyelids and lateral canthus.
- Spastic entropion—from ocular irritation (e.g., distichia, ectopic cilia, trichiasis, foreign body, irritant conjunctivitis); leads to excessive blepharospasm.
- Non-predisposed breeds—may be primary irritant causing secondary spastic entropion.
- Loss of orbital fat or periorbital musculature may lead to enophthalmos and entropion.
- Secondary cicatricial entropion—from scarring due to eyelid wounds or eyelid surgery.
- Cats—chronic infectious conjunctivitis or keratitis: may lead to functional entropion

caused by chronic blepharospasm (spastic entropion); also in older cats due to enophthalmos from retrobulbar fat loss.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Underlying causes of spastic entropion (eyelid hair anomalies, foreign bodies, infectious keratitis/conjunctivitis) should be ruled out and corrected, if possible, before an attempt at surgical correction is made.
- Puppies—common for first-time breeders of chow chows and Chinese Shar-Peis to mistakenly think that eyelids have not opened at 4–5 weeks of age, when puppies actually have severe blepharospasm and spastic entropion.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Observe patient with minimal restraint to assess degree of entropion without distortion from tension on eyelids or periocular area.
- Apply a topical anesthetic to reduce spastic component to differentiate spastic versus physiologic entropion.



TREATMENT

Puppies

- Do *not* initially perform skin resection surgery.
- If cornea ulcerated—topical antibiotic (e.g., neomycin/polymyxin B/bacitracin) ointment q6–8h.
- If mildly entropic and cornea not ulcerated, lubricate with artificial tear ointment q8–12h.
- If moderate to severe entropion with or without corneal ulceration, temporarily evert eyelid margins with sutures to break the irritation–spasm cycle; if successful, permanent procedure is unnecessary; may need to be repeated every 2–4 weeks until adult facial conformation is achieved.
- Semi-permanent eyelid eversion with hyaluronic acid filler injection—lasts up to several months, often until adult facial conformation is achieved.
- Permanent skin resection technique—postponed until patient's facial conformation matures (usually 1.5–2 years).

Medial Entropion

- Temporary eversion of medial canthus with sutures may aid in determining contribution of medial entropion to epiphora.

- Medial canthoplasty should be considered if entropion results in pigmentary keratitis, chronic epiphora, or corneal scarring.

Mature Dogs and Cats

- Chronic entropion—requires eyelid margin–everting surgery; ranges from simple Hertz-Celsius procedure to more radical lateral canthoplasty procedures; often combined with lid-shortening procedures.
- No history of previous entropion and clinical signs of acute condition—identify cause of spastic condition and correct; may attempt temporary eversion sutures before permanent skin resection.

E



MEDICATIONS

DRUG(S) OF CHOICE

- Topical ophthalmic ointment—triple antibiotic (in dogs only, q6–12h) or antibiotic based on culture and sensitivity testing; may be used if cornea is ulcerated, postoperatively, or as presurgical lubricant.
- Topical petrolatum-based artificial tear ointments (e.g., Puralube® q8–12h) may be used temporarily in mild cases without corneal ulceration.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

Temporary eversion suture technique—entropion may revert when sutures are removed or spontaneously pull through the skin; repeat as necessary until patient is mature enough to undergo more permanent repair. Consider hyaluronic acid filler injection as alternative.



MISCELLANEOUS

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of J. Phillip Pickett.

EOSINOPHILIA



BASICS

E

OVERVIEW

- Eosinophilia refers to an increased number of circulating eosinophils.
- Reference intervals may be difficult to accurately determine, as numbers do not tend to have normal (Gaussian) distribution. Absolute counts $>1.5 \times 10^3/\mu\text{l}$ often indicate clinically significant eosinophilia.
- Diseases associated with eosinophilia are highly variable. However, they often involve those causing release of cytokines including IL-5, IL-2, IL-3, and/or GM-CSF.
- Prevalence varies; 4.8% of cats and 10% of dogs have been identified with eosinophilia in large retrospective studies.

SIGNALMENT

- Breed and sex predilections are directly correlated to the characteristics of specific diseases.
- Rottweilers and German shepherd dogs show the highest overall prevalence of eosinophilia.

SIGNS

- Clinical signs directly associated with eosinophilia per se are lacking.
- Specific clinical signs are dependent on the disease causing the eosinophilia.

CAUSES & RISK FACTORS

- Diseases associated with eosinophilia are widely variable and can be categorized in many ways.
- Infectious diseases typically involve tissues rather than peripheral blood, and are more likely to be parasitic than bacterial.
- Tissues involved are frequently those that contain abundant mast cells, such as skin, lungs, and intestine, and often involve hypersensitivity.
- Metabolic—hypoadrenocorticism.
- Neoplastic—mast cell tumor; eosinophilic leukemia; lymphoma (both T-cell and B-cell); thymoma; mammary carcinoma; oral fibrosarcoma; transitional cell carcinoma.
- Immune mediated—hypereosinophilic syndrome (HES); idiopathic HES in Rottweilers; feline asthma; eosinophilic bronchopneumopathy; feline gastrointestinal eosinophilic sclerosing fibroplasia; flea bite allergy; eosinophilic granuloma complex.
- Infectious—*Angiostrongylus vasorum*; heartworm disease (*Dirofilaria immitis*); *Ehrlichia* spp. infections; *Anaplasma* spp. infections; histoplasmosis; sarcocytosis; *Aelurostrongylus* spp.; larval migration of various parasites.
- Toxic methimazole therapy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- HES represents an idiopathic response that may be due to an occult immunologic stimulus.
- Eosinophilic leukemia is a myeloproliferative disease that often has immature forms in circulation and in the bone marrow.
- Differentiation between HES and eosinophilic leukemia can be extremely difficult and is somewhat controversial.

CBC/BIOCHEMISTRY/URINALYSIS

- Caution should be taken in interpreting the results of some in-house hematology analyzers, as they only show good correlation with gold standard instruments. A blood smear should *always* be evaluated as part of the CBC.
- Eosinophils tend to be larger and hypolobulated compared to neutrophils.
- Feline eosinophils have small, rod-shaped granules.
- Sight hounds and sporadic other individuals have “gray eosinophils,” which have poorly staining granules and occasionally empty vacuoles in their cytoplasm.
- Eosinophils are grouped into one large category; bands, metamyelocytes, etc. are typically not divided out, as they are with neutrophils.

OTHER LABORATORY TESTS

Additional testing (e.g., adrenocorticotropic hormone (ACTH) stimulation test, fecal flotation, cytology, etc.) are dependent on the differential diagnosis/disease in question.

IMAGING

Diagnostic imaging utilized (e.g., radiographs, ultrasound, CT, etc.) is dependent on the differential diagnosis/disease in question.

DIAGNOSTIC PROCEDURES

Diagnostic procedures utilized (e.g., transtracheal wash, endoscopy, serologic testing, biopsy, etc.) are dependent on the differential diagnosis/disease in question.

PATHOLOGIC FINDINGS

- No specific lesions are ascribed solely to eosinophilia other than peripheral blood findings.
- Lesions are dependent on the disease(s) present.



TREATMENT

- No specific treatment is described exclusively for eosinophilia.
- The treatment employed is dependent on the cause of the eosinophilia.



MEDICATIONS

Dependent on cause.



FOLLOW-UP

Dependent on cause.



MISCELLANEOUS

SEE ALSO

Hypereosinophilic Syndrome (HES).

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone.
- HES = hypereosinophilic syndrome.

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EOSINOPHILIC GRANULOMA COMPLEX



BASICS

DEFINITION

- Cats—also called feline eosinophilic skin disease; term used for three distinct syndromes: eosinophilic plaque, eosinophilic granuloma, and indolent ulcer; grouped primarily according to their clinical similarities, their frequent concurrent (and recurrent) development, and their positive response to corticosteroids; reaction pattern and not a final diagnosis unless idiopathic.
- Dogs—eosinophilic granuloma in dogs (EGD) rare; specific differences from cats listed separately.

PATOPHYSIOLOGY

- Eosinophil—major infiltrative cell for eosinophilic granuloma and eosinophilic plaque, but not typically with indolent ulcer; most often associated with allergic or parasitic conditions but has a more general role in inflammatory reactions.
- Eosinophilic granuloma complex (EGC)—most often in cats with hypersensitivities to inhaled allergens, food, or insects, but can also be idiopathic with possible genetic causes.
- EGD—may have both a genetic predisposition and a hypersensitivity cause (especially in non-genetically susceptible breeds).

SYSTEMS AFFECTED

Skin/exocrine.

GENETICS

- Related individuals with disease development in a colony of specific pathogen-free cats indicate that genetic predisposition (possible inheritable dysfunction of eosinophilic regulation) may be significant component for development.
- Genetically predisposed development of hypersensitivity.

GEOGRAPHIC DISTRIBUTION

Seasonal incidence in some geographic locations—insect or environmental allergen exposure.

SIGNALMENT

Species

- Cats—eosinophilic granuloma, eosinophilic plaque, indolent ulcer.
- Dogs—eosinophilic granuloma.

Breed Predilections

- Cats—none.
- Dogs—EGD: Siberian husky (76% of cases), cavalier King Charles spaniel.

Mean Age and Range

- Eosinophilic granuloma and plaque—younger cats.
- Spontaneously regressing eosinophilic granuloma—<1 year.
- Indolent ulcer—any age.
- EGD—usually <3 years of age (80%).

Predominant Sex

- Cats (eosinophilic granuloma, indolent ulcer)—predilection for females reported;

eosinophilic plaque: no sex predilection.

- EGD—males (72% of cases).

SIGNS

General Comments—Cats

- Distinguishing among the syndromes depends on clinical signs.
- Lesions of more than one syndrome may occur simultaneously or may change over time.

Historical Findings—Cats

- Lesions may develop spontaneously and acutely.
- Eosinophilic granuloma—variable but typically nonpruritic.
- Eosinophilic plaque—severe pruritus.
- Indolent ulcer—pain and pruritus rare.
- Seasonal incidence possible (related to insects and allergy).
- Waxing and waning of clinical signs common in all syndromes.

Physical Examination Findings

- Eosinophilic plaque*—single or multiple, alopecic, erythematous, eroded/ulcerated well-demarcated and flat-topped ± white necrotic foci; most commonly seen on the abdomen and medial thighs, but may also see in mucocutaneous junctions and other areas of the skin; frequently moist or glistening; may appear oval or linear due to pattern of licking.
- Eosinophilic granuloma*—distinctly linear orientation on the caudal thigh; chin (“pouting cats”)—lip margin and chin swelling; paw pads—footpad swelling, pain, and lameness; oral cavity—ulceration common (especially on the tongue, palate); cats with oral lesions may be dysphagic, have halitosis, and may drool; can be located anywhere on the body; spontaneous regression—especially in young cats with the inheritable form.
- Indolent ulcer*—classically concave and indurated ulcerations with a granular, orange-yellow color, confined to the upper lips near philtrum or upper canine teeth.
- Peripheral lymphadenopathy possible for EGC lesions.
- EGD*—ulcerated plaques and nodules; green/orange color; most often affects the tongue and palatine arches; uncommon cutaneous lesions on the abdomen, cheek, digits, prepuce, and flanks.
- Cavalier King Charles spaniels*—lesions on the soft palate or near the tonsils.

CAUSES

- Hypersensitivity—flea or insect (mosquito bite), food hypersensitivity, and atopy; a heritable dysfunction has been proposed.
- Idiopathic.
- EGD—unknown; genetics in susceptible breeds; a hypersensitivity reaction often suspected (insect bite) in non-genetically susceptible breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Herpes virus dermatitis.
- Feline leukemia virus (FeLV) or feline immuno-

deficiency virus (FIV).

- Unresponsive lesions—pemphigus foliaceus, dermatophytosis and deep fungal infection, demodicosis, pyoderma, and neoplasia (metastatic adenocarcinoma, squamous cell carcinoma, and lymphoma).
- EGD—neoplasia, infectious and noninfectious granuloma.

CBC/BIOCHEMISTRY/URINALYSIS

CBC—mild to moderate eosinophilia.

OTHER LABORATORY TESTS

FeLV and FIV.

DIAGNOSTIC PROCEDURES

- Impression smears (cytology) from lesions—large numbers of eosinophils (indolent ulcer may be more neutrophilic).
- Comprehensive flea and insect control—assist in excluding flea or mosquito bite hypersensitivity.
- Food elimination trial and provocation—appropriate in all cases.
- Atopy—intradermal skin testing (preferred) or serum allergy testing followed by immunotherapy.
- Biopsy.

PATHOLOGIC FINDINGS

- Histopathologic diagnosis—mainly to rule out other differentials.
- Eosinophilic granuloma*—nodular to diffuse granulomatous dermatitis with flame figures, eosinophils, multinucleated histiocytic giant cells; mucinoses of epidermis/hair follicle outer root sheath, mural eosinophilic folliculitis/furunculosis, eosinophilic panniculitis possible.
- Eosinophilic plaque*—superficial to deep perivascular dermatitis with eosinophilia to interstitial to diffuse eosinophilia; mucinoses of epidermis/hair follicle outer root sheath, diffuse spongiosis of outer root sheath, eosinophilic microvesicles/microabscesses possible.
- Indolent ulcer*—variable; may be predominantly neutrophilic or eosinophilic.
- EGD—foci of palisading granulomas and flame figures; infiltrate with eosinophils mixed with macrophages.



TREATMENT

APPROPRIATE HEALTH CARE

- Most patients treated as outpatients unless severe oral disease prevents adequate fluid intake.
- Identify and eliminate offending allergen(s) before providing medical intervention.
- Atopy—immunotherapy: successful in a majority of cases; preferable to long-term corticosteroid administration.

NURSING CARE

Discourage patient from damaging lesions by excessive grooming.

DIET

No restrictions unless a food allergy is suspected. Elimination diet for suspected food allergy.

EOSINOPHILIC GRANULOMA COMPLEX

(CONTINUED)

CLIENT EDUCATION

- Inform clients about the possible allergic or heritable causes.
- Discuss the waxing and waning nature of these diseases.

E

SURGICAL CONSIDERATIONS

EGD—individual lesions may be excised/removed by carbon dioxide laser if being mechanically traumatized and medically unresponsive.



MEDICATIONS

DRUG(S) OF CHOICE

- Cases may improve with antibiotics—amoxicillin trihydrate-clavulanate 10–20 mg/kg q12h; cefovecin 8 mg/kg every 14 days; or clindamycin 11–22 mg/kg q24h.
- Oral corticosteroids—ongoing treatment necessary unless the primary cause is controlled; prednisolone 2–4 mg/kg q24h, then as required to control lesions; steroid tachyphylaxis may occur and may be specific to the drug administered; may be useful to change the form; other drugs: methylprednisolone 2–3 mg/kg q24h, dexamethasone 0.1–0.2 mg/kg q24–72h, and triamcinolone 0.2–0.3 mg/kg q24–72h; higher induction dosages may be required but should be tapered as quickly as possible.
- Cyclosporine modified, 7 mg/kg q24–48h.
- Topical—fluocinolone/dimethyl sulfoxide (DMSO; Synotic® lotion) to individual lesions; not practical and/or may cause systemic effects in patients with large numbers of lesions.

Alternate Therapies

- Chlorambucil 0.1–0.2 mg/kg q24–72h.
- α -interferon 300–1000 IU/day; limited success.
- Megestrol acetate—significant side effects (e.g., diabetes, mammary cancer, pyometra); use not recommended except in severe, recalcitrant cases.

EGD

- Oral prednisolone 0.5–2.2 mg/kg/day initially; then taper gradually.
- Some may undergo spontaneous remission.



FOLLOW-UP

PATIENT MONITORING

- Corticosteroids—baseline and frequent hemograms, serum chemistry profiles, and urinalyses with culture; excessive or too-frequent use of corticosteroids increases risk for development of diabetes mellitus and acquired skin fragility.
- Cyclosporine—baseline and frequent hemograms, serum chemistry profiles, and urinalyses with culture; measurement of plasma cyclosporine levels as needed to establish dosage within therapeutic levels (especially cats); avoid raw meat and keep cats indoors.
- Selective immunosuppressant drugs—frequent hemograms (biweekly at first, then monthly or bimonthly as therapy continues) to monitor for bone marrow suppression; routine serum chemistry profiles and urinalyses with culture (monthly at first, then every 3 months) to monitor for complications (renal disease, diabetes mellitus, and urinary tract infection).

EXPECTED COURSE AND PROGNOSIS

- Lesions should resolve permanently if a primary cause can be identified and controlled.
- Most lesions wax and wane, with or without therapy; an unpredictable schedule of recurrence should be anticipated.
- Drug dosages should be tapered to the lowest possible level (or discontinued, if possible) once the lesions have resolved.
- Lesions in cats with the inheritable disease may resolve spontaneously after several years.
- EGD—lesions may be recalcitrant to medical intervention.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Systemic glucocorticoids and immunosuppressive drugs should not be used during pregnancy.

SYNONYMS

- Eosinophilic granuloma—feline collagenolytic granuloma; feline linear granuloma.
- Indolent ulcer—eosinophilic ulcer; rodent ulcer; feline upper lip ulcerative dermatitis.

SEE ALSO

- Atopic Dermatitis.
- Food Reactions, Dermatologic.

ABBREVIATIONS

- DMSO = dimethyl sulfoxide.
- EGC = eosinophilic granuloma complex.
- EGD = eosinophilic granulomas in dogs.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.

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Acknowledgment The author acknowledges the prior contribution of Alexander H. Werner Resnick.



Client Education Handout
available online

EPILEPSY, GENETIC (IDIOPATHIC)—DOGS



BASICS

E

DEFINITION

Syndrome that is only epilepsy, with no demonstrable underlying brain lesion or other neurologic signs or symptoms; age-related; assumed genetic. The term "idiopathic" replaced by "genetic" according to the International League Against Epilepsy (ILAE) classification (see Appendix IX).

PATHOPHYSIOLOGY

- Exact mechanism unknown.
- Likely different mechanisms between breeds.

SYSTEMS AFFECTED

Nervous

GENETICS

Genetic basis suspected in Australian shepherd, beagle, Belgian shepherd (Groenendael and Tervuren), Bernese mountain dog, border collie, dachshund, English springer spaniel, Finnish spitz, German shepherd, golden retriever, keeshond, Irish wolfhound, Italian spinone, Labrador retriever, Shetland sheepdog, standard poodle, vizsla.

INCIDENCE/PREVALENCE

0.5–2.3% of all dogs.

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog

Breed Predilections

Beagles; all shepherds (German, Australian, Belgian); Bernese mountain dogs; boxers; cocker spaniels; border collies; dachshunds; golden retrievers; Irish setters; Labrador retrievers; poodles (all sizes); Saint Bernards; Shetland sheepdogs; Siberian huskies; springer spaniels; Welsh corgis; wirehaired fox terriers. Can occur in any breed.

Mean Age and Range

- Mean age 10 months–3 years.
- Range 6 months–5 years.

Predominant Sex

Male predisposition in Bernese mountain dog.

SIGNS

General Comments

- Seizures may be generalized (convulsive) from onset, or have a short aura (focal onset) with rapid secondary generalization.
- An aura (animal appears frightened, dazed, seeks attention, or hides, etc.) frequently precedes the generalized seizure.
- Focal seizures reported in the border collie, Finnish spitz, English springer spaniel, Labrador retriever, vizsla, Belgian shepherd, standard poodle.

Historical Findings

- First seizure—between 6 months and 5 years.
- Seizures—often when patient is resting

or asleep; often at night or early morning; frequency tends to increase if left untreated; affected animal falls on its side, becomes stiff, chomps its jaw, salivates profusely, urinates, defecates, vocalizes, and paddles with all limbs in varying combinations; short duration (30–90 seconds).

- Postictal behavior—confusion, disorientation; aimless, compulsive, blind, pacing; frequent polydipsia and polyphagia; recovery immediate or may take up to 24 hours.
- Dogs with established epilepsy might have clustered generalized seizures at intervals of 1–4 weeks.
- No asymmetry should be observed during seizure, e.g., twitching more pronounced on one side, limb contractions on one side, compulsive circling just prior to or after the seizure.
- Stimulus-induced seizures—seizures only upon specific stimulus (sound, event).

Physical Examination Findings

- Patients often have recovered at time of presentation.
- Patients may have postictal behavior.

CAUSES

Genetic in some breeds; of unknown cause in others.

RISK FACTORS

Known epilepsy in the family line.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Seizure pattern (breed, age at onset, type and frequency of seizures)—most important factor toward diagnosis.
- Acute onset of cluster seizures or status epilepticus—rule out toxicity or structural brain disease.
- >2 seizures within the first week of onset—consider diagnosis other than genetic epilepsy.
- Seizures at <6 months or >5 years of age—consider metabolic or intracranial structural disease; rule out hypoglycemia in older dogs.
- Focal seizures or presence of neurologic deficits—rule out intracranial structural disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Perform before initiating drug therapy as baseline data.

OTHER LABORATORY TESTS

Bile acids to rule out hepatic encephalopathy unnecessary in dogs with seizures without accompanying episodic abnormal behavior.

IMAGING

MRI—if seizure pattern does not fit genetic (idiopathic) epilepsy, neurologic deficits are present, or intracranial structural disease is suspected.

DIAGNOSTIC PROCEDURES

- Cerebrospinal fluid (CSF)—for suspected structural intracranial diseases.
- Electroencephalography—may see interictal spikes, polyspikes, and spike slow wave complexes.

PATHOLOGIC FINDINGS

- No primary lesion.
- Secondary neuronal loss and gliosis from prolonged seizures.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—recurrence of isolated seizures.
- Inpatient—for cluster seizures (>1 seizure q24h) or status epilepticus.

NURSING CARE

Inpatients with seizure disorders require constant monitoring.

DIET

- Dogs on chronic phenobarbital (PB) and potassium bromide (KBr) treatment often become overweight; weight-reducing program as necessary.
- KBr treatment—insure steady levels of salt in diet; increase in salt causes increase in bromide excretion preferentially over chloride, with subsequent decreased serum KBr levels; alternatively, decreased salt content increases KBr serum level.
- Trial with high-fat, low-carbohydrate diet—no improvement in seizure control.

CLIENT EDUCATION

- Severe cluster seizures and status epilepticus are life-threatening emergencies requiring immediate medical attention.
- Keep seizure calendar noting date, time, length, and severity of seizures to assess response to treatment.
- Once treatment instituted, medication is lifelong in most cases.
- Abrupt drug withdrawal may cause seizures.



MEDICATIONS

DRUG(S) OF CHOICE

- Initiate treatment at second generalized seizure if dog <2 years; when interictal period gradually shortens in others.
- Antiepileptic treatment—decreases frequency, severity, and length of seizures; perfect control rarely achieved.
- Tolerance and refractoriness to treatment may develop.

Phenobarbital

- Most efficacious antiepileptic drug (AED) in the dog.
- Traditional first-line drug; initial dosage 3–5 mg/kg PO q12h; steady state reached at 12–15 days, but levels decrease significantly in first 6 months owing to activation of lysosomal enzymes.
- Optimal therapeutic serum levels—100–120 µmol/L or 23–28 µg/mL.
- Oral loading dose (if needed)—6–10 mg/kg PO q12h for 2–3 days to reach therapeutic range rapidly.

Zonisamide

First-line drug when seizure frequency allows (<1/week); 5 mg/kg PO q12h; 10 mg/kg PO q12h as add-on to PB; half-life 15 hours;

(CONTINUED)

steady state 4 days; therapeutic range in human 10–45 µg/mL.

Levetiracetam

First-line drug when seizures have focal onset; <1 seizure/week; 20–70 mg/kg (smaller breeds require higher dosage) PO q8h; must be given q8h to reach adequate levels; no hepatic metabolism; safe; steady state 3 days; therapeutic range in human 10–40 µg/mL.

Potassium Bromide

- Traditional first-line drug; initial dosage 30 mg/kg PO q24h or divided q12h; half-life 24–46 days; steady state 3–4 months; varies with salt concentration in diet; bioavailability differs between dogs.
- Optimal therapeutic serum levels—20–25 mmol/L or 1.6–2 mg/mL; if sole antiepileptic drug, 25–32 mmol/L or 2–2.25 mg/mL can be safely used.
- Add on to PB if seizures uncontrolled with optimal PB level—beneficial and synergistic effect.
- Loading dose—may cause vomiting, diarrhea, profound longstanding sedation; if needed, double daily PO doses for 2 weeks.
- Renal insufficiency decreases bromide elimination; half initial dosage.

Diazepam (At-Home Use)

- To abort ongoing seizures—dogs with cluster seizures or status epilepticus.
- Insert 0.5–1 mg/kg injectable drug in rectum (or intranasal) via 1 inch teat cannula as soon as a seizure occurs; repeat 20 and 40 minutes later for a total of 3 insertions within 40 minutes; can be safely repeated once more in 24h period.
- Given early in course of ongoing seizures, helps abort subsequent seizures.
- Intranasal midazolam can also be used 0.5 mg/kg. Can be repeated once after 20 minutes.

CONTRAINDICATIONS

Aminophylline, theophylline.

PRECAUTIONS

α-adrenergic agonists (e.g., phenylpropanolamine)—CNS excitation.

POSSIBLE INTERACTIONS

- Cimetidine and chloramphenicol—interfere with PB metabolism; may cause toxic PB levels.
- PB lowers serum levels of zonisamide and levetiracetam.
- PB may lower T₄ and cause upward trend in thyroid-stimulating hormone (TSH) without signs of hypothyroidism.
- PB does not interfere with low-dose dexamethasone suppression tests regardless of dose and treatment.
- Zonisamide decreases total T₄.
- Whenever animals on lifetime medication, refer to manufacturer's drug profile or to pharmacist for interaction information.

ALTERNATIVE DRUG(S)

- With polypharmacy, initiate add-on gradually to avoid sedation.
- Gabapentin 10–20 mg/kg PO q8h; low efficacy as add-on; newer analog pregabalin may be more efficacious, 2–4 mg/kg q8h PO.
- Clorazepate 0.5–1 mg/kg PO q8h.
- Felbamate 30–70 mg/kg q12h–8h.
- Topiramate 2–10 mg/kg PO q12h.

EPILEPSY, GENETIC (IDIOPATHIC)—DOGS

- Phenytoin, valproic acid, carbamazepine, and ethosuximide—unsuitable pharmacokinetics in dogs.
- Others—acupuncture, vagal nerve stimulation, transcranial magnetic motor stimulation.
- CBD-infused oil 2.5 mg/kg (1.1 mg/lb) q12h.



FOLLOW-UP

PATIENT MONITORING

- Serum drug levels—preferentially at trough, at same time for each sampling; use same laboratory.
- Phenobarbital—measure PB level 4 weeks after initiating therapy; adjust dose as needed; then repeat level every 2 weeks until optimal levels reached; with chronic use perform CBC, biochemistry, and PB level every 6–12 months; tabulate albumin, liver enzymes, and serum drug levels to monitor trend; drug essentially hepatotoxic; most dogs eventually develop hepatotoxicity if serum levels >140 µmol/L (>33 µg/mL) for long time (>6–8 months); if hepatotoxicity suspected, perform bile acids.
- KBr—serum level (along with PB level) 4–6 weeks after initiating (should be 8–12 mmol/L or 0.5–1 mg/mL) and at 3–4 months; if diet change required, consider diet salt content; monitor level accordingly; monitor KBr level closely if renal insufficiency (isosthenuria or azotemia).
- Zonisamide—measure level at 1 week; monitor electrolytes and acid-base status to check for renal tubular acidosis.
- Levetiracetam—measure level at 4 days.

PREVENTION/AVOIDANCE

- Abrupt discontinuation of medication may precipitate seizures.
- Avoid salty treats in dogs treated with KBr.

POSSIBLE COMPLICATIONS

- Recurrent episodes of cluster seizures and status epilepticus.
- PB and KBr—polyuria, polydipsia, polyphagia, weight gain.
- Phenobarbital-induced corticosteroid alkaline phosphatase (C-AP) elevation occurs frequently; may be early sign of hepatotoxicity, but of less concern if alanine aminotransferase (ALT) is within reference range.
- PB-induced hepatotoxicity—after chronic treatment at high serum levels (>140 µmol/L or >33 µg/mL); often insidious in onset; only biochemical abnormality may be decreased albumin.
- Higher incidence of pancreatitis in patients treated with PB and/or KBr; once pancreatitis develops, recurrence is frequent.
- Phenobarbital—rare bone marrow suppression with severe neutropenia (± sepsis) early in course of treatment; discontinue drug.
- Paradoxical hyperexcitability; discontinue drug; risk factor for superficial necrolytic dermatitis.
- KBr—when levels are >22 mmol/L or >1.8 mg/mL, owners may complain of patient's unsteadiness while managing stairs.
- Zonisamide—mild sedation, decreased appetite, gastrointestinal signs.
- One case of

renal tubular acidosis and one case of acute idiosyncratic hepatic necrosis reported.

- Levetiracetam—transient sedation.

EXPECTED COURSE AND PROGNOSIS

- Treatment for life.
- Some dogs are well controlled with same drug and dosage for years; others remain poorly controlled despite polypharmacy.
- Patient may develop status epilepticus and die.
- Early treatment does not decrease occurrence of status epilepticus.
- Normal expected lifespan, but survival time shorter if episodes of status epilepticus.
- Treatment with 2 AEDs not linked to poor prognosis.
- Increased risk of premature death.
- Marked breed differences in incidence and mortality rates.
- Prognosis depends on combined veterinary expertise, therapeutic success, and owner's motivation.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Idiopathic epilepsy can be a reason for euthyroid sick syndrome in dogs.

AGE-RELATED FACTORS

If onset <2 years of age, epilepsy more likely to be difficult to control; condition may become intractable.

PREGNANCY/FERTILITY/BREEDING

- Avoid breeding affected animals.
- Reported association between estrus and onset of seizures in intact bitches with presumptive "idiopathic" epilepsy; two hormonally based patterns recognized: during heat; and during a specific time point at the end of diestrus.

SEE ALSO

- Seizures (Convulsions, Status Epilepticus)—Cats.
- Seizures (Convulsions, Status epilepticus)—Dogs.

ABBREVIATIONS

- AED = antiepileptic drug.
- ALT = alanine aminotransferase.
- C-AP = corticosteroid alkaline phosphatase.
- CSF = cerebrospinal fluid.
- ILAE = International League Against Epilepsy.
- KBr = potassium bromide.
- PB = phenobarbital.
- TSH = thyroid-stimulating hormone.

INTERNET RESOURCES

<http://www.canine-epilepsy.net>

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Author Joane M. Parent.



**Client Education Handout
available online**



BASICS

DEFINITION

Bleeding from the nose.

PATHOPHYSIOLOGY

Results from one of three abnormalities—coagulopathy; local disease or space-occupying lesion; vascular or systemic disease.

SYSTEMS AFFECTED

- Respiratory—hemorrhage; sneezing
- Gastrointestinal (GI)—melena.
- Hemic/lymphatic/immune—anemia.

GENETICS

Varies depending on underlying cause.

INCIDENCE/PREVALENCE

Varies depending on underlying cause.

SIGNALMENT

Species

Dog and cat.

Age, Breed, and Sex Predilections

Vary depending on underlying cause.

SIGNS

Historical Findings

- Nasal hemorrhage—unilateral or bilateral possible.
- Sneezing and/or stertorous respiration.
- Melena.
- With coagulopathy—hematochezia, melena, hematuria, or hemorrhage from other areas of the body.
- With hypertension—possibly blindness, intraocular hemorrhage, neurologic signs, cardiac or renal signs.

Physical Examination Findings

- Nasal hemorrhage.
- Melena—from swallowing blood or concurrent upper GI hemorrhage.
- Nasal stridor—may be present with neoplasia, foreign body, or advanced inflammatory disease.
- With coagulopathy—possibly petechiae, ecchymosis, hematomas, intracavitory bleeds, hematochezia, melena, and hematuria.
- With coagulopathy or hypertension—possibly retinal or intraocular hemorrhages or retinal detachment; with hypertension—possibly heart murmur or arrhythmia.

CAUSES

Coagulopathy

Thrombocytopenia

- Immune-mediated disease—idiopathic disease; drug reaction; modified live virus (MLV) vaccine reaction.
- Infectious disease—ehrlichiosis; anaplasmosis; Rocky Mountain spotted fever, babesiosis, feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV)-related illness.

- Bone marrow disease—neoplasia; aplastic anemia; infectious (fungal, rickettsial, or viral).
- Paraneoplastic disorder.
- Disseminated intravascular coagulation (DIC).

Thrombopathia

- Congenital—von Willebrand disease; thrombasthenia; thrombopathia.
- Acquired—nonsteroidal anti-inflammatory drugs (NSAIDs); clopidogrel; hyperglobulinemia (*Ehrlichia*, multiple myeloma); uremia; DIC.

Coagulation Factor Defects

- Congenital—hemophilia A (factor VIII deficiency) and hemophilia B (factor IX deficiency).
- Acquired—anticoagulant rodenticide (warfarin) intoxication, hepatobiliary disease, DIC.

Local Lesion

- Foreign body.
- Trauma.
- Infection—fungal (*Aspergillus*, *Cryptococcus*, *Rhinosporidium*); viral or bacterial. Usually blood-tinged mucopurulent exudate rather than frank hemorrhage.
- Neoplasia—adenocarcinoma; carcinoma; chondrosarcoma; squamous cell carcinoma; fibrosarcoma; lymphoma; transmissible venereal tumor.
- Dental disease—oronasal fistula, tooth root abscess.
- Lymphoplasmacytic rhinitis.

Vascular or Systemic Disease

- Hypertension—renal disease; hyperthyroidism; hyperadrenocorticism; pheochromocytoma; idiopathic disease.
- Hyperviscosity—hyperglobulinemia (multiple myeloma, *Ehrlichia*); polycythemia.
- Vasculitis—immune-mediated and rickettsial diseases.

RISK FACTORS

Coagulopathy

- Immune-mediated disease—young to middle-aged, small-to medium-sized female dogs.
- Infectious disease—dogs living in or traveling to endemic areas; tick exposure.
- Thrombasthenia—otter hounds.
- Thrombopathia—basset hounds, spitz.
- von Willebrand disease—Doberman pinschers, Airedales, German shepherds, Scottish terriers, Chesapeake Bay retrievers, and many other breeds; cats.
- Hemophilia A—German shepherds and many other breeds; cats.
- Hemophilia B—Cairn terriers, coonhounds, Saint Bernards, and other breeds; cats.

Space-Occupying Lesions

- Aspergillosis—German shepherds, Rottweilers, mesocephalic and dolichocephalic breeds.
- Neoplasia—dolichocephalic breeds.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

See Causes.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—if enough hemorrhage has occurred.
- Thrombocytopenia—possible.
- Neutrophilia—infection; neoplasia.
- Pancytopenia—if bone marrow disease.
- Hypoproteinemia—if enough hemorrhage has occurred.
- High blood urea nitrogen (BUN) with normal creatinine—possible, owing to blood ingestion.
- Hyperglobulinemia—possible with ehrlichiosis, multiple myeloma.
- Azotemia—with renal failure-induced hypertension.
- High alanine transaminase (ALT), aspartate aminotransferase (AST), and total bilirubin—with coagulopathy from severe hepatic disease.
- Urinalysis—usually normal; possible to see hematuria (if coagulopathy), isosthenuria (if renal failure-induced hypertension), and proteinuria (if glomerulotubular disease and hypertension).

OTHER LABORATORY TESTS

- Coagulation profile—prolonged times with coagulation factor defects; normal with thrombocytopenia and thrombopathia.
- Platelet function testing (e.g., buccal mucosal bleeding time, von Willebrand factor analysis)—may be abnormal with platelet dysfunction (platelet count and coagulation profile may be normal).
- Ehrlichia*, *Anaplasma*, Rocky Mountain spotted fever, or *Babesia* testing—may be positive in thrombocytopenia or thrombopathia-induced epistaxis.
- Aspergillus* serology—may help establish a diagnosis of fungal rhinitis; false-negative results are common, so results must be interpreted in light of other clinical and diagnostic findings.
- Thyroid hormone assay—elevated in cats with epistaxis due to hyperthyroid-induced hypertension.

IMAGING

- Thoracic radiograph—screen for metastasis.
- Nasal series—under anesthesia, including open-mouth ventrodorsal and skyline sinus views when space-occupying or local lesion is suspected; osteolysis with neoplasia and fungal sinusitis; foreign bodies usually not seen; dental disease may be identified.
- CT or MRI—more sensitive than radiographs.

DIAGNOSTIC PROCEDURES

- Blood pressure evaluation—indicated when coagulopathies and space-occupying lesions have been ruled out and particularly when azotemia or proteinuria is noted.

EPISTAXIS

(CONTINUED)

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- Rhinoscopy, nasal lavage, nasal biopsy (blind or guided via rhinoscopy or CT)—indicated for space-occupying disease; aimed at removing foreign bodies and evaluating and sampling nasal tissue for causal diagnosis (e.g., evaluate nasal tissue samples for neoplasia, inflammation, and infection via cytology and/or histopathology and bacterial/fungal culture and sensitivity testing).
- Bone marrow aspiration biopsy—indicated if pancytopenia identified.



TREATMENT

APPROPRIATE HEALTH CARE

- Coagulopathy—usually inpatient management.
- Space-occupying lesion or vascular or systemic disease—outpatient or inpatient management, depending on disease and its severity.
- Nasal tumors—radiotherapy; various response rates.

NURSING CARE

Provide basic supportive care if needed (fluids, nutrition).

ACTIVITY

Minimize activity or stimuli that precipitate hemorrhage episodes.

CLIENT EDUCATION

- Inform client about the disease process.
- Teach client how to recognize a serious hemorrhage (e.g., weakness, collapse, pallor, and blood loss >30 mL/kg bodyweight).

SURGICAL CONSIDERATIONS

- Surgery indicated if a foreign body is unable to be removed by rhinoscopy or blind attempt.
- Fungal rhinitis (e.g., *Aspergillus* and *Rhinosporidium*) require debulking (also see Medications).



MEDICATIONS

DRUG(S) OF CHOICE

General

- Whole blood, packed red blood cell (RBC), or hemoglobin solution transfusion—can be needed with severe anemia.
- Acepromazine (0.05–0.1 mg/kg SC/IV if normothermic and no platelet disorder present) to lower blood pressure and promote clotting; may help control serious hemorrhage.
- Discontinue all NSAIDs.

Coagulopathy

- Immune-mediated thrombocytopenia—prednisone (1.1 mg/kg q12h; taper over 4–6 months); other drugs can be used in addition to prednisone for refractive cases (see Thrombocytopenia, Primary Immune Mediated).

- Infectious disease—rickettsial disease (doxycycline 5 mg/kg PO q12h for 3–6 weeks); *Babesia* (imidocarb 6.6 mg/kg SC 2 doses 2 weeks apart, diminazene aceturate 5 mg/kg IM once, or 10 days of atovaquone 13.3 mg/kg PO q8h with azithromycin 10 mg/kg PO q24h).
- Bone marrow neoplasia—see Myeloproliferative Disorders.
- Thrombopathia and thrombasthenia—no treatment unless lymphoproliferative disease.
- von Willebrand disease—plasma or cryoprecipitate for acute bleeding; 1-desamino-8-d-arginine vasopressin (DDAVP) 1 µg/kg SC/IV diluted in 20 mL 0.9% NaCl given over 10 min may help control or prevent hemorrhage prior to invasive procedures; intranasal formulation (less expensive) may be used after passing through a bacteriostatic filter.
- Hemophilia A—plasma or cryoprecipitate for acute bleeding; no long-term treatment.
- Hemophilia B—plasma for acute bleeding; no long-term treatment.
- Anticoagulant rodenticide intoxication—plasma for acute bleeding; vitamin K at 5 mg/kg loading dose followed by 1.25 mg/kg q12h for 1 week (if warfarin formulation) to 4 weeks (longer-acting formulation).
- Hyperglobulinemia—plasmapheresis.
- Polycythemia—phlebotomy; hydroxyurea.
- Liver disease and DIC—treat and support underlying cause; plasma may be beneficial.

Space-Occupying Lesion

- Secondary bacterial infection—antibiotics based on culture and sensitivity testing.
- Fungal infection—for aspergillosis, topical treatment of nasal cavity and frontal sinuses with 1% clotrimazole in polyethylene glycol (see Precautions) or 1–5% enilconazole (see Aspergillosis, Nasal for protocol); for cryptococcosis—oral and injectable anti-fungal agents (see Cryptococcosis); for rhinosporidiosis—surgery followed by dapsone (1 mg/kg PO q8h for 2 weeks, then 1 mg/kg PO q12h for 4 months).

Vascular or Systemic Disease

- Hyperviscosity—treat underlying disease (e.g., ehrlichiosis, multiple myeloma, or polycythemia); plasmapheresis.
- Vasculitis—doxycycline for rickettsial disease (5 mg/kg q12h for 3–6 weeks); prednisone for immune-mediated disease (1.1 mg/kg q12h; taper over 4–6 months).

Hypertension

- Treat underlying disease—renal disease, hyperthyroidism, hyperadrenocorticism.
- Reduce weight if overconditioned.
- Restrict sodium.
- Calcium channel blockers—amlodipine (dogs: 0.1 mg/kg PO q12–24h; cats: 0.625–1.25 mg/cat PO q12–24h); treatment of choice.
- ACE inhibitors—benazepril (0.5 mg/kg q24h); enalapril (0.25–0.5 mg/kg q12–24h).

- Beta blockers—propranolol (0.5–1 mg/kg q8h); atenolol (0.25–1.0 mg/kg q12–24h).
- Diuretics—hydrochlorothiazide (2–4 mg/kg q12h); furosemide (0.5–2 mg/kg q8–12h).
- Phenoxybenzamine (0.2–1.5 mg/kg q12h) for pheochromocytoma.

CONTRAINDICATIONS

- Avoid drugs that may predispose patient to hemorrhage—NSAIDs; heparin; clopidogrel; phenothiazine tranquilizers.
- Topical antifungals—do not use in patients with disruption of the cribriform plate.

PRECAUTIONS

- Chemotherapeutic drugs (immune-mediated thrombocytopenia therapy, e.g., azathioprine)—monitor neutrophil counts and liver enzymes weekly until a pattern has been established that shows that the patient is tolerating the drug.
- Enalapril and/or diuretics—closely monitor patients with renal failure; avoid severe salt restriction when using angiotensin-converting enzyme (ACE) inhibitors.
- Avoid topical clotrimazole preparations with propylene glycol, as life-threatening mucosal irritation, ulceration, and nasopharyngeal swelling can occur.



FOLLOW-UP

PATIENT MONITORING

- Platelet count with thrombocytopenia.
- Coagulation profile with coagulation factor defects.
- Blood pressure with hypertension.
- Clinical signs.

PREVENTION/AVOIDANCE

- Restrict access to areas that might contain anticoagulant rodenticides.
- Practice dental preventative care.

POSSIBLE COMPLICATIONS

Anemia and collapse (rare).

EXPECTED COURSE AND PROGNOSIS

Varies depending on underlying cause.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Avoid teratogenic drugs (e.g., itraconazole).

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- ALT = alanine transaminase.
- AST = aspartate aminotransferase.
- BUN = blood urea nitrogen.
- DDAVP = 1-desamino-8-d-arginine vasopressin.
- DIC = disseminated intravascular coagulation.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.

(CONTINUED)

- GI = gastrointestinal.
- MLV = modified live virus.
- NSAID = nonsteroidal anti-inflammatory drug.
- RBC = red blood cell.

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Acknowledgment The author and book editors acknowledge the prior contribution of Mitchell A. Crystal.

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**Client Education Handout
available online**

EXOCRINE PANCREATIC INSUFFICIENCY



BASICS

E

DEFINITION

Syndrome that is caused by inadequate amounts of pancreatic digestive enzymes in the small intestinal lumen.

PATHOPHYSIOLOGY

- Most commonly caused by insufficient synthesis and secretion of pancreatic enzymes by the exocrine pancreas.
- In rare cases can be caused by an obstruction of the pancreatic duct or isolated lipase deficiency.
- Insufficient synthesis of pancreatic digestive enzymes can be due to destruction of acinar cells resulting from chronic pancreatitis (approximately 50% of cases in dogs and almost all cases in cats) or can be due to idiopathic pancreatic acinar atrophy (PAA; most common cause of exocrine pancreatic insufficiency in German shepherd dogs).
- Deficient exocrine pancreatic secretion results in maldigestion and nutrient malabsorption, leading to weight loss and loose stools with steatorrhea.
- Malabsorption contributes to small intestinal dysbiosis.

SYSTEMS AFFECTED

Nutritional—protein-calorie malnourishment.

GENETICS

Assumed to be hereditary in the German shepherd dog and probably transmitted by a complex trait (early studies have suggested an autosomal recessive trait, but this is no longer believed to be the case).

INCIDENCE/PREVALENCE

- PAA is very commonly seen in the German shepherd dog; it is less commonly seen in rough-coated collies and Eurasians.
- Other causes of exocrine pancreatic insufficiency (EPI) may be seen in all dog and cat breeds.
- Less common in cats than in dogs.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat.

Breed Predilections

German shepherd dogs, rough-coated collies, and Eurasians.

Mean Age and Range

- PAA in young adult dogs.
- Chronic pancreatitis in dogs and cats of any age.

Predominant Sex

No sex predilection.

SIGNS

General Comments

- Consider in young adult (age range approximately 1–4 years) German shepherd dogs

with weight loss and loose stools.

- Severity—varies depending on time until diagnosis and therapy.

Historical Findings

- Weight loss with normal to increased appetite.
- Chronically loose stools or diarrhea.
- Fecal volumes are larger than normal and may be associated with steatorrhea.
- Flatulence and borborygmus are commonly reported, especially in dogs.
- May show coprophagia and/or pica.
- May be accompanied by polyuria/polydipsia with diabetes mellitus as a sequel to chronic pancreatitis.

Physical Examination Findings

- Thin body condition.
- Decreased muscle mass.
- Poor-quality hair coat.
- Cats with steatorrhea may have greasy “soiling” of the hair coat in the perineal area, but this is seen in the minority of cases.

CAUSES

- PAA.
- Chronic pancreatitis.
- Pancreatic adenocarcinoma or other abdominal tumor leading to pancreatic duct obstruction

RISK FACTORS

- Breed—German shepherd dogs, rough-coated collies, and Eurasians.
- Any condition predisposing dogs or cats to chronic pancreatitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Secondary causes of chronic diarrhea and weight loss (e.g., hepatic failure, renal failure, hypoadrenocorticism, and hyperthyroidism in cats).
- Primary gastrointestinal disease (e.g., infectious, inflammatory, neoplastic, mechanical, or toxic).

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

Direct/Indirect Fecal Examinations

Negative for parasites.

Exocrine Pancreatic Function Tests—Trypsin-Like Immunoreactivity (TLI)

- Diagnostic test of choice in both dogs and cats.
- Principle of test—serum TLI can be measured by an assay that detects trypsinogen and trypsin that is directly released into the blood from pancreatic acinar cells; serum TLI is detected in the serum of all normal dogs and cats with a functional exocrine pancreatic mass.
- Serum TLI concentrations are dramatically reduced with EPI—dogs: cTLI $\leq 2.5 \mu\text{g/L}$; cats: fTLI $\leq 8.0 \mu\text{g/L}$.
- The TLI tests are species specific.
- Advantages—simple; quick; single serum specimen (fasted); highly sensitive and specific for EPI in both species.

Other Exocrine Pancreatic Function Tests

- Assays of fecal proteolytic activity using casein-based substrates have been used to diagnose EPI in both dogs and cats; however, fecal proteolytic activity is associated with false-positive and false-negative test results and should only be used in exotic species for which a serum TLI test is not available.
- An assay for the measurement of fecal elastase has been validated for the dog; however, this test is associated with a high rate of false-positive test results; therefore a positive test result, suggesting EPI, must be verified by measurement of a serum cTLI concentration.

Screening Tests for Malassimilation

Microscopic examination of feces for undigested food, assessment of fecal proteolytic activity, and the plasma turbidity test are unreliable and *not* recommended.

Cobalamin and Folate

- Often run as a panel with TLI.
- Used to assess for concurrent small intestinal dysbiosis or concurrent small intestinal disease (such as inflammatory bowel disease [IBD]).
- Cobalamin (vitamin B₁₂) is frequently deficient in both dogs and cats with EPI and can lead to treatment failure or complications if not addressed.

IMAGING

Abdominal radiography and ultrasonography are unremarkable unless the patient has concurrent conditions.

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Chronic pancreatitis—microscopically, acini and possibly islets are depleted and replaced by fibrous tissue; there may also be an active inflammatory infiltration.
- PAA—marked atrophy/absence of pancreatic acinar tissue on gross and histopathologic inspection in dogs with PAA.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient medical management.
- Patients with concurrent diabetes mellitus may initially require hospitalization if ill (e.g., diabetic ketoacidosis).

NURSING CARE

N/A

ACTIVITY

No restriction.

DIET

- Type of diet does not play a role in the management of EPI in dogs and cats.
- However, low-fat and high-fiber diets should be avoided.

(CONTINUED)

CLIENT EDUCATION

- Discuss hereditary nature in German shepherd dogs.
- Discuss expense of pancreatic enzyme supplementation and need for lifelong therapy.
- Discuss the possibility of diabetes mellitus in patients with chronic pancreatitis.

SURGICAL CONSIDERATIONS

Mesenteric torsion has been reported in German shepherd dogs with EPI in Finland, but not North America.

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

- Powdered pancreatic enzymes are the treatment of choice (as a reference these products should contain at least 70,000 USP of lipase per teaspoon). • In Europe, microencapsulated products are available; because the lipase is protected from gastric inactivation a much smaller amount is needed for treatment.
- Initially—mix enzyme powder in food at a dosage of 1 teaspoon/10 kg body weight with each meal; feed at least two meals daily to promote weight gain. • Preincubation of enzymes with food does *not* improve the effectiveness of oral enzyme therapy, but may negatively impact owner compliance.
- Approximately 85% of all dogs with EPI and virtually all cats with EPI are cobalamin deficient and require parenteral or oral cobalamin supplementation (see Cobalamin Deficiency for dosing). • Administration of a proton pump inhibitor (e.g., omeprazole at 0.7–1.0 mg/kg q12h) may improve the condition in nonresponsive patients. • Most dogs and cats respond to therapy within 5–7 days; after a complete response has been achieved, the amount of pancreatic enzyme supplement may be gradually reduced to a dose that prevents return of clinical signs. • Oral antibiotic therapy (tylosin: 25 mg/kg PO q12h) may be required for 4–6 weeks in patients with concurrent dysbiosis, but in most patients dysbiosis resolves spontaneously upon commencement of enzyme replacement therapy.
- Severely malnourished dogs may also require supplementation with tocopherol; body stores of other fat-soluble vitamins are probably also decreased in dogs and cats with EPI, but supplementation does not appear to be crucial.

CONTRAINDICATIONS

Avoid tablets and capsules, as mixing of enzymes and chyme is unpredictable.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- The cost of pancreatic enzyme replacement is very high; also, some cats refuse to consume the pancreatic enzyme supplement; these patients

can often be successfully managed by addition of fish oil to the enzyme supplement or administration of raw beef, pork, or game pancreas. • Each teaspoon of pancreatic enzyme supplement needs to be replaced with 1–3 ounces (approximately 30–90 g) of raw chopped pancreas.

- Raw pancreas can be kept frozen for months without losing enzymatic activity.

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

- Weekly for first month of therapy.
- Diarrhea improves markedly—fecal consistency typically normalizes within 1 week. • Gain in bodyweight. • Patients that fail to respond after 2 weeks of enzyme therapy and cobalamin supplementation should be treated for secondary intestinal dysbiosis. • Once bodyweight and condition normalize, gradually reduce daily dosage of enzyme supplements to a level that maintains normal fecal quality and bodyweight.

PREVENTION/AVOIDANCE

Do not breed patients that belong to a breed predisposed to PAA.

POSSIBLE COMPLICATIONS

- Approximately 20% of dogs fail to respond to pancreatic enzymes and need further evaluation and therapy. • Most patients with EPI have cobalamin deficiency and need to be managed accordingly. • Some dogs and cats treated with pancreatic enzyme supplements develop oral ulcerations; in most of these patients the dose of pancreatic enzyme supplements can be decreased, while maintaining therapeutic response; in a few patients, the dose of the pancreatic enzyme supplement needs to be adjusted frequently to avoid treatment failure and oral ulceration. • Two cats with EPI and vitamin K-responsive coagulopathy have been reported; thus, patients that present with a bleeding diathesis should be further evaluated and possibly treated with parenteral vitamin K supplementation.

EXPECTED COURSE AND PROGNOSIS

- Most causes are irreversible, and lifelong therapy is required. • Patients with EPI alone have a good prognosis with appropriate enzyme supplementation and supportive management.
- Prognosis is more guarded in patients with EPI and concurrent diabetes mellitus.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Dysbiosis. • Cobalamin deficiency. • IBD.
- Diabetes mellitus. • Associated vitamin K-responsive coagulopathy.

AGE-RELATED FACTORS

Consider EPI in young adult German shepherd dogs with weight loss and loose stools.

ZOONOTIC POTENTIAL

None

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PREGNANCY/FERTILITY/BREEDING

Do not breed animals with EPI suspected to be due to PAA.

SYNONYMS

None

SEE ALSO

- Cobalamin Deficiency.
- Diarrhea, Chronic—Cats.
- Diarrhea, Chronic—Dogs.
- Pancreatitis—Cats.
- Small Intestinal Dysbiosis.

ABBREVIATIONS

- cTLI = canine trypsin-like immunoreactivity.
- EPI = exocrine pancreatic insufficiency.
- fTLI = feline trypsin-like immunoreactivity.
- IBD = inflammatory bowel disease.
- PAA = pancreatic acinar atrophy.
- TLI = trypsin-like immunoreactivity.

INTERNET RESOURCES

<http://www.vetmed.tamu.edu/gilab>

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Client Education Handout
available online

FELINE CALICIVIRUS INFECTION



BASICS

DEFINITION

A common viral respiratory disease of domestic and exotic cats characterized by upper respiratory disease and oral ulceration, occasionally pneumonia or arthritis, and rarely a highly fatal systemic hemorrhagic disease (FCV-VSD).

PATHOPHYSIOLOGY

- Spread through ocular, nasal, and oral secretions.
- Transmission typically occurs through direct contact or fomite exposure; droplet transmission possible within 4–5 feet; replication takes place primarily in respiratory and oral tissues.
- Rapid cytolysis of infected cells results in tissue pathology and clinical disease.

SYSTEMS AFFECTED

- Gastrointestinal—ulceration of the tongue common; occasional ulceration of the hard palate and lips.
- Hemic/lymphatic/immune—hemorrhage; splenic necrosis (FCV-VSD).
- Hepatobiliary—hepatic necrosis (FCV-VSD).
- Musculoskeletal—acute arthritis.
- Ophthalmic—acute serous conjunctivitis without keratitis or corneal ulcers.
- Respiratory—rhinitis; interstitial pneumonia; ulceration of nose tip.
- Skin/exocrine—subcutaneous edema; ulcerations of pinnae or pawpads; pancreatic necrosis (FCV-VSD).

GENETICS

None

INCIDENCE/PREVALENCE

- Persistent infection common, resulting in virus-shedding carriers.
- Clinical disease—common in multicat facilities, shelters, breeding catteries.
- Routine vaccination—reduces incidence and severity of clinical disease; has not decreased prevalence of the virus.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Breed Predilections

None

Mean Age and Range

- Young kittens >6 weeks old—most common.
- Cats of any age may show clinical disease.

Predominant Sex

None

SIGNS

General Comments

Severity of disease is dependent on host immune status, virulence of infecting strain, and presence of co-infections. Most common manifestation involves self-limiting upper respiratory tract disease and oral ulceration.

Historical Findings

- Sudden onset.
- Anorexia.
- Serous ocular or nasal discharge, usually with little or no sneezing.
- Ulcers on tongue, hard palate, lips, tip of nose, or around claws.
- Dyspnea from pneumonia.
- Acute, painful lameness.

Physical Examination Findings

- Ranging from generally alert and in good condition to lethargy and decreased mentation.
- Fever.
- Ulcers of tongue/mouth may occur without other signs.
- Hypersalivation.
- Upper to lower respiratory tract disease—nasal discharge, or stertor; wheezes, crackles, or increased bronchovesicular sounds on pulmonary auscultation,
- Epistaxis or hematochezia with systemic hemorrhage (FCV-VSD).
- Facial and limb edema with crusting/ulcerations of face, pinnae, and feet due to vasculitis (FCV-VSD).
- Icterus (FCV-VSD).

CAUSES

- A small, nonenveloped single-stranded RNA virus, feline calicivirus (FCV).
- Numerous strains exist in nature, with varying degrees of antigenic cross-reactivity.
- More than one serotype.
- Relatively stable and resistant to many disinfectants.

RISK FACTORS

- Lack of vaccination or improper vaccination.
- Multicat facilities.
- Concurrent infections with other pathogens, e.g., feline herpesvirus (FHV), feline panleukopenia virus (FPV), feline immunodeficiency virus (FIV), feline leukemia virus (FeLV).
- Poor ventilation.
- Stress.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- FHV.
- Chlamydiosis.
- *Bordetella bronchiseptica*.

CBC/BIOCHEMISTRY/URINALYSIS

No characteristic or consistent findings.

OTHER LABORATORY TESTS

Often diagnosed on clinical signs.

IMAGING

Radiographs of lungs—consolidated lung tissue in cats with pneumonia.

DIAGNOSTIC PROCEDURES

- PCR—opharyngeal swabs most likely to detect virus; positive result does not prove that FCV is causative agent for disease due to persistently shedding cats.
- Cell cultures to isolate virus—oral pharynx; lung tissue; feces; blood; secretions from nose and conjunctiva.
- Immunofluorescent assays of lung tissue—viral antigen.
- Serologic testing on paired serum samples—detect rise in neutralizing antibody titers against virus; vaccination interferes with results from serum neutralization testing.

PATHOLOGIC FINDINGS

- Gross—upper respiratory infection; ocular and nasal discharge; pneumonia with consolidation of large portions of individual lung lobes; possible ulcerations on tongue, lips, and hard palate; systemic hemorrhages.
- Histopathologic—interstitial pneumonia of large portions of individual lung lobes; ulcerations on epithelium of tongue, lips, and hard palate; mild inflammatory reactions in nose and conjunctiva; systemic hemorrhages, vasculitis, or necrosis.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient, unless severe pneumonia, hemorrhage, or severe systemic disease.

NURSING CARE

- Clean eyes and nose as indicated with warm water or saline.
- Provide access to steam, such as in a bathroom, to clear secretions.
- Provide palatable, soft foods.
- Oxygen—with severe pneumonia.

ACTIVITY

Patients should be restricted from contact with other cats to prevent transmission of causative virus.

DIET

- No restrictions.
- Special diets—to entice anorectic cats to resume eating.
- Soft foods—if ulcerations restrict eating.

CLIENT EDUCATION

Discuss need for proper vaccination and to modify vaccination protocol in breeding catteries to include kittens before they

FELINE CALICIVIRUS INFECTION

(CONTINUED)

become infected (often at 6–8 weeks of age) from a carrier queen.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

- No specific antiviral drugs are clearly indicated.
- Broad-spectrum antibiotics—indicated for treatment of secondary bacterial infections (e.g., amoxicillin or amoxicillin-clavulanate at 22 mg/kg PO q12h; doxycycline at 5 mg/kg PO q12h).
- Secondary bacterial infections of affected cats not nearly as important as with FHV-1 infections.
- Antibiotic eye ointments—to reduce secondary bacterial infections of conjunctiva.
- Pain medication—as indicated for arthritis pain or significant ulceration.

CONTRAINdications

None

PRECAUTIONS

None

POSSIBLE INTERACTIONS

None

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Monitor for sudden development of dyspnea associated with pneumonia.
- No specific laboratory tests.

PREVENTION/AVOIDANCE

- American Association of Feline Practitioners—classifies FHV, FPV, and FCV as core vaccines; vaccinate all cats with either a modified live virus (MLV) or inactivated core vaccine on initial visit (as early as 6 weeks of age), repeat every 3–4 weeks until 16 weeks of age, and booster 1 year after last kitten vaccine; revaccinate every 3 years.
- Breeding catteries—respiratory disease is a problem; vaccinate kittens at earlier age, either with additional vaccination at 4–5 weeks or with intranasal vaccine at 10–14

days; follow-up vaccinations every 3–4 weeks until 16 weeks of age.

- Vaccination will not prevent virus infection in subsequent exposure, but can prevent serious clinical disease caused by most strains; FCV-VSD can occur in vaccinated cats.
- Environmental management—decrease housing density; isolate affected cats by >4 ft; beware of hygiene and fomites; disinfect with dilute (1 : 30) bleach.

POSSIBLE COMPLICATIONS

- Interstitial pneumonia—most serious complication; can be life-threatening.
- Secondary bacterial infections of lungs or upper airways.

EXPECTED COURSE AND PROGNOSIS

- Clinical disease—usually appears 3–4 days after exposure.
- With supportive care, infection usually self-limiting and cats with upper respiratory signs respond favorably within 7–10 days.
- Oral ulcerations typically improve in 2–3 weeks.
- Lameness usually resolves in 1–2 days.
- Prognosis excellent, unless severe pneumonia or systemic hemorrhagic disease develops.
- FCV-VSD may be severe and fatal.
- Recovered cats—persistently infected for long periods; will shed small quantities of virus in oral secretions continuously.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Affected cats may also be concurrently infected with FHV-1, especially in multicat and breeding facilities. FCV has been implicated in development of feline chronic gingivostomatitis.

AGE-RELATED FACTORS

Usually occurs in young kittens whose maternally derived immunity has waned.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Generally no problem, because most cats have been exposed or vaccinated before becoming pregnant.

SYNOMYS

- Feline picornavirus infection—FCV originally classified as a picornavirus; older literature refers to the infection by this name; no known picornavirus infects cats.

- Limping kitten syndrome.
- Hemorrhagic calicivirus.

SEE ALSO

- Chlamydiosis—Cats.
- Feline Herpesvirus Infection.
- Feline (Upper) Respiratory Infections.
- Rhinitis and Sinusitis.
- Stomatitis and Oral Ulceration.

ABBREVIATIONS

- FCV = feline calicivirus.
- FCV-VSD = feline calicivirus-virulent systemic disease.
- FeLV = feline leukemia virus.
- FHV = feline herpesvirus.
- FIV = feline immunodeficiency virus.
- FPV = feline panleukopenia virus.
- MLV = modified live virus.

INTERNET RESOURCES

[http://www.abcdcatsvets.org/
feline-calicivirus-infection-2012-edition](http://www.abcdcatsvets.org/feline-calicivirus-infection-2012-edition)

Suggested Reading

- Afonso MM, Gaskell RM, Radford A. Feline upper respiratory infections. In: Ettinger SJ, Feldman EC, Côté, E, eds. Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat, 8th ed. St. Louis, MO: Elsevier, 2017, pp. 1013–1016.
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Consulting Editor Amie Koenig

Acknowledgment The author and book editors acknowledge the prior contribution of Fred W. Scott.



Client Education Handout
available online

FELINE IDIOPATHIC LOWER URINARY TRACT DISEASE



BASICS

DEFINITION

Idiopathic lower urinary tract disease, commonly referred to as feline idiopathic cystitis (FIC), is a nonmalignant, sterile, inflammatory disease of the urinary bladder and urethra. It is the most common urinary disorder of young to middle-aged cats and is characterized by dysuria, pollakiuria, hematuria, peruria, and in some cases urinary obstruction. Clinical observations suggest that FIC is associated with different clinical phenotypes (acute self-limiting, chronic, nonobstructive, and obstructive forms) and pathologic phenotypes (ulcerative, inflammatory, hyperplastic, nonulcerative, and noninflammatory forms). Regardless of form, the terms idiopathic lower urinary tract disease and FIC represent an exclusionary diagnosis established only after known causes have been eliminated.

PATOPHYSIOLOGY

- Etiopathogenesis is uncertain.
- Urinary bladder abnormalities include alterations in urothelial barrier structure and function, differentiation and repair, signaling, eicosanoid biosynthesis, and innate immune and inflammatory responses.
- Association of FIC with stress (environmental, psychologic, physiologic, or comorbid pathologic stressors) and identification of multiple abnormalities of nervous and endocrine systems have led to hypothesis that systemic psychoneuroendocrine factors may have a role in the pathogenesis.
- Clinical and morphologic features of chronic forms of FIC are similar to those of an idiopathic cystopathy of humans called interstitial cystitis/painful bladder syndrome (IC/PBS). However, the extent to which the feline and human forms share pathogenic mechanisms has not yet been fully defined.

SYSTEMS AFFECTED

- Renal/urologic—lower urinary tract.
- Persistent urethral outflow obstruction results in postrenal azotemia.

INCIDENCE/PREVALENCE

- Incidence of hematuria, dysuria, and/or urethral obstruction (UO) in domestic cats has been previously reported to be ~0.5–1% per year.
- Hospital morbidity rate for FIC in cats with lower urinary tract signs is ~65%; it is the single most common cause of lower urinary tract signs in cats.

SIGNALMENT

Species

Cat

Mean Age and Range

- May occur at any age, but most commonly recognized in young to middle-aged adults (mean 3.5 years, range: 2–7 years).

- Uncommon in cats <1 and >10 years old.

SIGNS

Historical Findings

- Dysuria.
- Hematuria.
- Pollakiuria.
- Periuria.
- Urge incontinence.
- Outflow obstruction.

Physical Examination Findings

Thickened, firm, contracted bladder wall.

CAUSES

See Pathophysiology.

RISK FACTORS

- Male, middle-aged, and overweight cats, as well as cats housed indoors or living in a home with other cats, are at increased risk.
- Feeding dry food has not been consistently recognized as a risk factor.
- Stress may play a role in precipitating or exacerbating signs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Metabolic disorders including various types of uroliths/urethral plugs.
- Urinary tract infection (UTI) from bacteria, mycoplasma/ureaplasma, fungal agents, and parasites.
- Trauma.
- Neurogenic disorders including reflex dyssynergia, urethral spasm, and hypotonic or atonic bladder.
- Iatrogenic disease including reverse flushing solutions, indwelling and postsurgical urethral catheters, and urethrostomy complications.
- Anatomic abnormalities including urachal anomalies and acquired urethral strictures.
- Neoplasia.
- Clinical signs may be confused with constipation.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematuria and proteinuria without significant pyuria or bacteriuria—usually present.
- If UO persists, serum chemistry profiles reveal azotemia, hyperphosphatemia, hyperkalemia, and acidosis.

OTHER LABORATORY TESTS

- Absence of bacteriuria—verify by quantitative urine culture; collect urine specimens by cystocentesis to avoid contamination.
- Transmission electron microscopy has revealed calicivirus-like particles in some urethral plugs.

IMAGING

- Survey radiography may exclude radiopaque uroliths or urethral plugs.

- Ultrasoundography may exclude uroliths and thickening of bladder wall due to inflammation or neoplasia.

- Contrast cystography may exclude small or radiolucent uroliths, blood clots, urethral stricture, vesicourachal diverticula, and thickening of bladder wall due to inflammation or neoplasia.

DIAGNOSTIC PROCEDURES

- Cystoscopy may exclude uroliths and diverticula.
- Biopsies of urinary bladder wall may permit morphologic characterization of inflammatory or neoplastic lesions.

PATHOLOGIC FINDINGS

- Cystoscopy may reveal petechial hemorrhages (glomerulations) of urinary bladder mucosa.
- Mucosal ulceration or hyperplasia, submucosal edema, hemorrhage, neovascularization, fibrosis, and mononuclear inflammatory cell infiltrates are prominent features of chronic FIC.



TREATMENT

APPROPRIATE HEALTH CARE

- Patients with nonobstructive lower urinary tract diseases—typically managed as outpatients; diagnostic evaluation may require brief hospitalization.
- Patients with obstructive lower urinary tract diseases—usually hospitalized for diagnosis and management.

DIET

- Results of prospective, randomized, double-masked, controlled clinical trial provided evidence that feeding specific multipurpose therapeutic urinary food (Hill's c/d Multicare) enriched with omega-3 fatty acids (EPA and DHA) and antioxidants significantly reduced rate of recurrent episodes of FIC signs.
- Low-grade evidence that recurrence of signs may be minimized by feeding moist foods.
- Appropriate dietary management for persistent crystalluria associated with matrix-crystalline urethral plugs.

CLIENT EDUCATION

- Hematuria, dysuria, and pollakiuria—often self-limiting within 4–7 days in most cats. Signs may recur unpredictably; up to 65% of cats experience ≥1 episodes within 1–2 years.
- A lack of controlled studies demonstrating efficacy of most drugs used to treat this disorder symptomatically.
- Reduce environmental stress by minimizing impact of changes in the home and maintaining a constant diet. Environmental enrichment for indoor-housed cats consists of provision of necessary resources (food, water, litter boxes, space, play), providing a safe place to hide, refinement of cat-owner interactions, and management of conflict.

(CONTINUED)

FELINE IDIOPATHIC LOWER URINARY TRACT DISEASE

- Provide proper litter box hygiene.
- Males should be monitored for signs of UO.

SURGICAL CONSIDERATIONS

Do not perform perineal urethrostomy to minimize recurrent UO without localizing obstructive disease to penile urethra by contrast urethrography.



MEDICATIONS

DRUG(S) OF CHOICE

- Amitriptyline—empirically advocated to treat cats with severe recurrent or persistent signs; suggested dosage is 5–10 mg/cat q24h given at night; not recommended for treatment of acute, self-limiting episodes of FIC.
- Butorphanol, buprenorphine, and fentanyl—have been empirically recommended for short-term analgesia in cats with FIC; there have been no reports of controlled studies to evaluate their safety or efficacy.
- Prazosin—may be used to minimize reflex dyssynergia and functional urethral outflow obstruction; suggested dosage is 0.25–0.5 mg/cat PO q12–24h.
- Tolteridine may be considered as an anticholinergic and antispasmodic to minimize hyperactivity of bladder detrusor muscle and urge incontinence; suggested dose is 0.05 mg/kg PO q12h; there have been no controlled studies to evaluate its safety or efficacy.
- Glycosaminoglycans—empirically recommended to help repair glycosaminoglycan coating of urothelium; results of controlled clinical studies have not demonstrated any beneficial effects on reducing severity or frequency of clinical signs in cats with FIC.
- Feline facial pheromone—empirically recommended to decrease signs of stress in cats with FIC; results of controlled clinical studies have not demonstrated any beneficial effects in management of FIC.
- Corticosteroids—no detectable effect on remission of acute clinical signs demonstrated; predispose to bacterial UTIs, especially in cats with indwelling transurethral catheters.
- Nonsteroidal anti-inflammatory drugs (NSAIDs)—empirically recommended by

some because of their anti-inflammatory and analgesic properties; the safety of NSAIDs in the treatment of FIC has not been evaluated by controlled clinical trials.

- Antibiotics—no detectable effect on remission of clinical signs in cats demonstrated.

CONTRAINdications

- Phenazopyridine—may result in methemoglobinemia and irreversible oxidative changes in hemoglobin resulting in formation of Heinz bodies and anemia.
- Methylene blue—may cause Heinz bodies and severe anemia.
- Bethanechol—do not use in patients with UO.

PRECAUTIONS

- Cats with UO and postrenal azotemia are at increased risk for adverse drug events, especially with drugs and anesthetics that depend on renal elimination or metabolism.
- Indwelling transurethral catheters, especially when associated with fluid-induced diuresis, predispose patients to bacterial UTIs.



FOLLOW-UP

PATIENT MONITORING

Monitor hematuria by urinalysis; cystocentesis may cause iatrogenic hematuria, so naturally voided samples are preferred.

PREVENTION/AVOIDANCE

Best evidence suggests that multimodal approach to managing cats with acute nonobstructive FIC is advised, including multipurpose therapeutic urinary food proven to reduce rate of recurrent episodes of FIC signs (Hill's c/d Multicare); environmental enrichment; feeding moist food; and short-term administration of analgesics to control signs of pain.

POSSIBLE COMPLICATIONS

- Indwelling transurethral catheters—cause trauma; predispose to ascending bacterial UTIs.
- Perineal urethrostomies—predispose to bacterial UTIs and urethral strictures.

EXPECTED COURSE AND PROGNOSIS
Hematuria, dysuria, and pollakiuria often self-limiting within 4–7 days in most patients. These signs often recur unpredictably.



MISCELLANEOUS

AGE-RELATED FACTORS

Frequency of recurrence appears to decline with advancing age.

SYNONYMS

- Feline idiopathic cystitis.
- Feline interstitial cystitis.

SEE ALSO

- Dysuria, Pollakiuria, and Stranguria.
- Hematuria.
- Lower Urinary Tract Infection, Bacterial.
- Lower Urinary Tract Infection, Fungal.
- Urolithiasis, Struvite—Cats.

ABBREVIATIONS

- FIC = feline idiopathic cystitis.
- IC/PBS = interstitial cystitis/painful bladder syndrome.
- NSAID = nonsteroidal anti-inflammatory drug.
- UO = urethral obstruction.
- UTI = urinary tract infection.

Suggested Reading

Forrester SD, Towell TL. Feline idiopathic cystitis. *Vet Clin Small Anim* 2015, 45:783–806.

Kruger JM, Lulich JP, MacLeay J, et al. A randomized, double-masked, multicenter, clinical trial of two foods for long-term management of acute nonobstructive feline idiopathic cystitis (FIC). *J Am Vet Med Assoc* 2015; 247:508–517.

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Consulting Editor J.D. Foster

Acknowledgment The author and book editors acknowledge the prior contributions of Carl A. Osborne and Jody P. Lulich



Client Education Handout
available online

FELINE IMMUNODEFICIENCY VIRUS (FIV) INFECTION



BASICS

DEFINITION

A complex retrovirus that causes immunodeficiency in domestic cats; same genus (*Lentivirus*) as human immunodeficiency virus (HIV).

PATHOPHYSIOLOGY

- Infection causes immune dysfunction due to cytokine alterations, nonspecific hyperactivation of B and T lymphocytes, and apoptosis of T cells.
- Strain or subtype influences pathogenicity; subtypes A and B are most common in the United States.
- Acute infection—virus spreads from site of entry to lymph tissues and thymus via dendritic cells, first infecting T lymphocytes, then macrophages.
- Primary receptor is feline CD134; uses chemokine receptor CXCR4 as co-receptor.
- CD4+ and CD8+ T cells can be infected; virus selectively and progressively decreases CD4+ (T-helper) cells; inversion of the CD4+ : CD8+ ratio (from ~2 : 1 to <1 : 1) develops slowly, with absolute decrease of CD4+ T cells after several months of infection.
- Early infection and activation of CD4+ CD25+ regulatory T cells may limit effective immune response to FIV infection.
- Cats clinically asymptomatic until cell-mediated immunity is disrupted; humoral immune function declines in advanced stages of infection.
- T cells and macrophages—main cellular reservoirs of virus in affected cats; lymphoid tissues are reservoirs throughout the body.
- Astrocyte and microglial cells in brain and megakaryocytes and mononuclear bone marrow cells may be infected; neuronal loss may occur.
- Co-infection with feline leukemia virus (FeLV) may increase expression of FIV in many tissues, including kidney, brain, and liver.

SYSTEMS AFFECTED

- Hemic/lymphatic/immune—loss of CD4+ T cells; lymphocytic/plasmacytic infiltrates in tissues (especially gingiva, lymphoid tissues); lymphomas, mast cell tumors.
- Gastrointestinal—panleukopenia-like syndrome.
- Nervous—alterations in astrocyte function and neurotransmitter expression.
- Ophthalmic—anterior uveitis.
- Renal/urologic—nephropathy.
- Reproductive—fetal death or perinatal infections.
- Cardiovascular—possible myocarditis.
- Other body systems—secondary infections.

GENETICS

No predisposition for infection, but may play role in progression and severity.

INCIDENCE/PREVALENCE

United States and Canada—1–3% prevalence in healthy cat populations; 9–15% in sick cats.

GEOGRAPHIC DISTRIBUTION

Worldwide; variable seroprevalence.

SIGNALMENT

Species

Cat

Mean Age and Range

- Prevalence of infection increases with age.
- Mean age—6 years at time of diagnosis.

Predominant Sex

Male—more aggressive; roaming.

SIGNS

General Comments

- Diverse due to immunosuppressive nature.
- Cannot be clinically distinguished from FeLV-associated immunodeficiency.

Historical Findings

Recurrent minor illnesses, especially upper respiratory and gastrointestinal.

Physical Examination Findings

- Opportunistic infections.
- Lymphadenomegaly—mild to moderate.
- Gingivitis, stomatitis, periodontitis (25–50% of cases).
- Rhinitis, conjunctivitis, keratitis (30% of cases); often associated with feline herpesvirus and calicivirus infections.
- Persistent diarrhea (10–20% of cases); bacterial or fungal overgrowth, parasite-induced inflammation; direct effect of FIV on gastrointestinal epithelium.
- Chronic, nonresponsive, or recurrent infections of external ear and skin—bacterial infections or dermatophytosis.
- Fever and wasting—especially in later stage.
- Ocular disease—anterior uveitis; pars planitis; glaucoma.
- Neurologic abnormalities—disruption of normal sleep patterns; behavioral changes (pacing and aggression); motor and neurocognitive deficits; peripheral neuropathies.

CAUSES

- Cat-to-cat transmission—usually by bite wounds.
- Occasional perinatal transmission.
- Sexual transmission uncommon, although FIV has been detected in semen.

RISK FACTORS

- Male.
- Free-roaming or feral.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary bacterial, parasitic, fungal, or viral infections, especially FeLV.
- Toxoplasmosis—neurologic and ocular manifestations may be the result of *Toxoplasma* infection, FIV infection, or both.
- Nonviral neoplastic diseases.
- Chronic kidney disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia, lymphopenia, or neutropenia—common; but neutrophilia may occur in response to secondary infections; may also be normal.
- Urinalysis and serum chemistry profile—hypergammaglobulinemia, azotemia with isosthenuria, proteinuria (immune-mediated glomerulonephritis).

OTHER LABORATORY TESTS

Serologic Testing

- Detects antibodies to FIV.
- ELISA—routine screening; point-of-care and diagnostic laboratory kits; confirm positive results with additional testing, especially in healthy, low-risk cats.
- Western blot (immunoblot)—confirmatory testing of ELISA-positive samples.
- Kittens—when <6 months old may test positive owing to passive transfer of antibodies from FIV-positive queen; positive test does not indicate infection; retest at 8–12 months to determine infection.
- Vaccinated cats may test positive for FIV antibodies.

Others

- Virus isolation and subtyping.
- Reverse transcriptase polymerase chain reaction (RT-PCR)—useful in vaccinated cats or kittens with maternal antibody.
- CD4+ : CD8+ evaluation—helps determine extent of immunosuppression.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A

PATHOLOGIC FINDINGS

- Lymphadenopathy—initially, follicular hyperplasia and paracortical infiltration of plasmacytes; later, follicular hyperplasia with follicular depletion or involution; in terminal stages, lymphoid depletion.
- Lymphocytic and plasmacytic infiltrates—gingiva, lymph nodes and other lymphoid tissues, spleen, kidney, liver, and brain.
- Perivascular cuffing, gliosis, neuronal loss, white matter vacuolization, and occasional giant cells in the brain.

(CONTINUED)

FELINE IMMUNODEFICIENCY VIRUS (FIV) INFECTION

F

- Intestinal lesions similar to those seen with feline parvovirus infection.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient sufficient for most patients.
- Inpatient—with severe secondary infections until stable.

NURSING CARE

- Primary consideration—manage secondary and opportunistic infections.
- Supportive therapy—parenteral fluids and nutrition, as required.

ACTIVITY

Normal

DIET

Normal, may alter as necessary for cats with diarrhea, kidney disease.

CLIENT EDUCATION

- Inform client that infection is slowly progressive and healthy antibody-positive cats may remain healthy for years.
- Advise client that cats with clinical signs will have recurrent or chronic health problems that require medical attention.
- Discuss importance of keeping cats indoors to protect them from exposure to secondary pathogens and to prevent spread of FIV.

SURGICAL CONSIDERATIONS

- Oral treatment or surgery—dental cleaning, tooth extraction, gingival biopsy as needed; gingivitis and stomatitis may be refractory to treatment.
- Biopsy or removal of neoplastic lesions.



MEDICATIONS

DRUG(S) OF CHOICE

- Zidovudine (Retrovir®) 5–10 mg/kg PO q12h—antiviral agent; most effective against acute infection; monitor for bone marrow toxicity.
- Immunomodulatory drugs—may alleviate some clinical signs:
 - α -interferon (Roferon®-A)—diluted in saline at 30 units/day PO for 7 days, every other week; may increase survival rates and improve clinical status.
 - Feline omega-interferon (Virbagen® Omega)—1 million units/kg/day SC q24h for 5 days at 3 intervals (d0–4, d14–18, d60–64); lower-dose oral protocols may be effective.
- Antibacterial or antimycotic drugs—as indicated; prolonged therapy or high dosages may be required.

- Corticosteroids or gold salts—judicious but aggressive use may help control immune-mediated inflammation.
- Topical corticosteroids—for anterior uveitis; long-term response may be incomplete or poor; pars planitis often regresses spontaneously and may recur.
- Glaucoma—standard treatment.
- Vaccinate for respiratory and enteric pathogens based on individual risk assessment. Rabies vaccination according to regulatory guidelines.

CONTRAINDICATIONS

- Griseofulvin—avoid or use with extreme caution in FIV-positive cats; may induce severe neutropenia; neutropenia is reversible if drug is withdrawn early enough, but secondary infections can be life-threatening.

PRECAUTIONS

Systemic corticosteroids—use with caution; may lead to further immunosuppression.

ALTERNATIVE DRUG(S)

- Propionibacterium acnes* (ImmunoRegulin®)—0.5 mL/cat IV once or twice weekly.
- Acemannan (Carrisyn®)—100 mg/cat PO q24h.



FOLLOW-UP

PATIENT MONITORING

Varies according to secondary infections and other manifestations of disease.

PREVENTION/AVOIDANCE

- Prevent contact with FIV-positive cats.
- Quarantine and test incoming cats before introducing into multicat households.
- Vaccine no longer available in the U.S.

EXPECTED COURSE AND PROGNOSIS

- Approx. 20% of cats die within 2 years of diagnosis or 4.5–6 years after estimated time of infection, but >50% remain asymptomatic.
- In late stages of disease (wasting and frequent or severe opportunistic infections), life expectancy \leq 1 year.
- Overall survival time and quality of life for many FIV-positive cats will be similar to uninfected cats.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Secondary bacterial, viral, fungal, and parasitic disease.
- Lymphoid tumors.
- Immune-mediated disease.

AGE-RELATED FACTORS

Kittens (up to 4–6 months old) may test positive because of passive antibody transfer.

ZOONOTIC POTENTIAL

- None known.
- Potential transmission of secondary pathogens (e.g., *Toxoplasma gondii*) to immunocompromised humans.

PREGNANCY/FERTILITY/BREEDING

FIV-positive queens—reported abortions and stillbirths; transmission to kittens infrequent if queen is antibody-positive before conception; rate of transmission may be subtype or strain-dependent (>90% for experimental infections with some strains).

SYNOMYS

Feline immunodeficiency syndrome.

SEE ALSO

- Feline Calicivirus Infection.
- Feline Herpesvirus Infection.
- Feline Leukemia Virus (FeLV) Infection.
- Feline Stomatitis—Feline Chronic Gingivostomatitis (FCGS).
- Gingival Enlargement/Hyperplasia.

INTERNET RESOURCES

<https://catvets.com/public/PDFs/Practice-Guidelines/RetrovirusGLS-Summary.pdf>

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- HIV = human immunodeficiency virus.
- RT-PCR = reverse transcriptase polymerase chain reaction.

Suggested Reading

Hartmann K, Wooding A, Bergmann M. Efficacy of antiviral drugs against feline immunodeficiency virus. *Vet Sci* 2015, 2:456–476.

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Consulting Editor Amie Koenig



Client Education Handout
available online

FELINE INFECTIOUS DIARRHEA



BASICS

DEFINITION

- Diarrhea is defined as excess fecal water, increased quantity of fecal material, or increased frequency of bowel movements.
- Etiologies include viral, enteropathogenic bacterial, protozoal, fungal, or helminths; small bowel, large bowel, or mixed bowel diarrhea.
- Secondary systemic signs likely with infection by feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), feline enteric coronavirus (FECV), feline parvovirus (FPV), histoplasmosis.
- Presence of organisms on diagnostic screening does not indicate causation; patient factors (clinical signs, age, environmental exposure) should be considered before treatment.
- Some cats will have self-resolution; diagnostic testing may be appropriate for more severely affected animals or if clinical signs are persistent despite supportive care and having ruled out other causes of acute or chronic diarrhea; kittens with acute diarrhea should be screened for FPV.

PATHOPHYSIOLOGY

- Typically, fecal–oral route of infection.
- Diarrhea may result from decreased intestinal absorption or increased intestinal secretion caused by enterotoxins, osmotic forces, or epithelial damage.
- Immune response to infectious organisms can contribute to development of diarrhea; activated white blood cells release inflammatory mediators that stimulate secretion and damage intestinal epithelium.

SYSTEMS AFFECTED

- Cardiovascular—fluid balance.
- Gastrointestinal (GI).

GENETICS

Feline infectious peritonitis (FIP) more likely in purebred cats.

INCIDENCE/PREVALENCE

- 84% of cats from shelters had enteropathogens—no difference with or without diarrhea.
- FECV more common in cats with diarrhea.

GEOGRAPHIC DISTRIBUTION

- Widespread.
- Prevalence of etiologies varies by region.
- Histoplasma more common in eastern United States, Latin America.

SIGNALMENT

Species

Cat

Breed Predilections

Purebred cats have higher prevalence of FIP.

Mean Age/Range

Young cats more likely to develop diarrhea from FECV, FPV, *Cryptosporidium*, helminths; FIP has bimodal distribution (young and old).

Predominant Sex

FIP more frequent in males.

SIGNS

General Comments

Range from mild to severe.

Historical Findings

- Acute or chronic, small or large bowel diarrhea.
- Possibly lethargy, vomiting, weakness, weight loss, hyporexia.
- Crowded environment.

Physical Examination Findings

- Dehydration.
- Poor body condition.
- Fluid/gas-filled intestinal loops.
- Signs of sepsis or systemic inflammatory response syndrome (SIRS) possible—tachycardia, hypotension, hyper/hypothermia, tachypnea, pale mucous membranes.
- Abdominal masses or enlarged lymph nodes may be palpable (histoplasmosis, FIP).
- With systemic infections may note choriorretinitis, icterus, neurologic deficits.

CAUSES

- Viral—FECV, FPV, astrovirus, calicivirus, FIV, FeLV, torovirus-like agent.
- Bacterial—*Campylobacter* spp., *Clostridium perfringens* enterotoxin A, *Clostridium difficile* toxins, *Salmonella* spp., *Escherichia coli*, *Yersinia* spp.
- Helminth—*Toxocara* spp., *Ancylostoma* spp., *Strongyloides* spp., *Toxascaris leonine*, *Spirometra* spp., *Trichuris vulpis*.
- Protozoal—*Giardia* spp., *Tritrichomonas foetus*, *Toxoplasma gondii*.
- Coccidial—*Cryptosporidium* spp., *Cystoisospora* spp.
- Fungal—*Histoplasma capsulatum*.

RISK FACTORS

- Pediatric, young adult cats more commonly affected, particularly with helminths, viral, and coccidial disease.
- Crowding, poor sanitation increase risk of transmission.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute diarrhea—dietary indiscretion, foreign body, GI neoplasia; non-GI diseases: hyperthyroidism, iatrogenic, hepatotoxicity, renal disease, and other systemic diseases (frequently have hyporexia, vomiting, icterus).
- Chronic diarrhea—chronic enteropathy (dietary responsive, antibiotic responsive, dysbiosis, or inflammatory bowel disease),

primary GI neoplasia, pancreatic insufficiency, and hepatic or renal disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia with intestinal parasitism or histoplasmosis.
- Leukopenia with FPV, sepsis from salmonellosis or translocation, bone marrow involvement with histoplasmosis or FeLV.
- Anemia and microcytosis suggest GI hemorrhage or iron deficiency, particularly with high worm burden.
- Elevated liver enzyme activities or creatine kinase with toxoplasmosis.
- Hyperglobulinemia, elevated total bilirubin with FIP.
- Hemoconcentration, prerenal azotemia, electrolyte derangements with dehydration.
- Panhypoproteinemia if protein-losing enteropathy or GI blood loss.

IMAGING

- Abdominal radiographs if no response to symptomatic care to rule out other causes of diarrhea.
- Abdominal ultrasound recommended in nonpediatric patients with diarrhea nonresponsive to symptomatic care.
- Thoracic radiographs may show pulmonary disease or enlarged lymph nodes with histoplasmosis or toxoplasmosis.

DIAGNOSTIC PROCEDURES

- Fecal flotation—for intestinal parasitism; false negatives are possible as ova are intermittently shed; cats suspected to have intestinal parasitism should have multiple fecal flotations or be treated with anthelmintics.
- Fecal cytology—bacterial morphology (frequent spirochetes, spores) or presence of fungal or protozoal organisms.
- Giardia* ELISA.
- Tritrichomonas PCR using “colonic flush” technique.
- Histoplasma enzyme immunoassay (EIA)—urine.
- Toxoplasmosis immunofluorescence antibody test (IFA) for immunoglobulin (Ig) G and IgM, rising titer between acute and convalescent samples.
- FIV antibody, FeLV antigen ELISA.
- Infectious diarrhea PCR panels assess for range of infectious causes of diarrhea; caution should be used in interpretation; positive results do not necessarily indicate causation and false-negative results possible.

PATHOLOGIC FINDINGS

- Gross examination of intestinal mucosa may demonstrate parasites attached to intestinal mucosa with multifocal hemorrhagic ulcerations, submucosal congestion or hemorrhage, intestinal wall thickening, lymphadenopathy.
- Histopathology of intestine may show eosinophilic, neutrophilic, pyogranulomatous, or lymphoplasmacytic enteritis with varying

(CONTINUED)

FELINE INFECTIOUS DIARRHEA**F**

degrees of hemorrhage and necrosis, depending on etiology; may visualize causative agent.

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

- Mildly affected cats treated as outpatients.
- Moderate to severely affected cats may require IV fluids for dehydration/electrolyte management.
- Dextrose should be supplemented parenterally for hypoglycemia,

ACTIVITY

N/A

DIET

- Diets high in easily digestible protein, including adequate taurine.
- In anorexic pediatric patients, nasogastric tube feeding of liquid diet recommended if anorexia >48 hours.

CLIENT EDUCATION

- For most infectious organisms, environmental decontamination prevents reinfection and transmission to other pets/humans; isolation during hospitalization may be warranted depending on cause.
- Appropriate vaccination and deworming schedules should be followed.
- Cats with identified infectious causes of diarrhea should be isolated from other cats until clinical signs resolve; *Histoplasma* not directly transmitted from cat to other hosts.

SURGICAL CONSIDERATIONS

Viral and parasitic enterocolitis can result in intussusceptions.

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

- Many cases self-resolve with supportive care and time.
- Empiric therapy, pending diagnostics if clinical signs persist—probiotics (Visbiome® 112.5 billion bacteria/cat/day), or metronidazole 10 mg/kg PO q12h, with fenbendazole 50 mg/kg PO q24h for 5 days.
- Anthelmintics—fenbendazole 50 mg/kg PO q24h for 5 days; pyrantel pamoate 10 g/kg PO q24h for 3 days.
- Coccidiostatic—sulfadimethoxine 50–60 mg/kg PO q24h for 5–10 days; ponazuril 50 mg/kg PO once.
- Campylobacteriosis with persistent clinical signs—erythromycin 10–15 mg/kg PO q8h; azithromycin 5–10 mg/kg PO q24h.
- Histoplasmosis—itraconazole 5–10 mg/kg PO q12–24h: do not use compounded formulations.

- Toxoplasmosis—clindamycin 10–17 mg/kg PO/IM/IV q8–12h for 4 weeks.
- Trichomoniasis—ronidazole 30 mg/kg PO q24h for 14 days.
- Patients with sepsis or leukopenia should be treated with broad-spectrum antibiotics.
- Cats with confirmed salmonella should *not* be treated with antibiotics unless systemically ill.

CONTRAINdications

N/A

PRECAUTIONS

- Metronidazole dose should be reduced in animals with hepatic insufficiency.
- Clindamycin should be given with food or water to prevent development of esophageal strictures.
- Ronidazole can cause neurotoxicity and should be discontinued if clinical signs including anorexia develop.

POSSIBLE INTERACTIONS

Dependent on drug used; itraconazole has many interactions.

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

- Case-based, may include reassessment of anemia, leukopenia, or electrolyte derangements as appropriate.
- Persistent clinical signs after appropriate treatment suggest alternative cause of diarrhea.
- Patients with recurrent clinical signs should be retested, particularly if environmental reinfection possible (e.g., giardiasis, campylobacteriosis).

PREVENTION/AVOIDANCE

- Routine vaccination.
- Monthly flea and heartworm preventative with combination anthelmintic therapy.
- Maintain clean facilities and quarantine ill patients.
- Do not allow nonimmunocompetent patients to contact other animals until determined to be low risk.

POSSIBLE COMPLICATIONS

- Sepsis.
- Anemia.
- Dehydration, electrolyte, acid-base disturbances.

EXPECTED COURSE AND PROGNOSIS

- Usually good to excellent; underlying immunosuppressive conditions may increase susceptibility to infection and worsen prognosis.
- Infectious agents that cause systemic illness likely have worse prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

Young animals more susceptible.

ZOONOTIC POTENTIAL

- Toxoplasmosis—human abortion.
- Giardiasis—low risk of transmission.
- Cryptosporidiosis.
- Salmonellosis.
- Campylobacter jejuni*.
- Toxocara* spp. (ascarids)—visceral larval migrans, most common in children.
- Ancylostoma* (hookworms)—cutaneous larval migrans, most common in children.

PREGNANCY/FERTILITY/BREEDING

Patients exhibiting clinical signs of illness should not be bred. If illness develops while pregnant, take caution regarding drug choice.

SEE ALSO

- Acute Diarrhea.
- Campylobacteriosis.
- Clostridial Enterotoxicosis.
- Coccidiosis.
- Diarrhea, Chronic—Cats.
- Feline Infectious Peritonitis (FIP).
- Feline Panleukopenia.
- Giardiasis.
- Histoplasmosis.
- Hookworms (Ancylostomiasis).
- Roundworms (Ascariasis).
- Salmonellosis.
- Toxoplasmosis.
- Whipworms (Trichuriasis).

ABBREVIATIONS

- EIA = enzyme immunoassay.
- FECV = feline enteric coronavirus.
- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIV = feline immunodeficiency virus.
- FPV = feline parvovirus.
- GI = gastrointestinal.
- IFA = immunofluorescence antibody test.
- Ig = immunoglobulin.
- SIRS = systemic inflammatory response syndrome.

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FELINE INFECTIOUS PERITONITIS (FIP)



BASICS

DEFINITION

A systemic, immune-mediated, viral disease of cats characterized by insidious onset, persistent fever, pyogranulomatous tissue reaction, exudative effusions in body cavities, and high mortality.

PATHOPHYSIOLOGY

- The term feline coronavirus (FCoV) encompasses feline enteric coronavirus (FECV) and feline infectious peritonitis virus (FIPV).
- FECV is common and highly infectious; replicates locally in intestinal tract.
- FIPV infects monocytes/macrophages, which disseminate virus throughout body; localizes at vein wall and perivascular sites.
- FIP is an immune-mediated disease—perivascular accumulation of virus-infected macrophages and inflammatory cells produces pyogranulomatous inflammation in various organs.

SYSTEMS AFFECTED

- Multisystemic—pyogranulomatous or granulomatous lesions on omentum, serosal surface of abdominal organs, within abdominal lymph nodes, and submucosa of intestinal tract.
- Nervous—vascular lesions throughout CNS, especially in meninges.
- Ophthalmic—uveitis, chorioretinitis, and iritis.
- Respiratory—lesions on lung surfaces, pleural effusion.

INCIDENCE/PREVALENCE

- Prevalence of antibodies against FCoV—high, due to widespread presence of FECV, especially in multicat facilities.
- Incidence of FIP—low in most populations, especially in single-cat households.
- Because of difficulty in diagnosis, control, and prevention, outbreaks within breeding catteries may be catastrophic; in endemic catteries, risk of FCoV antibody-positive cat eventually developing FIP is usually <10%.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cats—domestic and exotic.

Breed Predilections

Some bloodlines or breeds of cats may be more susceptible.

Mean Age and Range

Highest incidence in kittens 3 months–2 years of age.

SIGNS

General Comments

- Variable, depending on effectiveness of cell-mediated immune response, and organ system(s) affected.
- Two classic forms—wet (effusive) and dry (noneffusive); depends on presence of effusion in body cavities; dry form may become wet form with disease progression.

Historical Findings

- Insidious onset.
- Gradual weight loss and inappetence.
- Stunted growth in kittens.
- Gradual increase in size of abdomen due to effusion.
- Persistent fever—fluctuating, antibiotic unresponsive.

Physical Examination Findings

- Depression.
- Fever.
- Poor condition.
- Stunted growth.
- Dull, rough hair coat.
- Icterus.
- Abdominal and/or pleural effusion.
- Palpable abdominal masses (granulomas or pyogranulomas).
- Ocular—anterior uveitis, keratic precipitates, iris color change, irregularly shaped pupil.
- Neurologic—seizure, ataxia, paresis/paralysis, abnormal behavior, cranial nerve deficits.

CAUSES

- Prevailing theory is that FECV mutates to FIPV during FECV infection in individual cats; weak cell-mediated immunity plays a role in development of FIP.
- FCoV has two genomic types (FCoV type 1 and 2) and two biotypes (FECV and FIPV).
- FCoV type 1 is predominant (>85%); both types 1 and 2 can cause FIP.
- FECV—enteritis; highly transmissible among cats.
- FIPV—systemic, fatal disease (FIP); cat-to-cat transmission unlikely.

RISK FACTORS

- Contact with FECV-shedding cat; >30% of cats are chronic shedders.
- Breeding catteries or multicat facilities.
- Less than 2 years of age.
- Feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV) infection.
- Certain cat breeds have higher incidence of FIP, especially dry form; some breeding pairs are prone to producing litters that develop FIP.



DIAGNOSIS

- Wet form—straightforward clinical diagnosis.
- Dry form—difficult to diagnose.

- Reverse-transcription polymerase chain reaction (RT-PCR) or immunohistochemistry on effusion or affected tissue confirmatory.
- No single diagnostic laboratory test.

DIFFERENTIAL DIAGNOSIS

- Fever of unknown origin—Infection, inflammation.
- Pleural effusion—cardiac disease; cardiac effusion has low specific gravity and cell count.
- Neoplasia—lymphoma, other causing abdominal organ enlargement/effusion.
- CNS signs—neoplasia, toxoplasmosis.
- Anemia and icterus—blood parasites causing hemolysis.
- Pansteatitis (yellow fat disease)—classic feel and appearance of fat within abdominal cavity; pain on abdominal palpation; often a fish-only diet.
- Leukopenia, enteritis—panleukopenia (see Feline Panleukopenia).

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with neutrophilia and lymphopenia.
- Mild to severe anemia.
- High total plasma protein, specifically globulin fraction (serum albumin : globulin typically <0.8).
- Hyperbilirubinemia and hyperbilirubinuria.

OTHER LABORATORY TESTS

- Serum antibody tests—detect antibodies against FCoV; positive tests not diagnostic of FIP (indicate only previous FECV infection); likelihood of FIP increases with titers $\geq 1 : 3200$, but low titers do not exclude FIP.
- RT-PCR—detect viral genome; positive tests on blood or stool not diagnostic of FIP; positive tests on effusion or tissues confirm FIP.
- Immunohistochemistry—detect virus in biopsy or tissue samples; excellent for confirming cause of specific lesions, especially abdominal disease, which often is not diagnosed as FIP.

IMAGING

- May confirm abdominal and pleural effusions.
- May detect granulomatous lesions.

DIAGNOSTIC PROCEDURES

- Thoracocentesis and/or abdominocentesis—fluid pale to straw colored, viscous with flecks of fibrin, specific gravity 1.017–1.047; fluid may be used for RT-PCR or immunohistochemistry.
- Laparoscopy—to observe specific lesions of peritoneal cavity and obtain biopsy samples.
- Exploratory laparotomy—may be indicated for difficult-to-diagnose patients.

PATHOLOGIC FINDINGS

Gross

- Variable, patient generally emaciated, with rough hair coat.

(CONTINUED)

- Abdomen and/or thoracic cavity—may contain thick, viscous exudates.
- White, rough, pyogranulomatous plaques or granulomas—may be on serosal surface of abdominal organs and omentum; fibrous strands may extend between organs.
- Discolored iris with anterior uveitis—may see keratic precipitates.
- Lesions in brain and/or spinal cord possible

Histopathologic

- Granulomas or pyogranulomas in any affected tissue.
- Lesions—perivascular; increase in size, involving large portions of tissue; microscopic appearance suggests diagnosis.

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

Inpatient or outpatient, depending on severity of disease and owner's willingness and ability to provide good supportive care.

NURSING CARE

- Therapeutic paracentesis—to relieve pressure/dyspnea from ascites or pleural effusions.
- Encourage cat to eat.

ACTIVITY

FIP transmission to other cats unlikely; no or low levels of FIPV shedding.

DIET

Any food that will entice patient to eat.

CLIENT EDUCATION

- Discuss various aspects of disease, including grave prognosis; once clinical FIP is confirmed, nearly 100% of cats will die of disease.
- Inform client of high prevalence of FECV infection but low incidence of FIP; <10% of FCoV antibody-positive cats <2 years of age eventually develop clinical disease.

SURGICAL CONSIDERATIONS

- Generally none.
- Rarely, inflammatory abdominal disease from FIP may cause intestinal obstruction.

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

- No cure; only symptomatic treatment is available.
- Immunosuppressive drugs (e.g., oral prednisolone)—may alleviate some symptoms.
- Feline omega interferon—unclear effectiveness in symptomatic management.
- Antibiotics—generally not necessary.

FELINE INFECTIOUS PERITONITIS (FIP)**ALTERNATIVE DRUG(S)**

Direct-acting antiviral drugs for FIP have shown effectiveness in treatment and are under development.

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

Monitor for development of pleural effusion or neurologic disease.

PREVENTION/AVOIDANCE

- Modified live intranasal vaccine—against FIPV; low efficacy; cannot rely on vaccination alone for control; will produce antibody-positive cats, complicating monitoring in catteries or colonies; not generally recommended.
- Mother/offspring—main method of transmission appears to be from asymptomatic carrier queens to their kittens at 4–7 weeks of age, after maternal immunity wanes; break cycle of transmission by early weaning at 4–5 weeks of age and isolating litter from direct contact with other cats, including queen.
- Routine disinfection to reduce FECV transmission—premises, cages, and water/food dishes; common disinfectants readily inactivate virus.
- Introduce only FCoV antibody-negative cats to catteries or colonies that are free of virus.
- Avoid breeding pairs that are prone to producing litters that develop FIP.

POSSIBLE COMPLICATIONS

Pleural effusion may require thoracocentesis; supportive care for other clinical signs.

EXPECTED COURSE AND PROGNOSIS

- Clinical course—a few days to several months until euthanasia is warranted.
- Prognosis grave once clinical signs occur; mortality nearly 100%.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

FeLV or FIV-positive cats—more prone to developing FIP.

PREGNANCY/FERTILITY/BREEDING

FIPV transmission from mother to offspring during pregnancy is presumed rare.

SYNONYMS

- Feline coronaviral polyserositis.
- Feline coronaviral vasculitis.
- Systemic feline coronavirus infection.

ABBREVIATIONS

- FCoV = feline coronavirus.
- FECV = feline enteric coronavirus.
- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIPV = feline infectious peritonitis virus.
- FIV = feline immunodeficiency virus.
- RT-PCR = reverse-transcription polymerase chain reaction.

INTERNET RESOURCES

<https://www.vet.cornell.edu/departments-centers-and-institutes/cornell-feline-health-center/health-information/feline-health-topics/feline-infectious-peritonitis>

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Acknowledgment The author and book editors acknowledge the prior contribution of Fred W. Scott.



**Client Education Handout
available online**

FELINE LEUKEMIA VIRUS (FeLV) INFECTION



BASICS

DEFINITION

A simple retrovirus (*Gammaretrovirus* genus) that causes immunodeficiency and neoplastic disease in domestic cats.

PATHOPHYSIOLOGY

- Four subgroups of feline leukemia virus (FeLV)—A, B, C, and T; FeLV-A most transmissible and present in all isolates; FeLV-B arises from recombination of FeLV-A *env* gene with endogenous retroviral sequences (50% of isolates); FeLV-C (1% of isolates) arises from mutation in *env* gene sequences; FeLV-T infects only T cells.
- Early infection (five stages)—(1) viral replication in tonsils and pharyngeal lymph nodes; (2) infection of circulating B lymphocytes and macrophages that disseminate virus; (3) replication in lymphoid tissues, intestinal crypt epithelial cells, bone marrow precursor cells; (4) release of infected neutrophils and platelets from bone marrow; and (5) infection of epithelial and glandular tissues, subsequent shedding of virus into saliva, urine.
- *Abortive infection*—if virus replication terminated at stage 1; no viremia.
- *Regressive or nonproductive infection*—immune response stops progression at stage 2 or 3 (4–8 weeks after exposure) and forces virus into latency after transient viremia; may be reactivated with immune suppression or other viral infections.
- *Progressive or productive infection*—immune response not effective, persistent viremia (stages 4 and 5) from 4–12 weeks after infection.
- Tumor induction—DNA provirus integrates into cat chromosomal DNA in critical regions near oncogenes (e.g., *c-myc* or genes influencing *c-myc* expression); thymic lymphosarcoma results.
- Feline sarcoma viruses—FeLV mutants; arise by recombination between FeLV and host genes; virus–host fusion proteins responsible for induction of fibrosarcomas.
- Pathogenesis influenced by presence of other viruses (e.g., feline foamy virus, feline coronavirus, feline immunodeficiency virus [FIV]) or endogenous retroviruses.

SYSTEMS AFFECTED

- Hemic/lymphatic/immune—bone marrow dyscrasia, neoplasia, immunosuppression.
- Nervous—degenerative myelopathy, neoplasia.
- Other body systems—immunosuppression with secondary infections or neoplasia.

GENETICS

N/A

INCIDENCE/PREVALENCE

- In United States, 2–3% in healthy cat population; worldwide infection rate 1–8% in healthy cats; 3–4 times greater in clinically ill cats.
- Decline in US prevalence since 1980s.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Mean Age and Range

- Prevalence highest between 1 and 6 years of age.
- Mean—3 years.

Predominant Sex

Male : female ratio—1.7 : 1.

SIGNS

General Comments

- Onset of FeLV-associated disease—months to years after infection.
- Associated diseases—non-neoplastic or neoplastic; most non-neoplastic or degenerative diseases result from immunosuppression.
- Regressive infections may be associated with cardiomyopathies, lymphomas, leukemias, anemia, other infections.
- Clinical signs of FeLV-induced immunodeficiency cannot be distinguished from FIV-induced immunodeficiency.

Historical Findings

- Outdoor cat.
- Multicat household.

Physical Examination Findings

- Depend on type of disease (neoplastic or non-neoplastic) and secondary infections.
- Lymphadenomegaly—mild to severe.
- Fever, wasting.
- Upper respiratory tract—rhinitis, conjunctivitis, keratitis.
- Persistent diarrhea—bacterial or fungal overgrowth, parasite-induced inflammation, direct effect on crypt cells.
- Gingivitis, stomatitis, periodontitis.
- Nonresponsive or recurrent infections of external ear and skin.
- Lymphoma—risk increased 62-fold in FeLV-infected cats; thymic and multicentric; extranodal lymphoma can affect eye, nervous system.
- Erythroid and myelomonocytic leukemias.
- Fibrosarcomas—coinfection with mutated sarcoma virus; frequently young cats.
- Peripheral neuropathies; progressive ataxia.

CAUSES

- Cat-to-cat transmission—close casual contact (grooming), shared dishes or litter pans, bites.
- Perinatal transmission—transplacental and transmammary transmission in ≥20% of surviving kittens from infected queens.

RISK FACTORS

- Age—kittens more susceptible than adults.
- Male—result of behavior.
- Free-roaming.
- Multicat household.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- FIV.
- Other infections—bacterial, parasitic, viral, or fungal.
- Nonviral neoplastic diseases.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—often severe, often nonregenerative; regenerative anemias usually associated with *Mycoplasma haemofelis* or *M. haemominutum* coinfections.
- Lymphopenia or lymphocytosis.
- Neutropenia—sometimes cyclic; may be response to secondary infections or immune-mediated disease.
- Thrombocytopenia and immune-mediated hemolytic anemia.
- Biochemistry/urinalysis abnormalities depend on affected organs.

OTHER LABORATORY TESTS

- Immunochromatography (lateral flow) and ELISA—point-of-care screening, detect antigen in plasma, serum, saliva, tears; more sensitive than immunofluorescent antibody (IFA) for early or transient infection; single positive test does not predict persistent viremia (retest in 12 weeks); confirm positive tests with another method.
- IFA—identify FeLV antigen in leukocytes and platelets in fixed smears of whole blood or buffy coat; positive result indicates productive bone marrow infection; 97% of IFA-positive cats persistently infected and viremic for life; antigen usually detected by 4 weeks after infection, but may be up to 12 weeks; for leukopenic cats, use buffy coat smears rather than whole blood smears; confirm positive tests.
- FeLV vaccination does not interfere with antigen testing.
- PCR for proviral DNA in blood or tissue—denotes exposure, confirm with antigen test; proviral DNA detectable 1–2 weeks after infection; proviral loads can differentiate cats with regressive versus progressive infections.
- Reverse transcription PCR (RT-PCR) for viral RNA (virus circulating or replicating within cells) in saliva or blood—denotes viremia and FeLV shedding; first test to become positive as early as 1 week after infection.
- Multiple tests over several months may be needed to clarify FeLV status and whether infection progressive or regressive; a few cats have persistently discordant ELISA-positive and IFA-negative tests or test positive only sporadically.

IMAGING

Thymic atrophy (fading kittens); mediastinal mass and pleural effusion with thymic lymphoma.

(CONTINUED)

FELINE LEUKEMIA VIRUS (FeLV) INFECTION

DIAGNOSTIC PROCEDURES

Bone marrow aspiration or biopsy—arrest in erythroid differentiation; true aplastic anemia with hypocellular bone marrow may be seen; some cases of anemia result from myelophthisis.

PATHOLOGIC FINDINGS

- Bone marrow hypercellularity with neoplastic disease.
- Lymphocytic and plasmacytic infiltrates of gingiva, lymph nodes, other lymphoid tissues, spleen, kidney, liver.
- Intestinal lesions—feline panleukopenia-like syndrome.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient for most cats.
- Inpatient—may be required with severe secondary infections, anemia, cachexia.
- Blood transfusions—emergency support; may need multiple transfusions; passive antibody transfer (if vaccinated donor) reduces level of FeLV antigenemia in some.
- Management of secondary and opportunistic infections.

NURSING CARE

Supportive therapy (e.g., parenteral fluids, nutritional supplements) as indicated.

ACTIVITY

Normal

DIET

Normal, may alter as necessary for cats with diarrhea, kidney disease.

CLIENT EDUCATION

- Keep cats indoors and separated from FeLV-negative cats to protect from secondary pathogens and prevent spread of FeLV.
- Discuss good nutrition, routine husbandry to control secondary infections.

SURGICAL CONSIDERATIONS

- Biopsy or removal of tumors.
- Oral treatment or surgery—dental cleaning, tooth extraction, gingival biopsy.



MEDICATIONS

DRUG(S) OF CHOICE

- Antiretroviral therapy not routinely indicated due to inconsistent evidence of efficacy and potential adverse effects; immune modulator therapy also unproven.
 - Zidovudine (Retrovir® 5–10 mg/kg PO q12h)—clinical improvement, does not clear virus.

- α -interferon (Roferon®-A in saline 30 U/day PO for 7 days every other week).
- Feline recombinant interferon omega (Virbagen® Omega 1 million U/kg SC for 5 days starting days 0, 14, 60)—may increase survival rates and improve clinical status.
- *Mycoplasma haemofelis* infection—see Mycoplasmosis for recommended treatment.
- Lymphoma—management with standard chemotherapy protocols; remission periods average 3–4 months.
- Myeloproliferative disease, leukemias—more refractory to treatment.
- Vaccinate for respiratory and enteric pathogens based on individual risk assessment. Rabies vaccination according to regulatory guidelines.

CONTRAINDICATIONS

Modified live vaccines—potential for disease in severely immunosuppressed cats.

PRECAUTIONS

Systemic corticosteroids—potential for further immunosuppression.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

Immunomodulatory drugs—*Propionibacterium acnes* (ImmunoRegulin® 0.5 mL/cat IV once or twice weekly); acemannan (Carrisyn® 100 mg/cat/day PO).



FOLLOW-UP

PATIENT MONITORING

Varies according to clinical manifestations.

PREVENTION/AVOIDANCE

- Prevent contact with FeLV-positive cats.
- Quarantine and test incoming cats before introduction to multicat households.
- Screen blood donor cats for FeLV-regressive infections using PCR for proviral DNA.

Vaccines

- Most commercial vaccines induce virus-neutralizing antibodies, reported efficacy ranges from <20% to almost 100%, depending on methodology; canarypox-FeLV recombinant vaccine does not contain adjuvant.
- Test cats for FeLV before initial vaccination.
- Vaccinate kittens at 8–9 and 12 weeks of age; boost at 1 year of age; revaccinate every 2–3 years if cat is in low risk environment; annually if high risk..

EXPECTED COURSE AND PROGNOSIS

Persistently viremic cats: >50% succumb to related diseases within 2–3 years after infection.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Secondary infections.
- Neoplasia (lymphoid, fibrosarcoma).
- Immune-mediated disease.

AGE-RELATED FACTORS

- Neonatal kittens—most (70–100%) susceptible to infection.
- Older kittens—<30% susceptible to infection by 16 weeks of age; may develop regressive infections.

ZOONOTIC POTENTIAL

Probably low, but controversial.

PREGNANCY/FERTILITY/BREEDING

- Abortions, stillbirths, and fetal resorptions occur in about 80% of FeLV-positive queens.
- Transmission from queen to kittens—in at least 20% of live births.

SEE ALSO

- Anemia, Nonregenerative.
- Feline Immunodeficiency Virus (FIV) Infection.
- Feline Stomatitis—Feline Chronic Gingivostomatitis (FCGS).
- Lymphoma—Cats.
- Myeloproliferative Disorders.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- IFA = immunofluorescent antibody.
- RT-PCR = reverse transcription polymerase chain reaction.

INTERNET RESOURCES

<http://www.abcdcatsvets.org/feline-leukaemia-virus-infection>

Suggested Reading

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Client Education Handout available online

FELINE PANLEUKOPENIA



BASICS

DEFINITION

A viral infection of cats characterized by sudden onset, vomiting and diarrhea, severe dehydration, and high mortality.

PATHOPHYSIOLOGY

Feline parvovirus (FPV) infects and causes acute death of rapidly dividing cells.

SYSTEMS AFFECTED

- Gastrointestinal—crypt cells of jejunum and ileum are destroyed causing blunted villi; malabsorption of nutrients; acute vomiting and diarrhea; dehydration; and secondary bacteremia.
- Hemic/lymphatic/immune—severe panleukopenia; atrophy of thymus.
- Nervous and ophthalmic—in neonates, rapidly dividing granular cells of cerebellum and retinal cells of eye destroyed; cerebellar hypoplasia with ataxia and retinal dysplasia result.
- Reproductive—in utero infection in nonimmune queens leads to fetal death or neurologic abnormalities.

GENETICS

N/A

INCIDENCE/PREVALENCE

- Unvaccinated populations—most severe and important feline infectious disease.
- Routine vaccination—almost total control of disease.
- Extremely contagious.
- Extremely stable virus, survives for years on contaminated premises.

GEOGRAPHIC DISTRIBUTION

Worldwide in unvaccinated populations.

SIGNALMENT

Species

- Felidae—all, domestic and exotic.
- Canidae—susceptible to canine parvovirus; some exotic canids may be susceptible to FPV.
- Mustelidae—especially mink; may be susceptible.
- Procyonidae—raccoon and coatiundi; susceptible.

Breed Predilections

None

Mean Age and Range

- Unvaccinated and previously unexposed cats of any age can become infected once maternal immunity has been lost.
- Kittens 2–6 months of age—most susceptible to develop severe disease.
- Adults—often mild or subclinical infection.

Predominant Sex

N/A

SIGNS

Historical Findings

- History of recent exposure (e.g., from shelter population).
- Newly acquired kitten.
- Kitten 2–4 months old from premises with history of feline panleukopenia (FP).
- No vaccination history or last vaccinated when <16 weeks of age.
- Sudden onset, with vomiting, diarrhea, depression, complete anorexia.

Physical Examination Findings

- Mental dullness/lethargy.
- Typical “panleukopenia posture”—sternum and chin resting on floor, feet tucked under body, top of scapulae elevated above the back.
- Dehydration—appears rapidly; may be severe.
- Vomiting, diarrhea.
- Body temperature—usually mild to moderately increased or decreased in early stages; becomes severely low as patients become moribund.
- Abdominal pain.
- Small intestine—either turgid or flaccid.
- Subclinical or mild infections common, especially in adults.
- Ataxia from cerebellar hypoplasia—kittens infected in utero or neonatally; evident at 10–14 days of age and persist for life: hypermetria; dysmetria; base-wide stance; alert, afebrile, and otherwise normal; retinal dysplasia sometimes seen.

CAUSES

FPV

- Small, single-stranded DNA virus.
- Single antigenic serotype.
- Antigenic cross-reactivity with canine parvovirus (CPV) type 2 and mink enteritis virus.
- Extremely stable against environmental factors, temperature, and most disinfectants.
- Requires a mitotic cell for replication.

CPV Types 2a, 2b, and 2c

- CPV-2a, CPV-2b, and CPV-2c can produce FP in domestic and/or exotic cats.
- Properties of CPV similar to FPV.

RISK FACTORS

- Factors that increase mitotic activity of small intestinal crypt cells such as intestinal parasites or pathogenic bacteria.
- Secondary or coinfections—viral upper respiratory infections.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Panleukopenia-like syndrome of feline leukemia virus (FeLV) infection—chronic

enteritis and panleukopenia, frequently anemia; patient positive for FeLV antigen.

- Salmonellosis—can cause severe gastroenteritis; white blood cell (WBC) count usually high.
- Acute poisoning—similar to acute disease; depression; subnormal temperature; WBC count normal.
- Many diseases cause mild clinical signs hard to differentiate from mild FP; total WBC count always low during acute infection with FPV, even in subclinical infections.

CBC/BIOCHEMISTRY/URINALYSIS

- Panleukopenia—most consistent finding; WBC counts usually between 500 and 3,000 cells/ μ L during acute disease.
- Biochemical findings usually nonspecific—hypoproteinemia, hypoalbuminemia, hypcholesterolemia possible.

OTHER LABORATORY TESTS

- CPV antigen fecal immunoassay (Cite Canine Parvovirus Test Kit, IDEXX Labs)—not licensed for FP; detects FPV antigen in feces.
- Chromatographic test strip—feces for FPV and CPV.
- Serologic testing—paired serum samples detect rising antibody titer.
- PCR testing—confirms FPV in blood, feces, or tissue; positive result with recent modified live virus (MLV) vaccination.

DIAGNOSTIC PROCEDURES

- Viral isolation from feces or affected tissues (e.g., thymus, small intestine, spleen).
- Electron microscopy of feces—detects parvovirus, presumably FPV.

PATHOLOGIC FINDINGS

Gross

- Rough hair coat, weight loss.
- Severe dehydration.
- Evidence of vomiting and diarrhea.
- Edematous, turgid small intestine.
- Petechial or ecchymotic hemorrhages in jejunum and ileum.
- Thymic atrophy.
- Gelatinous or liquid bone marrow.
- In utero or neonatal infection—gross hypoplasia of cerebellum.

Microscopic

- Dilated small intestinal crypts with sloughing of epithelial cells.
- Shortened and blunt intestinal villi.
- Lymphocytic depletion of follicles of lymph nodes, Peyer's patches, spleen.
- Neonatal and fetal infection—disorientation and depletion of granular and Purkinje cells of cerebellum.
- Eosinophilic intranuclear inclusions in affected tissues during early infection.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Main principles of treatment—rehydration; antibiotic therapy; supportive care (antiemetics and analgesics as needed).
- Inpatient—severe cases.
- Outpatient—mild cases.

NURSING CARE

- IV fluid therapy—essential in severe cases; correct dehydration and provide electrolytes; add dextrose if patient is hypoglycemic.
- SC fluids—mild cases without dehydration or shock.
- Antiemetic therapy should be considered in vomiting patients.
- Whole blood, packed red blood cells, or fresh frozen plasma transfusions—if clinical signs of anemia are present or serum albumin <2 g/dL.

ACTIVITY

Keep patient indoors during acute disease.

DIET

Temporarily withhold food until vomiting is controlled.

CLIENT EDUCATION

- Inform client that current and future cats in household must be vaccinated for FPV before exposure.
- Inform client that virus will remain infectious for years unless environment can be adequately disinfected with dilute bleach.

SURGICAL CONSIDERATIONS

None



MEDICATIONS

DRUG(S) OF CHOICE

Broad-spectrum antibiotics (e.g., ampicillin or ampicillin–sulbactam IV, amoxicillin or amoxicillin–clavulanate PO)—counter secondary bacteremia from intestinal bacterial translocation.

CONTRAINdications

Oral medications until vomiting/gastroenteritis has been controlled.

ALTERNATIVE DRUG(S)

None



FOLLOW-UP

PATIENT MONITORING

- Monitor hydration and electrolyte balance closely.
- Monitor CBC every 24–48h until recovery.

PREVENTION/AVOIDANCE

- Contaminated environments (e.g., cages, floors, food and water dishes) should be disinfected with 1 : 32 dilution of bleach.
- FPV resistant to most commercial disinfectants.

Vaccines

- FP vaccines are core vaccines—to be given to all cats.
- FP is preventable by routine vaccination of kittens.
- MLV vaccines are available for parenteral injection or intranasal administration; MLV vaccine is preferred, with exceptions, as it may provide better protection.
- Inactivated vaccine is available for parenteral injection.
- Do not use MLV vaccines in pregnant cats or kittens younger than 4 weeks old.
- Immunity—long duration, perhaps even for life.
- Kittens—vaccinate as early as 6 weeks of age, then every 3–4 weeks until 16–20 weeks of age; American Association of Feline Practitioners vaccination guidelines now recommend the last vaccine to be given when kitten is at least 16 weeks old, instead of 12 weeks, because maternal antibodies may not have waned until 16 weeks of age.
- Boosters—1 year after last kitten vaccine; then repeat every 3 years.

POSSIBLE COMPLICATIONS

- Shock, sepsis—severe dehydration, hypoglycemia, hypoproteinemia bacterial translocation, electrolyte imbalance.
- Chronic enteritis—fungal or other cause.
- Teratogenic effects (cerebellar hypoplasia resulting in ataxia for life)—virus infection of fetus.
- Concurrent infection with intestinal parasites.

EXPECTED COURSE AND PROGNOSIS

- Most cases acute, lasting only 5–7 days.
- Guarded prognosis during acute disease, especially if WBC count <2,000 cells/ μ L.
- Approximately 50% mortality has been reported.
- If patient survives acute disease, recovery usually rapid and uncomplicated.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Viral upper respiratory diseases—feline viral rhinotracheitis and feline calicivirus infection.

AGE-RELATED FACTORS

- Clinical—typically in kittens.
- Subclinical—usually adults.

FELINE PANLEUKOPENIA

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

- Unvaccinated pregnant cats at great risk of infection.
- Fetuses almost always become infected with fatal or teratogenic effects, even when dam has subclinical infection.
- Fetal resorption, abortion, fetal mummification, stillbirth, or birth of weak, fading kittens.
- Kittens may have cerebellar hypoplasia.

SYNONYMS

- Feline distemper.
- Feline parvovirus infection.
- Feline viral enteritis.

ABBREVIATIONS

- CPV = canine parvovirus.
- FeLV = feline leukemia virus.
- FP = feline panleukopenia.
- FPV = feline parvovirus.
- MLV = modified live virus.
- WBC = white blood cell.

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Acknowledgment The author and book editors acknowledge the prior contribution of Fred W. Scott.



Client Education Handout
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FELINE (UPPER) RESPIRATORY INFECTIONS



BASICS

DEFINITION

- Viral, bacterial, fungal etiologies.
- Most cats harbor viral causes and become clinical with stress.
- Viral upper respiratory infection (URI) very common; secondary bacterial infections common; primary bacterial rhinitis uncommon.
- Most organisms spread through direct contact, air (droplets from coughing, sneezing, or discharge), and contaminated surfaces (e.g., shared bowls, cages).
- Illness typified by rhinosinusitis, conjunctivitis, lacrimation, salivation, oral ulcerations.

PATOPHYSIOLOGY

- Feline herpesvirus (FHV) induces marked rhinitis, sneezing, and conjunctivitis, and may lead to chronic signs; cats are infected for life, with latent virus sequestered in trigeminal nerve ganglion.
- FHV infects epithelial cells of respiratory tract, conjunctiva, and/or cornea; during primary infection or recrudescence, direct effect is cytolysis of infected cells and necrosis of affected tissues; inflammatory disease can occur via immune-mediated response to infection; turbinate lysis can occur.
- Feline calicivirus (FCV) has predilection for epithelial cells of oral cavity and upper respiratory tract; causes rhinitis, stomatitis, oral ulceration: ulcers start as vesicles; some strains infect lungs and can cause focal alveolitis and interstitial pneumonia; other strains cause "limping syndrome."
- FCV—virulent systemic disease (VSD) caused by hypervirulent strains that can infect endothelium of liver, lungs, and pancreas, leading to severe systemic illness characterized by vasculitis; results in edema, alopecia, ulcers, and can cause multiple organ dysfunction syndrome (MODS), systemic inflammatory response syndrome (SIRS), disseminated intravascular coagulation, death.
- *Chlamydophila felis* predominantly infects conjunctiva and causes conjunctivitis; has also been associated with URI.
- Bacterial infection—often secondary to viral disease, trauma, allergic rhinitis.
- *Cryptococcus* affects rostral nasal cavity resulting in rhinitis and turbinate lysis; granulomatous protuberances can occur; destruction of adjacent facial bones facilitates spread of infection to contiguous regions, such as bridge and side of nose, nasal planum, or hard palate, resulting in facial distortion; infection can spread through cribriform plate, resulting in meningoencephalitis, cryptococcal optic neuritis, secondary retinitis.

SYSTEMS AFFECTED

- Respiratory—nasal and upper airway, including sinuses, lower airway.

- Ophthalmologic—conjunctiva.
- Musculoskeletal—FCV.
- Integument/mucous membranes—FHV, *Cryptococcus*.
- Neurologic—*Cryptococcus*, lymph.
- VSD can affect many organ systems.

GENETICS

N/A

INCIDENCE/PREVALENCE

- FHV and FCV most common causes of URI.
- Over 90% of cats are seropositive for FHV.
- Conjunctivitis is most common disease caused by FHV, most common feline ophthalmic disease.
- Carrier states exist for FHV, FCV (10–75%).
- *C. felis*—1–5% for cats without signs of respiratory tract disease, 10–30% for cats with conjunctivitis or URI.
- *Bordetella bronchiseptica*—seroprevalence of 24–79%, isolation rates up to 47% reported.

GEOGRAPHIC DISTRIBUTION

- Ubiquitous.
- *Cryptococcus*—worldwide, associated with pigeon guano.

SIGNALMENT

- Species—cat.
- Breed predilection—N/A.
- Mean age/range—more common in younger cats, though viral flare-ups can occur through life.
- Predominant sex—N/A.

SIGNS

Historical Findings

- Exposure to other cats common; stress, steroids, immunosuppression may precipitate clinical signs for viral causes.
- Caretakers may report upper respiratory signs, weight loss, anorexia, gagging, halitosis, depression.

Physical Examination Findings

- Depend on organism.
- Frequently—sneezing, nasal discharge, stertor, halitosis, ocular discharge, inappetence.
- FHV—fever, sneezing, nasal discharge, conjunctivitis, ulcerative stomatitis, ulcerative keratitis, blepharospasm, salivation, depression, anorexia.
- FCV—fever, salivation and ulceration of tongue, hard palate, or nostrils, stomatitis, gingivitis, rhinitis, conjunctivitis, coughing, dyspnea, lameness.
- With VSD—peripheral edema, dermal ulcers, icterus possible.
- *B. bronchiseptica*—fever, sneezing, ocular discharge, nasal discharge, lymphadenopathy, coughing, dyspnea, cyanosis.
- *Cryptococcus*—sneezing, nasal discharge, ocular discharge, gagging, dysphagia, stertor, upper airway obstruction, facial deformity, lymphadenopathy, neurologic abnormalities, optic neuritis, chorioretinitis.

- *C. felis*—conjunctivitis, occasional sneeze, fever.
- *Mycoplasma* spp.—conjunctivitis, ocular and nasal discharge, dyspnea.

CAUSES

- Viral—FHV, FCV, influenza.
- Primary bacterial—*B. bronchiseptica*, *C. felis*, *Streptococcus canis*, *Mycoplasma* spp.
- Secondary bacterial invaders—*Corynebacterium* spp., *Escherichia coli*, *Pasturella multocida*, *Pseudomonas aeruginosa*, *Streptococcus* spp., *Staphylococcus* spp.
- Fungal—*Cryptococcus neoformans*, *Sporothrix schenckii*, *Aspergillus* spp., *Penicillium* spp.

RISK FACTORS

- Stress/steroids.
- Decreased immune function, feline immunodeficiency virus (FIV)/feline leukemia virus (FeLV) infection.
- Multicat households, shelters, young cats.



DIAGNOSIS

- Direct fluorescent staining of conjunctival scraping—FHV.
- PCR for *B. bronchiseptica* (controversial if positive), *Chlamydophila felis*, FCV, FHV, H7N2 influenza virus, influenza A virus (including H7N2, H3N2, H1N1, H3N8), *Mycoplasma felis*.
- Viral isolation.
- *Mycoplasma* culture.
- *Cryptococcus*—direct microscopic visualization of organisms in nasal discharge or tissue: cytology or histopathology, culture, serology; latex agglutination to identify antigen.

DIFFERENTIAL DIAGNOSIS

- Nasopharyngeal polyps.
- Nasopharyngeal stenosis.
- Foreign body.
- Neoplasia.
- Dental disease—tooth root abscess.
- Anatomic defects.
- Trauma.
- Burn—caustic agent or electrical.

CBC/BIOCHEMISTRY/URINALYSIS

Generally normal with most etiologies—with virulent systemic FCV may see inflammatory leukogram, thrombocytopenia, elevated liver enzymes/total bilirubin.

OTHER LABORATORY TESTS

- Culture of upper airways.
- Lymph node cytology.
- Nasal biopsies.

IMAGING

- Skull radiographs generally not helpful.
- Thoracic radiography—generally normal, may see pulmonary involvement if fungal disease or pneumonia.

(CONTINUED)

FELINE (UPPER) RESPIRATORY INFECTIONS

F

- CT of head—may show mass, turbinate lysis, increased soft tissue within nasal passages, lymphadenopathy.

DIAGNOSTIC PROCEDURES

- Conjunctival scraping may identify FHV.
- Rhinoscopy—in cats with *Cryptococcus*.
- Upper airway exam.
- Bronchoalveolar lavage if pneumonia suspected.
- FIV antibody, FeLV antigen testing.

PATHOLOGIC FINDINGS

Histopathology—lymphoplasmacytic stomatitis; FCV; vasculitis; FCV-VSD; bacterial rhinitis, suppurative inflammation; *Cryptococcus* organisms on nasal or lymph node biopsy.



TREATMENT

APPROPRIATE HEALTH CARE

- Most cats managed as outpatient; isolate if hospitalized, as many organisms highly contagious and airborne.
- Moderate to severely affected cats may require IV fluids for hydration.
- May require supplemental oxygen.

ACTIVITY

N/A

DIET

- Enteral feeding recommended if anorexia persists >48 hours.
- Nasogastric feeding may not be appropriate if there is severe nasal discharge.
- Cats with severe oral ulceration may need enteric feeding while ulcers heal.

CLIENT EDUCATION

Most agents are contagious.

SURGICAL CONSIDERATIONS

Corneal ulcers can be deep, may require surgical intervention.



MEDICATIONS

DRUG(S) OF CHOICE

- Many cases will self-resolve.
- Antibiotics not recommended for cats with only serous discharge; observation without antibiotics recommended for up to 10 days for acute-onset mucopurulent/purulent discharge without systemic signs (fever, lethargy, anorexia) or specific etiology identified by exam or history; susceptibility profiles of organism may be helpful for chronic cases.

- First choices—doxycycline 10 mg/kg PO q24h, usually effective for *B. bronchiseptica*, *C. felis*, *Mycoplasma* spp.; amoxicillin 22 mg/kg, PO, q12h.
- Other options—amoxicillin-clavulanate 15–20 mg/kg PO q12h, azithromycin 5–15 mg/kg PO q24h, marbofloxacin 2.5–5 mg/kg PO q24h, pradofloxacin 5–10 mg/kg PO q24h.
- Antifungals—fluconazole 50 mg/cat PO q12–24h, itraconazole 10 mg/kg PO q24h; compounded formulations not recommended.
- Antivirals—famciclovir 62.5 mg/cat PO q12h, cidofovir topical 0.5% 1 drop OU q12h.

CONTRAINdications

Use azole drugs with caution in patients with liver disease.

PRECAUTIONS

Doxycycline can cause esophagitis and esophageal strictures—follow with food and/or water.

POSSIBLE INTERACTIONS

Azole antifungals have many drug interactions.



FOLLOW-UP

PATIENT MONITORING

- Viral—most cases improve within 1 week; could take up to 6 weeks to resolve.
- Persistent clinical signs after appropriate treatment suggest alternative cause.

PREVENTION/AVOIDANCE

- Vaccination.
- FCV, FHV—core vaccines; modified live and inactivated virus vaccines give reasonable protection, mild clinical signs may be seen; vaccines do not prevent infection or viral latency, although shedding post challenge may be reduced.
- Vaccination against *C. felis* and *B. bronchiseptica* is noncore.
- Do not allow non-immunocompetent patients to contact other animals until determined to be low risk.
- Bleach diluted 1 : 30 with water mixed with detergent is effective at eliminating most respiratory pathogens from environment.

POSSIBLE COMPLICATIONS

- Pneumonia.
- Septicemia (rare).

EXPECTED COURSE AND PROGNOSIS

- Good to excellent; underlying immunosuppression may increase susceptibility to infection, worsen prognosis.
- FHV—generally, mortality low and prognosis good, except for young kittens and aged cats.
- FCV-VSD—poor, mortality >50%.



MISCELLANEOUS

AGE-RELATED FACTORS

Young animals more susceptible.

ZOONOTIC POTENTIAL

- *B. bronchiseptica* rare cause of zoonotic infections.
- Human conjunctivitis caused by feline chlamydia has been reported.

PREGNANCY/FERTILITY/BREEDING

Animals who are actively ill should not be bred. FHV can cause abortions.

SEE ALSO

- Chlamydiosis—Cats.
- Cryptococcosis.
- Feline Calicivirus Infection.
- Feline Herpesvirus Infection.
- Mycoplasmosis.
- Rhinitis and Sinusitis.

ABBREVIATIONS

- FCV = feline calicivirus.
- FeLV = feline leukemia virus.
- FHV = feline herpesvirus-1.
- FIV = feline immunodeficiency virus.
- MODS = multiple organ dysfunction syndrome.
- SIRS = systemic inflammatory response syndrome.
- VSD = virulent systemic disease.
- URI = upper respiratory infection.

INTERNET RESOURCES

<https://catvets.com/guidelines/practice-guidelines/feline-vaccination-guidelines>

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FEVER



BASICS

DEFINITION

F Higher than normal body temperature because of changed thermoregulatory set point in hypothalamus; normal body temperature in dogs and cats 100.2–102.8 °F (37.8–39.3 °C). Fever of unknown origin (FUO)—at least 103.5 °F (39.7 °C) on at least four occasions over 14-day period and illness of 14 days' duration without obvious cause.

PATHOPHYSIOLOGY

Exogenous or endogenous pyrogens reset thermoregulatory center to higher temperature, activating physiologic responses to raise body temperature. Physiologic consequences include increased metabolic demands, muscle catabolism, bone marrow suppression, heightened fluid and caloric requirements, and possibly disseminated intravascular coagulation (DIC) and shock.

SYSTEMS AFFECTED

- Cardiovascular—tachycardia.
- Hemic/lymphatic/immune—bone marrow depression, DIC.
- Nervous—cerebral edema, depression.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Some breed-associated conditions may result in FUO (e.g., shar-pei fever).

SIGNS

General Comments

- Fever lowers bacterial division and increases immune competence.
- Prolonged fever >105 °F (>40.5 °C) leads to dehydration and anorexia.
- Fevers >106 °F (>41.1 °C) may lead to cerebral edema, bone marrow depression, arrhythmia, electrolyte disorders, multiorgan damage, DIC.

Historical Findings

- Clinical history (e.g., contact with infectious agents, lifestyle, travel, recent vaccination, drug administration, insect bites, previous illness, allergies) and physical examination (including retinal examination) may help identify underlying disease condition.
- Fever patterns (e.g., sustained, intermittent) rarely helpful.

Physical Examination Findings

- Hyperthermia.
- Lethargy.
- Inappetence.
- Tachycardia.

- Tachypnea.
- Hyperemic mucous membranes.
- Dehydration.
- Shock.

CAUSES

Infectious Agents

- Viruses—feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), parvo, distemper, herpes, calici.
- Bacteria—endotoxins, *Mycoplasma*, *Bartonella*, *Leptospira*, *Borrelia burgdorferi*, others.
- Systemic fungi—*Histoplasma*, *Blastomyces*, *Coccidioidomycetes*, *Cryptococcus*.
- Vector borne—*Rickettsia*, *Borrelia*, *Ehrlichia*, *Anaplasma*, *Neorickettsia*.
- Parasites and protozoa—*Babesia*, *Toxoplasma*, aberrant larva migrans, *Dirofilaria* thromboemboli, *Leishmania*, *Cytauxzoon*, *Hepatozoon*, *Neospora*.

Immune-Mediated Processes

Systemic lupus erythematosus, immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, pemphigus, polyarthritis, polymyositis, rheumatoid arthritis, vasculitis, hypersensitivity reaction, transfusion reaction, infection secondary to inherited or acquired immune defects.

Endocrine and Metabolic

Hyperthyroidism, hypoadrenocorticism (rare), pheochromocytoma, hyperlipidemia, hypernatremia.

Neoplasia

Lymphoma, myeloproliferative disease, plasma cell neoplasm, mast cell tumor, malignant histiocytosis, metastatic disease, necrotic tumor, and solid tumor, particularly in liver, kidney, bone, lung, lymph nodes.

Other Inflammatory Conditions

Cholangiohepatitis, hepatic lipidosis, toxic hepatopathy, cirrhosis, inflammatory bowel disease, pancreatitis, peritonitis, pleuritis, granulomatous diseases, portosystemic shunting, thrombophlebitis, infarctions, pansteatitis, panosteitis panniculitis, hypertrophic osteodystrophy, blunt trauma, cyclic neutropenia, intracranial lesions, pulmonary thromboembolism.

Drugs and Toxins

Tetracycline, sulfonamide, penicillins, nitrofurantoin, amphotericin B, barbiturates, iodine, atropine, cimetidine, salicylates, antihistamines, procainamide, heavy metals.

FUO—Dogs

- Infection (28%)—discospondylitis, fungal infections, endocarditis, abscesses, bacteremia, septic arthritis, septic meningitis, pyothorax, pulmonary foreign body/abscess, stump pyometra, pneumonia, osteomyelitis, peritonitis, prostatitis, pancreatitis,

pyelonephritis, sepsis secondary to immunodeficiency, leptospirosis, leishmaniasis, toxoplasmosis, Lyme disease, infection with *Ehrlichia*, *Anaplasma*, *Bartonella*, others.

- Immune-mediated disease (27%)—polyarthritis, meningitis, vasculitis, others.
- Bone marrow disease, including neoplasia (16%).
- Neoplasia (7%).
- Miscellaneous (10%)—hypertrophic osteodystrophy, lymphadenitis, panosteitis, portosystemic shunting, shar-pei fever.
- Undiagnosed (12%).

FUO—Cats

- Most virally mediated (e.g., FeLV, FIV, feline infectious peritonitis [FIP], less commonly parvo, herpes, calici).
- Occult bacterial infection with atypical bacteria, sometimes secondary to bite wounds (e.g., *Yersinia*, *Mycobacteria*, *Nocardia*, *Actinomyces*, *Brucella*).
- Pyothorax.
- Additional causes—pyelonephritis, blunt trauma, penetrating intestinal lesion, dental abscess, systemic fungal disease, lymphoma, solid tumors.
- Immune disorders, endometritis, discospondylitis, pneumonia, endocarditis rare.

RISK FACTORS

- Recent travel.
- Exposure to biologic agents.
- Immunosuppression.
- Very young or old animals.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiate fever from hyperthermia. Temperatures up to 103 °F (39.4 °C) may be caused by stress or illness. Temperatures >104 °F (>40 °C) almost always important. Temperatures >107 °F (>41.7 °C) usually not fever, more likely to be primary hyperthermia.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and blood smear—leukopenia or leukocytosis, left shift, moncytosis, lymphocytosis, thrombocytopenia or thrombocytosis, spherocytes, organisms.
- Biochemistry profile and urinalysis vary with organ system involved.

OTHER LABORATORY TESTS

- If infectious disease suspected, attempt to culture an organism—urine culture, blood cultures (i.e., three anaerobic/aerobic cultures, taken 20 min apart; try to use as much volume as possible to increase diagnostic yield; use special blood culture bottles), fungal and cerebrospinal fluid cultures, synovial and prostatic fluid, biopsy specimens.

(CONTINUED)

FEVER**F**

- FeLV and FIV test, Snap 4DX test, serologic tests or PCR for *Toxoplasma*, *Borrelia*, *Mycoplasma*, *Bartonella*, *Anaplasma*, *Ehrlichia*, *Rickettsia*, FIP, systemic mycoses.
- Fecal examination.
- Tracheal wash or bronchoalveolar lavage.
- If immune disorders suspected—cytologic examination of synovial fluid; Coombs' test, rheumatoid factor, antinuclear antibodies.
- Pancreatic lipase immunoreactivity.
- T₄ in cats.

IMAGING**Radiography**

- Abdominal radiographs—tumors and effusion.
- Thoracic radiographs—pneumonia, neoplasia, pyothorax.
- Survey skeletal radiographs—bone tumors, multiple myeloma, osteomyelitis, discospondylitis, panosteitis, hypertrophic osteopathy, hypertrophic osteodystrophy.
- Dental/skull radiographs—tooth root abscess, sinus infections, foreign bodies, neoplasia.
- Contrast radiography (e.g., gastrointestinal and excretory urography).

Ultrasonography

- Abdominal (plus directed aspirate or biopsy)—abdominal neoplasia, abscess or other site of infection (e.g., pyelonephritis, pancreatitis, pyometra).
- Echocardiography if endocarditis suspected.

Nuclear Imaging

- Radionuclide scanning procedures to evaluate for bone tumors, osteomyelitis, pulmonary embolism.
- CT, MRI, or positron emission tomography scan if indicated.

DIAGNOSTIC PROCEDURES

- Arthrocentesis (culture and cytology).
- Bone marrow aspirate and biopsy if malignancy or myelodysplasia suspected.
- Lymph node, skin, or muscle biopsy if clinically indicated.
- Fine-needle aspirate or biopsy of any mass or abnormal organ.
- Central spinal fluid tap if neurologic signs.
- Endoscopy and biopsy if gastrointestinal signs.
- Exploratory laparotomy—last resort if all other diagnostic tests fail to determine cause and patient not improving.

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

Goals of treatment—reset thermoregulatory set point to lower level; remove underlying cause.

NURSING CARE

- Fluid administration (IV) often lowers body temperature.
- Topical cooling if fever is severe (convection cooling with fans, evaporative cooling with alcohol on foot pads, axilla, and groin).
- Only use antipyretic treatment when fever is prolonged and life-threatening (>106 °F, >41.1 °C) and topical cooling is unsuccessful. Impaired patients (e.g., with heart failure, seizures, or respiratory disease) require antipyretic treatment earlier. Antipyretic treatment may preclude elucidation of cause, delay correct treatment, and complicate patient monitoring (e.g., reduction of fever is important indication of response to treatment).

DIET

Febrile patients in hypercatabolic state require high caloric intake.

CLIENT EDUCATION

Work-up of patients with FUO often extensive, expensive, and invasive, and may not result in definitive diagnosis.

SURGICAL CONSIDERATIONS

Surgery may be necessary in some animals (e.g., pyometra, peritonitis, pyothorax, liver abscess, neoplasms).

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

Do not use broad-spectrum (i.e., "shotgun") treatment in place of thorough diagnostic workup unless patient's status is critical and deteriorating rapidly.

Antibiotics

- Based on results of bacterial culture or serology.
- In emergency situations, combination antibiotic therapy can be started after culture specimens obtained (e.g., cephalothin 20 mg/kg IV q6–8h; combined with enrofloxacin 10 mg/kg IV q24h). Additional antimicrobials depend on main clinical suspicion based on preliminary laboratory and clinical evidence.
- Do not give antibiotics longer than 1–2 weeks if ineffective.

Antipyretics

- Aspirin—dogs: 10 mg/kg PO q12h; cats: 6 mg/kg PO q48h.
- Deracoxib—dogs: 1–2 mg/kg/day.
- Carprofen—dogs: 2 mg/kg q12h.
- Meloxicam—0.1 mg/kg/day.
- Dipyrrone—dogs: 25 mg/kg IV.
- Flunixin meglumine—dogs: 0.25 mg/kg SC once (give IV fluids).

Glucocorticoids

- Do not use unless infectious causes have been ruled out.
- May mask clinical signs, may lead to immunosuppression, and not recommended for use as antipyretics; administration of corticosteroids to cats with intractable FUO after ruling out infectious diseases may promote favorable response.
- Primarily indicated for fever associated with immune-mediated disease and certain steroid-responsive tumors (e.g., lymphoma).

PRECAUTIONS

Side effects of antipyretics include emesis, diarrhea, gastrointestinal ulceration, renal damage, hemolysis, hepatotoxicity.

POSSIBLE INTERACTIONS

Combination of nonsteroidal anti-inflammatory drugs and steroids raises risk of gastrointestinal hemorrhage.

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

- Body temperature at least q12h.
- If cause of fever not found, repeat history and physical exam along with screening laboratory tests.
- If fever develops or worsens during hospitalization, consider nosocomial infection or superinfection.

EXPECTED COURSE AND PROGNOSIS

Vary with cause; in some patients (more commonly cats), underlying cause cannot be determined.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Young animals—infectious disease more common; prognosis better.
- Old animals—neoplasia and intra-abdominal infection more common; signs tend to be more nonspecific; prognosis often guarded.

SYNOMYNS

Pyrexia

SEE ALSO

Heat Stroke and Hyperthermia.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation.
- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIV = feline immunodeficiency virus.
- FUO = fever of unknown origin.

Authors Maria Vianna and Jörg Bucheler

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FLEA BITE HYPERSENSITIVITY AND FLEA CONTROL



BASICS

DEFINITION

Flea bite hypersensitivity (FBH)—allergic reaction to antigens in flea saliva.

F

Flea Life Cycle

- *Ctenocephalides felis* (cat flea)—not host specific; parasitizes cats, dogs, wildlife.
- Adult fleas mate on host and within 24 hours females lay up to 50 eggs per day.
- Eggs fall off pets into the environment and hatch.
- Larvae have negative phototropism and infest carpets, upholstery, and under furniture.
- Eggs from wildlife and feral cats survive in moist, protected areas.
- Larvae undergo molts until they pupate; the cocoon enhances survival.
- Adults emerge when environmental conditions and host availability are favorable.
- Less than 5% of the total flea burden is found as adults on the pet.
- The majority of the biomass is found as immature stages in the home and in peridomestic areas.

PATHOPHYSIOLOGY

- Antigens in flea saliva cause FBH.
- Major allergen—*Ctef1*, an 18-kD protein.
- Flea saliva—contains histamine-like compounds that irritate skin.
- Both immunoglobulin (Ig) E and IgG anti-flea antibodies reported.
- Immediate and delayed hypersensitivity reactions reported.
- Mast cell degranulation follows antigen exposure.
- FBH is associated with a T_H2 response.

SYSTEMS AFFECTED

Skin

GENETICS

No known inheritance pattern.

INCIDENCE/PREVALENCE

- Varies with climatic conditions and flea population.
- In areas where fleas are prevalent, FBH is considered the most common skin disease.

GEOGRAPHIC DISTRIBUTION

May occur anywhere; nonseasonal in climates that are warm and humid.

SIGNALMENT

Species

Dogs and cats.

Breed Predilections

None

Mean Age and Range

Typically signs by 5 years of age, but may be seen at any age.

SIGNS

Historical Findings

- Pruritus.
- Lack of consistent or effective flea control.

Physical Examination Findings

- Determined by the severity of the reaction.
- Finding fleas and flea dirt is supportive but not essential for diagnosis.
- Sensitive animals require a low exposure and tend to overgroom, removing evidence of infestation.
- Dogs—lesions concentrated in the caudal-dorsal lumbosacral region; caudal-lateral aspect of the thighs, lower abdomen, and inguinal region; primary lesions are papules; secondary lesions (hyperpigmentation, lichenification, alopecia, and scaling) and pyotraumatic dermatitis ("hotspots") are common. Erythema and papules around the umbilicus are highly suggestive ("peri-umbilical rush")
- Cats—head and neck pruritic papular dermatitis and/or a generalized distribution including dorsal lumbosacral area, caudomedial thighs, and abdomen. Also common clinical signs are self-induced symmetrical alopecia and lesions of the eosinophilic granuloma complex.

CAUSES

See Pathophysiology.

RISK FACTORS

Exposure to fleas; atopy may predispose dogs to FBH.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Food allergy.
- Atopy.
- Ectoparasitism.
- Dermatophytosis.
- Pyoderma.
- Any pruritic skin disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Usually normal.
- Cats—occasional eosinophilia.

OTHER LABORATORY TESTS

- Skin scrapings—negative.
- Flea combings—may find fleas or flea dirt.
- Intradermal allergen testing (IDT), radioallergosorbent test (RAST), and ELISA—variable accuracy; both false-positive and false-negative results reported.

DIAGNOSTIC PROCEDURES

- Diagnosis based on historical information, clinical signs, and response to anti-flea treatment.
- Fleas or flea dirt is supportive but not mandatory.
- Identification of *Dipylidium caninum* segments in stool is supportive.
- The only way to confirm FBH is by response to treatment.

PATHOLOGIC FINDINGS

- Superficial perivascular to interstitial dermatitis.
- Eosinophils often the predominant cell type.
- Eosinophilic intra-epidermal microabscesses may be visible.
- In cats—superficial or deep perivascular to interstitial dermatitis with numerous eosinophils and mast cells.
- Histopathologic evaluation—

does not differentiate FBH from other hypersensitivities.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient therapy.

NURSING CARE

N/A

DIET

N/A

CLIENT EDUCATION

- Inform owners that there is no cure for FBH; flea-allergic animals often become more sensitive to flea bites as they age.
- Hypoallergenization is not effective.
- Medications that stop itching are meant to bring relief while flea control is instituted.



MEDICATIONS

DRUG(S) OF CHOICE

Itch Relief

Corticosteroids

- Anti-inflammatory dosages for symptomatic relief while instituting adequate flea control. Use only as much as is needed and for the shortest duration to achieve the desired effect.
- Oral—prednisolone: cats, 1–2 mg/kg PO q24h for 5–7 days then taper; dogs, 0.5–1 mg/kg PO q24h for 7 days then taper, or for 4 days without tapering.

Oclacitinib

- Anti-itch, mild to moderate anti-inflammatory properties approved for allergic itch relief in dogs only. Usually a 7–10-day period is enough to control the itch while the anti-flea treatment is enhanced.
- Oral: 0.4–0.6 mg/kg q12h for 14 days, then reduce frequency to q24h.

Antihistamines

Little to no effect.

Flea Control

The most important therapy is the immediate reduction or elimination of adult fleas on the host. In a highly infested environment, it is recommended to treat the surroundings as well.

Pet-Targeted Flea Control

- Oral:
 - Nitenpyram—adulticide; has the fastest onset, but short acting; for dogs q24h, for cats q48h.
 - Spinosad—monthly oral treatment for dogs and cats.
 - Isoxazolines—very effective antiparasitic drugs, lotilaner, and sarolaner monthly and fluralaner trimonthly.
 - Topical/spot-on:
 - Dinotefuran/pyriproxyfen—rapid-acting spot-on product for dogs and cats; a second canine product

(CONTINUED)

FLEA BITE HYPERSENSITIVITY AND FLEA CONTROL

contains high-dose permethrin and should not be used on cats. • Fipronil plus insect growth regulator (IGR)—spot-on treatment for cats and dogs; spray treatment for dogs.

- Imidacloprid plus IGR—monthly spot-on treatment for cats and dogs; a second canine product contains permethrin and should not be used on cats; also available as a collar.

- Indoxycarb—monthly spot-on, dogs only, activated by flea digestive enzymes, contains permethrin, should not be used on cats.

- Selamectin—for dogs and cats, monthly spot-on; also has insect development inhibitor (IDI) action. • Selamectin plus sarolaner spot-on for cats—monthly spot-on.

- Fluralaner spot-on for dogs and cats—tri-monthly treatment. • Sprays—usually contain pyrethrins and pyrethroids with IGR.

IGRs

S-methoprene and pyriproxyfen are analogues of insect juvenile hormone that bind to immature stages and prevent maturation.

IDIs

Lufenuron and selamectin inhibit chitin synthesis in egg shell, immature stages, and adults.

Premises-Targeted Flea Control

- Indoor treatment: • Vacuuming significantly reduces the flea burden: removing eggs, larvae, and adult fleas; particularly carpets, furniture and the floor under furniture. • “Foggers/bombs” and premises sprays—contain organophosphates, pyrethrins, and/or IGRs. Etofenprox plus IGR and permethrin/pyrethrin plus IGR, available in inverted aerosol sprays; apply according to manufacturer’s directions; treat all areas of the house; can be applied by the owner. • Foggers/bombs do not effectively penetrate all areas commonly inhabited by fleas such as under furniture; handheld sprays are highly effective against biomass, may be directed where flea populations reside, and have long residual activity. • Professional exterminator—discuss products with representative.

Environment-Targeted Flea Control

- Outdoor treatment—concentrate in shaded areas; sprays usually contain pyrethroids or organophosphates and an IGR; owners should be educated on areas of application based on likelihood of reinfestation from feral cats and wildlife.
- Nematode (*Steinernema carpocapsae*)—may

kill *C. felis* larvae and pupae, but efficacy is unknown; no knowledge of the effects these worms might have on beneficial insects, mammals, or humans.

CONTRAINdications

N/A

PRECAUTIONS

- Label instructions—must be strictly followed.
- Spinosad can potentiate neurologic side effects of high-dose ivermectin—but is safe when combined with heartworm preventive dose.
- Isoxazolines should be used with caution in animals with preexisting epilepsy.
- Pyrethrin/pyrethroid-type flea products—adverse reactions include depression, hypersalivation, muscle tremors, vomiting, ataxia, dyspnea, and anorexia: do not use in cats.
- Organophosphates—inappropriate given the current alternatives.

ALTERNATIVE DRUG(S)

- Powders and dips—adverse reactions and toxicity make their use inappropriate given the current alternatives. Shampoos containing D-limonene on cats can cause acute necrotizing dermatitis and septicemia.
- Over-the-counter products often contain the same ingredient(s), but the absence of proper education frequently leads to failure in flea control.



FOLLOW-UP

PATIENT MONITORING

- Pruritus—a decrease means the FBH is being controlled. • Fleas and flea dirt—absence is not always a reliable indicator of successful treatment.

PREVENTION/AVOIDANCE

- Warm climates and infested premises require year-round flea control.
- Seasonally warm climates—begin flea control when temperatures consistently remain above freezing.

POSSIBLE COMPLICATIONS

- Secondary bacterial folliculitis.
- Acute moist dermatitis.
- Acral lick dermatitis.

EXPECTED COURSE AND PROGNOSIS

Prognosis is excellent if strict flea control is instituted.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Anemia—could result from heavy flea burden, especially in puppies or kittens. • *Dipylidium caninum* due to ingestion of the flea.

F

AGE-RELATED FACTORS

Package should be consulted for the minimum approved age for application.

ZOONOTIC POTENTIAL

- Humans can be bitten by fleas; the resulting papular rash can be mild to extensive, depending on numbers of fleas and individual hypersensitivity reactions.
- *C. felis* can transmit zoonotic agents, including *B. henselae* (cat scratch disease), *R. felis* (murine typhus, flea-borne typhus), and *D. caninum* (tapeworms).

PREGNANCY/FERTILITY/BREEDING

- Corticosteroids and organophosphates—do not use in pregnant bitches and queens.
- The safe use of sarolaner and afoxolaner has not been evaluated in breeding, pregnant, or lactating dogs.

SYNONYMS

- Flea bite allergy.
- Flea allergy dermatitis.

ABBREVIATIONS

- ELISA = enzyme-linked immunosorbent assay.
- FBH = flea bite hypersensitivity.
- IDI = insect development inhibitor.
- IDT = intradermal allergen testing.
- Ig = immunoglobulin.
- IGR = insect growth regulator.
- RAST = radioallergosorbent test.

INTERNET RESOURCES

<http://capcvet.org>

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Steven A. Levy.



**Client Education Handout
available online**

GASTRITIS, CHRONIC



BASICS

DEFINITION

Inflammation of the stomach leading to clinical signs of >3 weeks' duration.

G

PATHOPHYSIOLOGY

- Inflammation may be secondary to drugs, infection, neoplasia, toxins/irritants, foreign material, food antigens or bacterial antigens; may be primary as a form of inflammatory bowel disease (IBD).
- Visceral receptors stimulated by inflammation, distension, etc. send signals via vagal and sympathetic nerves to vomiting center (medulla oblongata).

SYSTEMS AFFECTED

- Gastrointestinal (GI).
- Musculoskeletal—weight loss, muscle wasting, weakness.
- Integument—hair coat changes.
- Respiratory—respiratory aspiration pneumonia.

GENETICS

N/A

INCIDENCE/PREVALENCE

Common

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Norwegian lundehund—chronic atrophic gastritis with IBD (lymphoplasmacytic); can progress to adenocarcinoma.
- Basenji and Drentse Patrijshond—chronic hypertrophic gastritis.

Mean Age and Range

Any age.

Predominant Sex

None

SIGNS

Historical Findings

- Vomiting is most common—digested or undigested food, bile, frank blood, digested blood ("coffee grounds"); variable frequency.
- Hyporexia to anorexia.
- Melena.
- Polydipsia.
- Diarrhea with concurrent intestinal disease.
- Retching.
- Burping.
- Weight loss.

Physical Examination Findings

- Abdominal distension ± pain.
- Ptyalism.
- Muscle wasting, weight loss, coat changes.
- Pallor if bleeding ulcer.
- Dehydration or hypovolemia.

CAUSES

- Food sensitivity.
- IBD.
- Toxins, e.g., heavy metals, environmental irritants (cleaners, herbicides).
- Metabolic/endocrine disease—renal disease, liver disease, hypoadrenocorticism, pancreatitis, hyperthyroidism.
- Neoplasia—

large or small cell lymphoma, adenocarcinoma, polyp, gastrinoma, leiomyosarcoma, plasma cell tumor, mast cell tumor.

- Foreign material.
- Drugs—nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, chemotherapeutics.
- Parasitism—*Toxocara* spp., *Physaloptera* spp. (dogs and cats), *Ollulanus tricuspis* (cats).
- Helicobacter* spp.
- Pythiosis.
- Canine distemper virus.
- Hypergastrinemia—gastrinoma, achlorhydria, Basenji gastroenteropathy, hepatic or renal disease.
- Miscellaneous—stress, emphysematous gastritis (gas-forming organisms/severe signs), benign gastric emphysema (milder disease/air trapping), eosinophilic sclerosing fibroplasia.

RISK FACTORS

- Drugs (e.g., NSAIDs).
- Unsupervised/free-roaming pets—exposure to toxin.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any cause of GI signs.
- Esophageal disease—differentiate vomiting from regurgitation.
- Hypertrrophic pyloric gastropathy.
- Bilious vomiting syndrome.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemoconcentration if dehydrated.
- Anemia—if blood loss (regenerative anemia if acute blood loss such as ulceration; microcytic, hypochromic with chronic blood loss).
- Thrombocytosis with chronic blood loss leading to iron deficiency.
- Eosinophilia with parasitism, neoplasia, or eosinophilic gastritis.
- Biochemistry—prerenal or renal azotemia; increased blood urea nitrogen (BUN) : creatinine ratio with GI bleeding; hyperkalemia and hyponatremia with hypoadrenocorticism; hypochloremic metabolic alkalosis with gastric outflow obstruction.
- Urinalysis—unremarkable.

OTHER LABORATORY TESTS

- Gastrin levels—elevated with gastrinoma; may be elevated with azotemia or use of antacids.
- T₄.
- Fecal float.
- Baseline cortisol ± adrenocorticotropic hormone (ACTH) stimulation test.
- Pythium ELISA.
- Iron panel (iron deficiency with bleeding).

IMAGING

- Abdominal radiographs—radiopaque foreign material, thickened gastric wall, gastric distension.
- Contrast radiography—radiolucent foreign material, outflow obstruction, delayed emptying, wall defects or thickening.
- Ultrasonography—wall thickening, layering loss, ulcer, foreign object, mass.

DIAGNOSTIC PROCEDURES

- Upper GI endoscopy—visualize gastric mucosa, identify ulcer or mass, retrieve foreign object, biopsy (even when grossly

normal), removal of small mass lesions (cautery), evaluate duodenum.

- Exploratory laparotomy—perforated ulcer, full-thickness biopsy, partial gastrectomy, mass removal.
- Wireless capsule endoscopy—identify mass or ulcer.

PATHOLOGIC FINDINGS

- IBD—variable inflammatory infiltrate: lymphoplasmacytic, eosinophilic, neutrophilic, granulomatous/histiocytic gastritis (investigate for infectious cause).
- Helicobacter* spp. do not always convey pathology—significant populations deep in gastric glands may warrant treatment.
- Special stains—further evaluation of potential neoplasia and infectious organisms.



TREATMENT

APPROPRIATE HEALTH CARE

- Many treated as outpatients pending diagnostic testing or treatment trials (i.e., diet, drugs).
- Inpatient management warranted if significant dehydration or hypovolemia present.

NURSING CARE

- IV fluids based on patient status; *caution* for fluid overload with hypoproteinemia.
- Enteral nutrition (nasoesophageal, nasogastric, or esophageal tubes) with persistent anorexia.
- Severe hypoalbuminemia—consider albumin, plasma, or colloids.

ACTIVITY

Restrict postoperatively if surgery performed.

DIET

- Novel protein or hydrolyzed diet when allergy or IBD suspected; initial response expected within 2 weeks; worsening warrants diet change or other intervention; if improvement noted, continue beneficial diet for several months before reintroducing other foods to assess tolerance.
- Challenge with original diet can prove food hypersensitivity; rarely pursued.
- Low-fat diet if hyperacidity or gastric ulcer.
- Frequent, small meals (q4–6h) may provide benefit.
- Small late-night meal may decrease bilious vomiting.
- Calorie requirement/diet guideline increases compliance.
- Unflavored or topical flea, tick, and heartworm preventatives.
- Treats limited to prescription diet.
- If commercial diet declined, consider home-cooked diet formulated by veterinary nutritionist.

CLIENT EDUCATION

- Review multiple etiologies.
- Least invasive testing first when patient status allows; biopsy for definitive diagnosis if extra-intestinal causes ruled out and patient fails diet and drug trial (i.e., anthelmintic).

(CONTINUED)

GASTRITIS, CHRONIC**G****MEDICATIONS****DRUG(S) OF CHOICE**

- Anthelmintic—fenbendazole (50 mg/kg PO q24h for 5 days), pyrantel pamoate + febantel.
- Gastroprotectants—proton pump inhibitor (PPI), i.e., omeprazole (1 mg/kg PO q12h 30–60 min before meal); also consider sucralfate, H₂ receptor antagonist, and others per ACVIM consensus (see Suggested Reading).
- Antiemetics—maropitant (1 mg/kg SC or IV q24h; 2 mg/kg PO q24h), ondansetron, metoclopramide, mirtazapine.
- Prokinetics—metoclopramide (0.2–0.4 mg/kg PO q8h; CRI 1–2 mg/kg/day), cisapride, ranitidine, low-dose erythromycin.
- IBD suspected/confirmed—glucocorticoid (i.e., prednisone 2 mg/kg PO q24h or divided q12h; prednisolone for cat) when no clinical response to other therapeutic trials or in advanced disease; taper by 20–25% increments over time to lowest effective dose; discontinue when possible; total dose not >60 mg per day (dog); use with diet.
- If glucocorticoid not tolerated and/or relapse, consider second drug; see Alternative Drug(s).
- *Helicobacter* gastritis—several protocols have been described (e.g., metronidazole, amoxicillin, clarithromycin); see Suggested Reading.

CONTRAINDICATIONS

- Do not use prokinetics if GI obstruction possible.
- Do not use antacids or PPIs with atrophic gastritis and achlorhydria.

PRECAUTIONS

- Immune modulation predisposes to secondary infections.
- Steroids can cause GI ulceration, diabetes mellitus, or fluid overload (especially cat: congestive heart failure); patient monitoring and client education are vital to success.
- Prolonged use of antacids or PPIs can lead to overgrowth of bacteria.

POSSIBLE INTERACTIONS

- Sucralfate will decrease absorption of other medications; separate by 2 hours from other medications.
- Omeprazole affects clearance of many drugs.
- Never use NSAIDs with glucocorticoids; high risk for GI erosion or ulcer.

ALTERNATIVE DRUG(S)

- IBD—if steroid and diet alone do not achieve disease remission, if patient relapses, and/or if steroid side effects are undesirable, second agent may be considered; options:

cyclosporine, mycophenolate, chlorambucil, azathioprine (never in cats); find lowest effective dose.

- Monitoring—exam, labwork (CBC, chemistry) for myelosuppression and other concerns (i.e., hepatic toxicity with cyclosporine, chlorambucil, and azathioprine).
- Budesonide (steroid; 1–3 mg/patient depending on size) may have fewer systemic side effects; adrenal pituitary axis is affected.

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

- Depends on patient severity and medication chosen; minimum—physical exam within 2 weeks of starting treatment.
- Recheck abnormal labwork (i.e., electrolytes, proteins) and monitor for medication side effects (i.e., hyperglycemia, anemia, myelosuppression, hepatopathy, etc. based on specific drugs selected).
- Recurrence warrants repeat diagnostics; repeat biopsy may be indicated (i.e., patients previously in remission of IBD can progress to lymphoma).
- Lack of response—change in medical management (i.e., alternative diet or drug); repeat biopsy (primary disease may have been missed) and labwork (CBC, chemistry, fecal, T₄) for emerging comorbidity.

PREVENTION/AVOIDANCE

- Avoid drugs with high incidence of GI upset (i.e., doxycycline, NSAIDs).
- Avoid rapid diet change.
- Prevent free-roaming and potential for dietary indiscretion—may need basket muzzle in dogs.

POSSIBLE COMPLICATIONS

- Gastroesophageal reflux.
- Delayed gastric emptying/motility disorders.
- Erosions/ulcers.
- Aspiration pneumonia.
- Electrolyte or acid-base imbalances.
- Progression from superficial to atrophic gastritis.
- Debilitation/death in refractory cases.
- Steroids—diabetes mellitus, heart failure, calcinosis cutis, muscle weakness, ulcers.
- Other immune-modulating drugs—bone marrow suppression, pancreatitis, hepatitis, GI upset.

EXPECTED COURSE AND PROGNOSIS

- Varies with cause.
- Medication tapered to lowest effective dose ± stopped with diet.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

- Foreign objects—more common in young animals.
- Food-responsive enteropathy—often younger animals.
- IBD—often middle-aged to older.
- Neoplasia—middle-aged to older animals more common.

ZOONOTIC POTENTIAL

Potential/uncommon concern secondary to parasites (i.e., *Toxocara spp.*—larval migrans).

PREGNANCY/FERTILITY/BREEDING

- Prednisone—abortion, teratogenic, can induce parturition.
- Azathioprine—fetal harm; decrease sperm production.
- Cyclosporine—fetal toxicity.

SEE ALSO

- Biliary Vomiting Syndrome.
- Gastroduodenal Ulceration/Erosion.
- Gastroenteritis, Eosinophilic.
- *Helicobacter spp.*
- Hypertrophic Pyloric Gastropathy, Chronic.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- GI = gastrointestinal.
- IBD = inflammatory bowel disease.
- NSAID = nonsteroidal anti-inflammatory drug.
- PPI = proton pump inhibitor.

INTERNET RESOURCES

- <https://veterinarianpartner.vin.com/default.aspx?pid=19239&id=4951472>
- <https://veterinarianpartner.vin.com/default.aspx?pid=19239&id=4951476>

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Acknowledgment The author and book editors acknowledge the prior contribution of Michelle Pressel



Client Education Handout
available online

GESTATIONAL DIABETES MELLITUS



OVERVIEW

Diabetes mellitus (DM), which occurs during mid to late gestation, most likely due to insulin resistance from increased progesterone and growth hormone production by the mammary glands.

SIGNALMENT

- Middle-aged intact female dogs.
- Mean age—6 years.
- Nordic spitz breeds are overrepresented.
- Not reported in cats.

SIGNS

- Polyuria.
- Polydipsia.
- Polyphagia.
- Weight loss.
- Lethargy.
- Vomiting.
- Ketosis.

CAUSES & RISK FACTORS

- Late-term pregnancy.
- Diestrus.
- Exogenous progesterone supplementation.
- Acromegaly.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Acromegaly—affected bitches are listless and have increased abdominal size, increased interdental spaces, polyuria/polydipsia, weight gain, and excessive skin folds in the facial/neck areas.

CBC/Biochemistry/Urinalysis

- Hyperglycemia.
- Glucosuria.
- Metabolic acidosis if ketonemic or ketonuric.

Other Laboratory Tests

Urine culture—urinary tract infections can contribute to insulin resistance.

Imaging

- Ultrasonography—assess fetal viability; deceased puppies may affect treatment decisions.
- Radiographs—determine fetal size and relative risk for dystocia.

Diagnostic Procedures

N/A



TREATMENT

- Nonpharmacologic considerations—management of gestational DM requires intensive fluid and insulin therapy.

Continued glucose toxicity can destroy the pancreatic beta cells' capacity to produce insulin, leading to permanent DM.

- Ovariectomy is recommended. While the diabetes may resolve at the end of diestrus or after parturition, it will return on subsequent cycles and then has a greater potential to become permanent.



MEDICATIONS

DRUG(S) OF CHOICE

- Insulin—if ketosis not present, start at an insulin dose of 0.25 U/kg SC q12h of intermediate or long-acting insulin; will likely need to increase the dose to achieve glycemic control. If ketoacidosis is present, regular insulin (0.1–0.2 U/kg IM q4–6h) may be necessary to achieve initial glycemic control before switching to longer-acting insulin.
- Aglepristone—10 mg/kg SC days 1, 2, 9, and 17 from diagnosis. This medication is a progesterone receptor blocker, but does not affect progesterone levels. Treatment reserved for cases in which ovariectomy is not possible or authorized by the owners.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Care must be taken to avoid insulin overdose causing hypoglycemia during the immediate postpartum period (or the end of diestrus), because the speed at which insulin resistance resolves and exogenous insulin requirements decrease is unpredictable.

PREVENTION/AVOIDANCE

Ovariectomy to remove source of progesterone.

POSSIBLE COMPLICATIONS

Lack of prompt resolution of hyperglycemia may result in diabetes mellitus becoming permanent.

EXPECTED COURSE AND PROGNOSIS

- Diabetes usually resolves at parturition or at the end of diestrus. More likely to be transient DM if pregnancy terminated, whereas insulin-treated bitches more likely to develop permanent DM.
- May abort the litter or have dystocia as a result of the effects of chronic hyperglycemia.
- Small, unthrifty puppies may result from an abnormal placental blood supply. Conversely, some fetuses in a hyperglycemic environment experience an abnormally increased growth

rate (macrosomia). These puppies tend to be large, leading to dystocia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Pregnancy

AGE-RELATED FACTORS

Older bitches are more likely to develop permanent DM.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

May abort the litter or have dystocia as a result of the effects of chronic hyperglycemia. There is thought to be a genetic component, due to a breed predisposition. It is not advised to continue to breed affected individuals.

SEE ALSO

Diabetes Mellitus without Complication—Dogs.

ABBREVIATIONS

- DM = diabetes mellitus.

Suggested Reading

Johnson CA. Glucose homeostasis during canine pregnancy: insulin resistance, ketosis, and hypoglycemia. Theriogenology 2008, 70(9):1418–1423.

Author Carla Barstow

Consulting Editor Erin E. Runcan

G

GIARDIASIS



BASICS

OVERVIEW

- Enteric infection of dogs and cats with protozoan parasite, *Giardia duodenalis*.
- Direct transmission by ingestion of cysts that are immediately infective when shed in feces.
- Trophozoites, motile (flagellated) organisms released from ingested cysts, attach to surface of enterocytes in small intestine with ventral sucking disc; move from site to site.
- Can cause small bowel diarrhea, but infection often asymptomatic.

G

SIGNALMENT

More common in dogs than cats.

SIGNS

- Clinical signs more common in young hosts; adults usually asymptomatic.
- Signs can be acute, transient, intermittent, or chronic.
- Malabsorption syndrome with soft, frothy, greasy, voluminous feces (diarrhea), usually with rancid odor.

CAUSES & RISK FACTORS

- Transmitted by ingestion of cysts from feces in/on food, water, environment, or fur.
- Indirect water-borne transmission most common; cool, moist conditions favor cyst survival.
- Higher risk of infection in puppies and kittens, in high-density populations, and in animals with compromised immunity.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious and noninfectious causes of small bowel diarrhea, maldigestion, and malabsorption syndromes, especially pancreatic exocrine insufficiency or inflammatory bowel disease.
- In cats, differentiate from infection with *Tritrichomonas foetus*.

CBC/BIOCHEMISTRY/URINALYSIS

Generally within normal limits.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Detection of *Giardia* trophozoites, cysts, or antigen in feces.
- Trophozoites (15 × 8 µm) detectable in fresh feces (especially diarrheic feces) and in duodenal aspirates obtained by endoscopy; trophozoites identified on Diff-Quik® or Lugol's iodine-stained fecal smear by teardrop shape with two prominent nuclei. Trophozoites

identified in wet mount diluted in saline by "falling leaf" motility; flotation media may lyse trophozoites, interfering with accurate identification.

- Cysts, ~12 µm long, oval with 2–4 nuclei, shed intermittently; centrifugal flotation of fresh feces in zinc sulfate (specific gravity 1.18) preferred method for identification of cysts. Three samples collected at 2–3-day intervals should be examined to detect >70% of infections; cysts become distorted (crescent-shaped) in sugar or other flotation solution with specific gravity >1.25; formalin–ethyl acetate sedimentation is useful in cases of steatorrhea.
- ELISA-based kits available for in-house detection of *Giardia* antigen in feces have high sensitivity; kits should be used to confirm suspicious cases rather than for screening healthy animals; if clinical signs resolve, continued antigen testing not recommended.
- PCR testing—commercial laboratories; studies have shown variable (usually poorer) sensitivity compared to other methods.



TREATMENT

- Outpatient, unless debilitated or dehydrated.
- Drug therapy should be combined with environmental cleaning and disinfection plus bathing of patient.
- Giardia* vaccines commercially available; efficacy is poor and vaccine not widely used.



MEDICATIONS

DRUG(S) OF CHOICE

- All extra-label.
- Fenbendazole—50 mg/kg PO q24h for 3 days (dogs) or 5 days (cats); second course of treatment may be necessary.
- Metronidazole—20–22 mg/kg PO q12h for 5–8 days in dogs.
- Metronidazole benzoate—22–25 mg/kg PO q12h for 5–7 days in cats.
- Fenbendazole (50 mg/kg PO q24h) plus metronidazole (25 mg/kg PO q12h) for 5 days—may provide better resolution and reduction in cyst shedding.
- Combination febantel, pyrantel pamoate, and praziquantel product—use for 3 days at label dose for *Giardia*.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Metronidazole—efficacy reportedly 50–67% in dogs; bitter taste; can cause anorexia, vomiting, vestibular signs.
- Albendazole (25 mg/kg PO q12h for 2 days in dogs or 5 days in cats) is effective but not

recommended because it can be teratogenic and cause anorexia, depression, vomiting, ataxia, diarrhea, abortion, and myelosuppression.



FOLLOW-UP

- Repeat fecal examinations to confirm efficacy of treatment and detect reinfection.
- Chronic infection can lead to debilitation.



MISCELLANEOUS

ZOONOTIC POTENTIAL

- In North America, *Giardia* is the most common intestinal parasite in humans. Dog and cat isolates are host specific, with little data to demonstrate transmission from pets to humans.
- Most *Giardia* infections in humans are anthropotic or originate from livestock.
- Zoonotic transmission from pets to immunosuppressed humans may occur.

PREGNANCY/FERTILITY/BREEDING

Do not use albendazole in pregnant animals.

INTERNET RESOURCES

- <https://capcvet.org>
- <https://www.cdc.gov/parasites/giardia>

Suggested Reading

Bowman DD. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis, MO: Elsevier Science, 2009, pp. 89–91.

Uehlinger FD, Naqvi SA, Greenwood SJ, et al. Comparison of five diagnostic tests for *Giardia duodenalis* in fecal samples from young dogs. Vet Parasitol. 2017, 244:91–96.

Authors Matt Brewer and Katy A. Martin

Consulting Editor Amie Koenig

GLAUCOMA



BASICS

DEFINITION

- A group of diseases where elevated intraocular pressure (IOP) causes optic nerve and retinal degeneration with subsequent loss of vision.
- Diagnosis—IOP >20 mmHg (dogs) or >25 mmHg (cats) as determined by tonometry, with changes in vision or the appearance of the globe, optic nerve, and/or retina.

PATHOPHYSIOLOGY

- Multifactorial disease where obstruction of aqueous humor outflow leads to increased IOP and optic nerve degeneration.
- Elevated IOP induces mechanical changes (stretching of sclera in lamina cribrosa damages optic nerve axons) and vascular changes (decreased ocular perfusion causes ischemic damage to retina), resulting in ganglion cell death and optic nerve atrophy.

SYSTEMS AFFECTED

- Ophthalmic.
- Nervous.

GENETICS

- Primary angle-closure glaucoma (PACG; dogs)—complex trait with multiple genetic risk factors and uncertain mode of inheritance.
- Primary open-angle glaucoma (POAG; dogs)—monogenic (*ADAMTS10*) and autosomal recessive.
- Primary congenital glaucoma (PCG; cats)—monogenic (*LTPB2*) and autosomal recessive.

INCIDENCE/PREVALENCE

- Dogs—prevalence depends on breed; primary and secondary glaucoma are each listed as approximately 0.8% of all hospital admissions in the North American Veterinary Medical Database (NAVMDB).
- Cats—relatively uncommon; less than 0.3% of diagnoses in NAVMDB.

SIGNALMENT

Species

- Dog—primary and secondary common.
- Cat—primary rare; secondary more common (due to intraocular neoplasia or chronic uveitis).

Breed Predilections

- PACG—Alaskan Malamute, American cocker spaniel, Australian cattle dog, basset hound, Boston terrier, bouvier des Flandres, bullmastiff, Chinese Shar-Pei, chow chow, Dalmatian, Dandie Dinmont terrier, English cocker spaniel, English springer spaniel, flat-coated retriever, golden retriever, Great Dane, Labrador retriever, Newfoundland, poodle, Samoyed, Shiba Inu, shih tzu, Siberian husky, Welsh springer spaniel.

- POAG—beagle, Norwegian elkhound, petit basset griffon Vendéen.
- PCG—Siamese cats.
- Other forms of primary glaucoma—Burmese, Persian, Siamese cats.

Mean Age and Range

- Primary (dogs)—any age; predominantly affects middle-aged (4–9 years).
- Secondary (cats)—usually affects older cats (>6 years).

Predominant Sex

Females suffer PACG compared to males at a ratio of 2 : 1.

SIGNS

General Comments

All well-equipped small animal hospitals should have a tonometer.

Historical Findings

- Dogs—owners may note pain (blepharospasm, tenderness about the head), serous to seromucoid ocular discharge, red or cloudy eye, dilated pupil, or altered vision; in chronic cases, globe enlargement may be apparent.
- Cats—signs are more subtle; eye may not appear painful, red, or cloudy; owners may note dilated pupil, vision changes, or enlarged globe.

Physical Examination Findings

Acute Primary

- High IOP (often >30 mmHg).
- Blepharospasm.
- Enophthalmos with elevated third eyelid.
- Episcleral injection.
- Diffuse corneal edema.
- Mydriasis.
- Vision loss—may be detected by lack of menace response, dazzle reflex, and/or direct or consensual pupillary light reflex.
- Optic nerve may be normal or swollen and hyperemic.

Chronic (End Stage)

- High or normal IOP.
- Buphthalmos.
- Descemet's streaks (Haab's striae).
- Subluxated lens with an aphakic crescent.
- Optic nerve head atrophy will appear dark and cupped.
- Retinal atrophy detected by peripapillary or generalized tapetal hyper-reflectivity.

Secondary

- High IOP.
- Episcleral injection.
- Corneal edema.
- Aqueous flare.
- Iris changes (miosis or mydriasis, posterior synechia, iris bombe).
- Hyphema.
- Anterior lens luxation.
- Intumescent cataracts.
- Intraocular mass.

CAUSES

- Congenital—severe dysgenesis/lack of formation of the iridocorneal angle.
- Primary—developmental iridocorneal angle anomalies that impede aqueous humor outflow.
- Secondary—obstruction of aqueous humor outflow by various mechanisms, e.g., uveitis (inflammatory cells or debris), anterior lens luxation (lens or attached vitreous), red blood cells, or neoplastic cells.

RISK FACTORS

- Age.
- Breed.
- Chronic uveitis.
- Goniodygenesis—developmental defect of iridocorneal angle.
- Lens luxation.
- Hypermature or intumescent cataracts.
- Hyphema.
- Intraocular neoplasia.
- Topically applied mydriatics—may precipitate acute glaucoma in predisposed animals.
- Primary glaucoma is bilateral and often asymmetric; the unaffected fellow eye is at risk for developing glaucoma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- See Red Eye.
- Conjunctivitis—normal IOP and pupil size with conjunctival hyperemia (diffuse, red discoloration) instead of episcleral vessel engorgement.
- Uveitis—initially low IOP with miotic pupil.

IMAGING

Ocular ultrasound—facilitates evaluation of eye with opaque ocular media; may identify cause of secondary glaucoma (lens luxation, intraocular tumor).

DIAGNOSTIC PROCEDURES

- Rebound or applanation tonometry—essential for diagnosis of glaucoma.
- Gonioscopy—referral procedure that allows for evaluation of iridocorneal angle and assists with diagnosis of primary vs. secondary glaucoma.
- Systemic workup may be indicated in cases of secondary glaucoma due to chronic uveitis, hyphema, or intraocular neoplasia.

PATHOLOGIC FINDINGS

- Histopathologic evaluation is required for all eyes enucleated due to intractable glaucoma.
- Iridocorneal angle morphology assists diagnosis of primary vs. secondary glaucoma.
- Loss of retinal ganglion cells.
- Gliosis and “cupping” of optic nerve head.

(CONTINUED)

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

- Acute—outpatient medical management vs. referral.
- Chronic—outpatient medical management vs. salvage surgical management.

CLIENT EDUCATION

- Warn client that primary glaucoma is a bilateral disease; more than 50% of dogs develop glaucoma in the other eye within 8 months without prophylactic therapy.
- Warn client that up to 50% of dogs will be blind in the affected eye within the first year regardless of therapy.

SURGICAL CONSIDERATIONS

- Acute, visual eyes (dogs)—referral surgical procedures aim to control IOP by decreasing aqueous humor production (transscleral or endoscopic cyclophotocoagulation), increasing outflow (gonioimplants), or both; medical treatment is still required long term to control IOP and inflammation.
- Blind, painful eyes (dogs and cats)—salvage procedures include enucleation, evisceration with intrascleral prosthesis (if no intraocular infection or neoplasia), and intravitreal gentamicin or cidofovir injection to minimize long-term medical therapy.

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

Use multiple agents to lower IOP into the normal range as quickly as possible in an attempt to salvage vision and maintain comfort. Topical hypotensive drugs have largely replaced systemic therapy due to higher efficacy and fewer side effects.

Acute Primary (Dogs)

- Prostaglandin analog—latanoprost 0.005% q12h. In emergency, apply one drop to affected eye, followed by another drop in 30 min. Recheck IOP in 1–2 hours.
- Carbonic anhydrase inhibitor—dorzolamide 2% q8h. Use in combination with latanoprost for long-term therapy.
- Topical corticosteroids—0.1% dexamethasone or 1% prednisolone acetate q12h. Use to control intraocular inflammation from initial hypertensive episode.
- ± Topical beta blocker—timolol maleate 0.5% q12h. Minimal effect on lowering IOP in companion animals. Use as auxiliary or prophylactic medication.

- ± Hyperosmotic agent—mannitol 1–2 g/kg IV over 20 min. In emergency, use to dehydrate vitreous humor and lower IOP if topical medications ineffective.

Secondary (Dogs and Cats)

- Identify and treat primary disease.
- Topical corticosteroids—to reduce inflammation if no ulcerative keratitis.
- Topical carbonic anhydrase inhibitors.
- ± Topical beta blockers.

CONTRAINDICATIONS

- Topical atropine—do not use with glaucoma.
- Prostaglandin analogs/miotic agents—do not use with primary anterior lens luxation or uveitis; mostly ineffective in cats.

PRECAUTIONS

- Systemic absorption of topical beta blockers may cause bronchoconstriction and bradycardia in small dogs and cats.
- Hyperosmotic agents may initiate acute pulmonary edema in patients with cardiovascular disease or hypervolemia.

POSSIBLE INTERACTIONS

Concurrent administration of latanoprost with a topical nonsteroidal anti-inflammatory drug such as flurbiprofen 0.03% may decrease its hypotensive effect.

ALTERNATIVE DRUG(S)

- Prostaglandin analogs—travoprost 0.004% q12h, bimatoprost 0.03% q12h.
- Carbonic anhydrase inhibitor—brinzolamide 1% q8h.
- Beta blockers—levobunolol 0.5% q12h, betaxolol 0.5% q12h.
- Osmotic agents—hypertonic hydroxyethyl starch 6–7.5% (4 mL/kg IV over 15–20 min).

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

- IOP—monitored often (weekly to monthly) after starting initial therapy, then q3–4 months long term. Client's daily observation of comfort and vision is most important.
- Monitor for drug reactions.

PREVENTION/AVOIDANCE

- Primary—bilateral disease; recommend that a veterinary ophthalmologist examine the unaffected eye to determine its risk of developing glaucoma.
- Prophylactic therapy for the predisposed, unaffected eye delays onset of glaucoma—0.25% demecarium bromide (miotic) q12h, or 0.5% timolol maleate q12h, or 2% dorzolamide q8–12h.

POSSIBLE COMPLICATIONS

- Blindness.
- Chronic ocular pain.

EXPECTED COURSE AND PROGNOSIS

- Chronic disease that requires constant medical treatment (even with surgical intervention).
- With medical treatment only—most patients ultimately become blind.
- Referral surgical treatment—better chance of retaining vision longer; most patients do not remain visual for more than 2 years after initial diagnosis.
- Secondary to lens luxation—may carry fair prognosis with referral for successful removal of luxated lens and postoperative medical therapy.
- Secondary to anterior uveitis—may carry fair prognosis with control of uveitis.

G**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

- All listed drugs may affect pregnancy.
- Primary and lens luxation cases—Inherited; do not breed affected animals.

SEE ALSO

- Anterior Uveitis—Cats.
- Anterior Uveitis—Dogs.
- Lens Luxation.
- Red Eye.

ABBREVIATIONS

- IOP = intraocular pressure.
- PACG = Primary angle-closure glaucoma.
- POAG = Primary open-angle glaucoma.
- PCG = Primary congenital glaucoma.
- NAVMDB = North American Veterinary Medical Database.

Suggested Reading

- Miller PE. The glaucomas. In: Maggs DJ, Miller PE, Ofri R, eds. Slatter's Fundamentals of Veterinary Ophthalmology, 6th ed. St. Louis, MO: Elsevier, 2018, pp. 279–305.
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Author Erin M. Scott**Consulting Editor** Kathern E. Myrna**Acknowledgment** The author and book editors acknowledge the prior contribution of J. Phillip Pickett.**Client Education Handout available online**

GLUCOSURIA



BASICS

DEFINITION

Glucosuria is detected via routine laboratory testing, most commonly with reagent test strips. Persistent glucosuria is an abnormal finding.

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PATHOPHYSIOLOGY

- Glucose is a small molecule that is freely filtered through the glomerulus into the ultrafiltrate.
- Glucose is actively reabsorbed in the proximal renal tubule by a sodium-glucose co-transport system. Physiologic levels of filtered glucose are mostly reabsorbed, leaving excreted levels too low to detect using screening tests.

Hyperglycemic Glucosuria

- Glucosuria will be present when blood glucose concentration exceeds renal tubular epithelial transport maximum. This varies by species, with dogs typically above 180 mg/dL and cats typically above 280 mg/dL.
- If hyperglycemia is present, determine whether glucosuria transient or persistent.

Transient

- Physiologic—usually transient and associated with release of endogenous “stress” hormones (catecholamines, glucagon, corticosteroids); especially common in cats. Serum may be normoglycemic or hyperglycemic at urine collection because different concentrations of glucose excreted in urine over time equilibrate in bladder.
- Pharmacologic—may occur following administration of glucose-containing solutions (e.g., dextrose); administration of drugs (glucocorticoids, growth hormone, thiazide diuretics, morphine, epinephrine) may also result in hyperglycemia and glucosuria.
- Toxic—ethylene glycol.
- Pathologic—possible with acute pancreatitis.

Persistent

Pathologic conditions that can result in persistent glucosuria (due to hyperglycemia) include diabetes mellitus, hyperadrenocorticism, acromegaly, extreme stress, hyperthyroidism in cats.

Normoglycemic Glucosuria

Impaired renal proximal tubular epithelial cell reabsorptive capacity.

Congenital

Primary glucosuria—Scottish terriers; Fanconi syndrome: basenji dogs; also sporadic in Norwegian elkhounds, Shetland sheepdogs, miniature schnauzers, Labrador retrievers, border terriers, whippets, Yorkshire terriers, and mixed-breed dogs; decreased reabsorption of glucose, amino acids, and phosphorus plus decreased secretion of hydrogen ions.

Acquired

- Fanconi syndrome due to toxicity such as heavy metal poisoning (e.g., lead, mercury, copper, copper associated hepatitis) or dried chicken treats made in China, drugs (e.g., gentamicin, cephalosporins, outdated tetracycline, cisplatin, streptozotocin), chemicals (Lysol, maleic acid), other miscellaneous causes.
- Acute renal failure with significant tubular lesions.

SYSTEMS AFFECTED

- Renal—normoglycemic patients have abnormal renal tubular epithelial cell function; dogs with Fanconi syndrome may develop metabolic acidosis and chronic kidney disease (CKD) with secondary multisystem involvement; glucosuria predisposes to bacterial urinary tract infection.
- Endocrine—hyperglycemic patients may have diabetes mellitus and/or hyperadrenocorticism.
- Liver—copper associated hepatitis; centrilobular hepatitis with copper accumulation.

SIGNALMENT

- Adult dogs and cats develop persistent hyperglycemic glucosuria due to adult-onset diabetes mellitus.
- Dogs with congenital Fanconi syndrome typically develop clinical disease due to defective reabsorption of glucose and amino acids at 4–5 years of age; no sex predilection.
- Familial renal tubular disorders have been reported (see Pathophysiology).
- Primary renal glucosuria (Scottish terriers) may be recognized at early age as incidental finding.
- Copper associated hepatitis with acquired Fanconi syndrome (Labrador retrievers).
- Dogs (any breed or age) fed dried chicken treats made in China.

SIGNS

Clinical signs variable depending upon primary cause.

Historical Findings

- Persistent glucosuria results in polyuria (osmotic diuresis), leading to compensatory polydipsia.
- Glucosuria predisposes to urinary tract infections; clinical signs associated with upper and/or lower urinary tract infection.
- Breed and therapeutic history (see Pathophysiology) are important.

Physical Examination Findings

- Patients with hyperglycemic glucosuria may exhibit systemic signs; see diabetes mellitus chapters.
- Patients with normoglycemic glucosuria may have normal body functions.
- Dogs with Fanconi syndrome may develop signs of metabolic acidosis, electrolyte abnormalities, and CKD.

CAUSES

Hyperglycemic Glucosuria Transient

- Physiologic—stress; common in cats.
- Pharmacologic—see Pathophysiology.

Persistent

- Diabetes mellitus; insulin deficiency or resistance.
- Hyperadrenocorticism; insulin resistance.
- Acute pancreatitis; insulin deficiency or resistance.
- Less common causes include pheochromocytoma, acromegaly, hyperglucagonemia, hyperpituitarism, hyperthyroidism, and chronic liver failure (due to failure to metabolize glucagon).

Normoglycemic Glucosuria

Congenital

- Primary renal glucosuria (Scottish terrier).
- Fanconi syndrome.
- Congenital diseases may be associated with renal dysfunction (Norwegian elkhound).

Acquired

- Acute kidney injury associated with proximal tubular dysfunction.
- Fanconi syndrome.
- CKD (rare).

RISK FACTORS

Vary with underlying causes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Persistent hyperglycemic glucosuria in fasted patients is frequently associated with endocrinopathies (diabetes mellitus, hyperadrenocorticism).
- Acute pancreatitis.
- Renal tubular reabsorptive dysfunctions cause normoglycemic glucosuria.
- Stressed patients exhibit mild transient hyperglycemia and glucosuria.

LABORATORY FINDINGS

Screening Tests

Normally negative (urine glucose concentration below detection).

Glucose Oxidase Tests

- Reagent strips use glucose oxidase method that is specific for glucose; positive values occur with urine glucose concentrations greater than 100 mg/dL.
- Methodology is a two-step enzymatic process—glucose oxidase catalyzes glucose and produces gluconic acid and hydrogen peroxide; peroxidase catalyzes reaction of hydrogen with chromagen to produce color change on reagent pad; the test is time dependent, which varies with manufacturer; pigmenturia can complicate color interpretation.
- False negatives can be seen with ascorbic acid, exposure to formalin, ketonuria, marked bilirubinuria, highly concentrated urine, and refrigerated urine samples that have not been warmed to room temperature prior to performing the test.
- False positives can be seen with exposure to oxidizing agents such as hydrogen peroxide or chlorine bleach (most commonly with samples obtained from table top or floor).
- Specific for glucose; more sensitive

HEARTWORM DISEASE—CATS



BASICS

OVERVIEW

- Disease caused by infection with *Dirofilaria immitis*. • Microfilaremia uncommon (<20%) and usually transient if present. • Prevalence one-tenth that of unprotected dogs. • Low average worm burden. • Worms are physically smaller but recent evidence suggests lifespan is similar to that in the dog.

SIGNALMENT

- No age or breed predisposition. • Males more commonly infected naturally and easier to infect experimentally.

SIGNS

Historical Findings

- Coughing (this sign is relatively uncommon with heart failure). • Cough will commonly occur early in disease prior to established adult infection. • Heartworm-associated respiratory disease (HARD)—clinical signs and pulmonary pathology that occur 2–4 months post infection even when adult infection is never established. • Dyspnea.
- Vomiting (undetermined cause).
- Pulmonary thromboembolism (PTE) frequently results in acute respiratory failure and death. • Vomiting and respiratory signs predominate in chronic disease.

Physical Examination Findings

- Usually normal. • Increased bronchovesicular sounds. • Arrhythmia, murmur, or gallop rhythm should increase suspicion of primary cardiac disease.

CAUSES & RISK FACTORS

- Outdoor cats at increased risk (2 : 1).
- Feline leukemia virus (FeLV) infection not predisposing factor.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Asthma. • Cardiomyopathy. • Chylothorax.
- *Aelurostrongylus abstrusus* infection.
- *Paragonimus kellicotti* infection.

CBC/BIOCHEMISTRY/URINALYSIS

- Varies with stage of disease. • Mild nonregenerative anemia. • Eosinophilia inconsistent. • Concurrent basophilia should increase suspicion. • Hyperglobulinemia.

OTHER LABORATORY TESTS

Microfilaria Concentration Tests

Very low sensitivity, high specificity.

Heartworm Antigen Tests

- ELISA or immunochromatographic tests.
- Tests that detect circulating adult heartworm antigen (HWAg) more specific than antibody tests. • Positive antigen test

result is strong evidence of adult heartworm infection. • Low worm burdens (fewer than five worms) and single-sex infections commonly result in false-negative antigen tests. • Data suggest heat treatment of samples prior to testing may significantly increase test sensitivity; negative result does not rule out heartworm disease: more than 40% of cats with adult infection are antigen-negative; many cats are symptomatic (HARD) well before antigen test would become positive.

Heartworm Antibody Tests

- ELISA or immunochromatographic tests.
- Tests that detect circulating antibodies to immature and adult heartworm antigen are most sensitive tests for feline heartworm disease.
- Positive result does not confirm *adult* infection; usually becomes positive within 4 months of infection. • The more intense the antibody response, the more likely adult infection. • May become negative in adult infections perhaps associated with Ag:Ab complexing.

IMAGING

Radiography

- Enlarged (pulmonary artery, >1.6 times width of ninth rib). • Blunted, tortuous pulmonary arteries. • Patchy perivascular pulmonary infiltrates. • Pleural effusion may be present.
- Chylothorax has been documented with spontaneously occurring and experimentally induced heartworm infections in cats.

Echocardiography

- Dilated main pulmonary artery.
- Identification of worms in heart or main pulmonary artery; most commonly seen in right pulmonary artery but also in right ventricle and atrium (hyperechoic “=” sign). • Sensitive test in hands of experienced echocardiographer.
- Excludes or confirms other primary cardiac diseases (cardiomyopathy).



TREATMENT

- Currently no approved or recommended medical adulticide therapy. • Surgical or catheter-based extraction may be most reasonable option. • Symptomatic cats should be stabilized (see below) prior to consideration of worm extraction. • Spontaneous “cure” probably more common in cats than dogs.



MEDICATIONS

DRUG(S) OF CHOICE

Initial Stabilization

- Supplemental oxygen. • Theophylline (sustained-release formulation) 15–25 mg/kg PO q24h in evening. • Prednisolone 1–2 mg/kg PO q12–24h for 10–14 days; then gradually taper and discontinue. • Doxycycline therapy

10 mg/kg PO q24h for 30 days (to eliminate endosymbiont *Wolbachia*) may hasten worm death and reduce severity of pulmonary inflammation secondary to worm embolization.

- Cautious balanced fluid therapy if indicated.
- Medical adulticide therapy not currently recommended. • Supportive care for PTE the same as initial stabilization (see above).

CONTRAINdications/POSSIBLE INTERACTIONS

- Aspirin therapy—no documented benefit.
- Current information does not support use of melarsomine (Immiticide®) in cats.



FOLLOW-UP

PATIENT MONITORING

Serial evaluation of clinical response, thoracic radiographs, and heartworm antigen and antibody tests is most informative.

PREVENTION/AVOIDANCE

- Ivermectin 24 µg/kg PO q30 days.
- Milbemycin oxime 0.5 mg/kg PO q30 days. • Selamectin 6.6–12 mg/kg cutaneously q30 days. • Moxidectin 1–2 mg/kg cutaneously q30 days. • Administration of these drugs in cats is not precluded by antibody or antigen seropositivity.



MISCELLANEOUS

ABBREVIATIONS

- FeLV = feline leukemia virus.
- HARD = heartworm-associated respiratory disease.
- HWAg = adult heartworm antigen.
- PTE = pulmonary thromboembolism.

INTERNET RESOURCES

<https://www.heartwormsociety.org/veterinary-resources/american-heartworm-society-guidelines>

Suggested Reading

Little SE, Raymond MR, Thomas JE, et al. Heat treatment prior to testing allows detection of antigen of *Dirofilaria immitis* in feline serum. Parasit Vectors 2014; 7:1.

Thomason JD, Calvert CA. Heartworm disease. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, eds., Manual of Canine and Feline Cardiology, 5th ed. St. Louis, MO: Saunders Elsevier, 2016.

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Acknowledgment The author and book editors acknowledge the prior contribution of Matthew W. Miller



**Client Education Handout
available online**

HEARTWORM DISEASE—DOGS



BASICS

DEFINITION

Disease caused by infestation with *Dirofilaria immitis*.

PATHOPHYSIOLOGY

- Severity directly related to worm number, duration of infestation, host response, and host activity level.
- Endothelial damage leads to myointimal proliferation and inflammation predisposing to periarterial edema.
- Lobar arterial enlargement, tortuosity, and obstruction cause impaired compliance, loss of collateral recruitment, pulmonary hypertension (PH), right-sided congestive heart failure (rCHF), thrombosis.
- Pulmonary damage exacerbated after death of adult worms and with exercise.

SYSTEMS AFFECTED

- Respiratory—PH, thromboembolism, allergic pneumonitis (some occult infections), eosinophilic granulomatosis (uncommon).
- Cardiovascular—severe PH causes right ventricular hypertrophy and, in some dogs, rCHF (ascites).
- Hemic/lymphatic/immune—venous inflow to the heart can become obstructed by worms causing traumatic hemolytic anemia and cardiogenic shock (caval syndrome).
- Renal/urologic—immune-complex glomerulonephritis.

INCIDENCE/PREVALENCE

Virtually 100% in unprotected dogs living in highly endemic regions.

GEOGRAPHIC DISTRIBUTION

- Most common in tropical and subtropical zones; endemic in North, Central, and South America, southern Europe, and Australia.
- Diagnosed in all 50 states of United States; common along Atlantic/Gulf coasts and Ohio/Mississippi river basins.
- Ubiquitous mosquito vector in endemic areas.

SIGNALMENT

Breed Predilections

- Medium-to-large breed dogs > small dogs.
- Outdoor dogs > indoor dogs.

Mean Age and Range

Infestation can occur at any age; most affected dogs 3–8 years old.

Predominant Sex

Males > females.

SIGNS

Historical Findings

- Dogs often asymptomatic or exhibit minimal signs such as occasional coughing (mild infestation).
- Coughing and exercise intolerance associated with moderate pulmonary damage (moderate infestation).
- Cachexia, exercise intolerance, syncope, and/or abdominal distention (rCHF) in

severely affected dogs.

- Cardiogenic shock, pigmenturia, abdominal distention (rCHF) in dogs with caval syndrome.

Physical Examination Findings

- No abnormalities—dogs with mild and some with moderate infestation.
- Labored breathing and/or crackles—dogs with severe PH or pulmonary thromboembolism (PTE).
- Tachycardia, weight loss, exercise intolerance, syncope, coughing, pale or light pink mucous membranes, dyspnea.
- Ascites, jugular vein distention/pulsation, hepatomegaly (rCHF).
- Hemoptysis—occasionally.
- Pale mucous membranes, dyspnea, weak pulses.

RISK FACTORS

- Residence in endemic areas.
- Outside habitat.
- Lack of prophylaxis.
- Environmental temperature >57 °F (14 °C).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of PH and thrombosis (e.g., hyperadrenocorticism, protein-losing nephropathy or enteropathy).
- Chronic obstructive lung disease.
- Pneumonia.
- Allergic lung disease.
- Other causes of ascites (e.g., dilated cardiomyopathy).
- Other causes of hemolytic anemia (e.g., immune-mediated).

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia—absent, mild, or moderate depending on chronicity, severity, thromboembolic complications.
- Eosinophilia and basophilia—vary.
- Inflammatory leukogram and thrombocytopenia associated with thromboembolism.
- Hyperglobulinemia—inconsistent finding.
- Hemoglobinemia—evident with caval syndrome and less often thromboembolism.
- Proteinuria—common with severe and chronic infestation; due to immune-complex glomerulonephritis or amyloidosis.
- Hemoglobinuria—caval syndrome or severe lysis with thromboembolism.

OTHER LABORATORY TESTS

- Highly specific, sensitive serologic tests identify adult female *D. immitis* antigen; test 7 months after end of previous transmission season; false positives possible with *Spirocera* infestation; in author's experience, false negatives occur more commonly in shelter animals due to antigen-antibody complexes (antigen blocking); if infestation suspected with negative antigen test, consider heartworm heat treatment antigen ELISA testing.
- Antigenemia absent in absence of adult female worms.
- Weak positive test verified by repeat testing using different test and/or microfilaria testing.
- Strong reaction indicates relative high worm burden or recent worm

death and highly predictive of thromboembolic complications post adulticide therapy.

- Microfilaria testing—mainly to confirm weak positive antigen tests, determine microfilarial status prior to using milbemycin preventatives, and identify microfilaria that may contribute to development of resistance when treated chronically with macrolide preventative.

IMAGING

Radiography

- Use DV projection.
- Main pulmonary artery segment enlargement, lobar arterial enlargement, tortuosity/pruning vary from absent to severe; right caudal artery > left caudal artery > cranial arteries.
- Parenchymal lung infiltrates of variable severity—surround lobar arteries; may extend into most or all of one or multiple lung lobes with thromboembolism and/or PH.
- Diffuse, symmetric, alveolar, interstitial infiltrates occur secondary to allergic reaction to microfilaria (allergic pneumonitis) in about 10% of occult infestations.

H

Echocardiography

- Often unremarkable; may reflect right ventricular dilation and wall hypertrophy, tricuspid regurgitation, PH, small left heart due to underloading (pulmonary obstruction/hypertension).
- Parallel, linear echodensities produced by heartworms may be detected in right ventricle, right atrium, pulmonary arteries.

DIAGNOSTIC PROCEDURES

ECG

- Usually normal.
- May reflect right ventricular hypertrophy in dogs with severe infestation.
- Heart rhythm disturbances—occasionally seen (atrial premature contractions and atrial fibrillation most common) in severe infestation.

PATHOLOGIC FINDINGS

- Large right heart.
- Pulmonary arterial myointimal proliferation.
- PTE.
- Pulmonary hemorrhage.
- Hepatomegaly and congestion in dogs with rCHF.



TREATMENT

APPROPRIATE HEALTH CARE

- Most dogs hospitalized during adulticide administration.
- Eliminate microfilaria with monthly prophylaxis and doxycycline/minocycline; milbemycin may cause rapid decrease in microfilaria numbers and should be used with caution in that scenario; dogs should be rendered microfilaria free 3–4 months post diagnosis.
- Hospitalization recommended for dogs experiencing thromboembolic complications.

ACTIVITY

Severely restrict activity for 4–6 weeks after adulticide administration.

HEARTWORM DISEASE—DOGS

(CONTINUED)

CLIENT EDUCATION

- Good prognosis for animals with mild to moderate disease.
- Post-adulticide pulmonary complications likely in patients with moderate to severe pulmonary artery pathology and those with high worm burden.
- Reinfestation can occur without appropriate prophylaxis.

SURGICAL CONSIDERATIONS

- Treatment of choice for caval syndrome.
- Worm removal from right heart and pulmonary artery via jugular vein, by use of fluoroscopy and long, flexible alligator forceps or horsehair brush, highly effective for treating high worm burden when employed by experienced operator.



MEDICATIONS

DRUG(S) OF CHOICE

- Stabilize animals in rCHF with diuretics, angiotensin-converting enzyme (ACE) inhibitor, pimobendan, sildenafil, cage rest, and moderate sodium restriction before adulticide treatment.
- Stabilize pulmonary failure with oxygen supplementation, antithrombotics (e.g., clopidogrel and heparin), and/or anti-inflammatory dosages of corticosteroid depending on clinical and radiographic findings.
- Doxycycline/minocycline (5–10 mg/kg PO q12h) for 4 weeks followed by 1 month wait period is used prior to adulticide therapy to kill *Wolbachia*, a Gram-negative, endo-symbiotic, intrafilarial bacterium associated with inflammation of the lungs and kidneys; the author practices adulticide therapy after 4 weeks of treatment.
- Adulticide—melarsomine dihydrochloride (2.5 mg/kg IM/dose): injections given into epaxial muscles using 22-gauge needles; apply pressure over injection site during and after needle withdrawal.
- Graded-kill protocol recommended in most cases—administer one injection followed in 1 month by two injections (first injection on left or right epaxial muscles, followed by injection on opposite side 24h later).
- For severe heartworm infestation with high worm burdens, administer one injection every 4–6 weeks for a total of three injections; maintain strictest patient confinement practical for 4–6 weeks; perform antigen test 6 months after third injection.
- Allergic pneumonitis—administer prednisone or prednisolone (2 mg/kg PO q12–24h for several days) and then immediately administer melarsomine.
- Rapid microfilaricidal therapy (e.g., milbemycin or high-dose ivermectin) not recommended—eliminate microfilaria with monthly prophylaxis and doxycycline/minocycline; confirm elimination of microfilaria by testing 3–4 months after initiating therapy.

PRECAUTIONS

- Adulticide treatment—not indicated in patients with renal failure, hepatic failure (icterus), or nephrotic syndrome.
- Caval syndrome—remove worms surgically and stabilize patient with conservative management for at least 1 month prior to adulticide therapy.

ALTERNATIVE DRUG(S)

- Sodium heparin (75–100 units/kg SC q8h), clopidogrel (2–4 mg/kg PO q24h), or low molecular weight heparin (dalteparin: 100 units/kg SC q12–24h) for 1–3 weeks before, during, and for 3 weeks after adulticide administration are controversial recommendations for most severe cases; therapy is combined with strict, extended cage confinement.
- Sodium heparin (200–500 units/kg SC q8h) recommended for dogs with PTE or hemoglobinuria with goal of prolonging activated partial thromboplastin time (APTT) 1.5–2 times baseline.
- Soft or slow kill methods using any macrocyclic lactone alone are not recommended.



FOLLOW-UP

PATIENT MONITORING

- Perform antigen test 6 months after adulticide treatment; some dogs with persistent, low-grade antigenemia may not require retreatment.
- Weak antigenemia indicates most worms killed, pulmonary pathology will improve, and ivermectin prophylaxis will likely eventually kill remaining worms.

PREVENTION/AVOIDANCE

- Heartworm prophylaxis should be provided for all dogs at risk—author recommends year-round prophylaxis; otherwise begin with mosquito season and continue for 1 month following first frost.
- In highly endemic areas, consider combination of heartworm prophylaxis, insect repellents, and ectoparasiticides.
- Antigen test 7 months after end of previous season.
- Ivermectin (Heartgard®, Iverhart®, Tri-Heart®)—highly effective, monthly preventative; safe for microfilaremic dogs.
- Milbemycin oxime (Interceptor®, Sentinel®, Trifexis®)—highly effective, monthly prophylaxis; acute reactions may occur when given to microfilaremic dogs.
- Moxidectin (Advantage® Multi, ProHeart® 6)—topical solution administered monthly; slow-release injectable formulation (ProHeart® SR12) available in some countries.
- Selamectin (Revolution®)—highly effective monthly topical preparation.
- Administer to puppies as soon after 8 weeks of age as dictated by seasonal risk.
- All prophylactic drugs can be administered safely to collies at labeled dosages.
- For dogs infected with adult worms not already on prophylaxis, any of above drugs can be started immediately and should be started within 1 month of diagnosis; author recommends against using milbemycin in

microfilaremic dogs.

- All macrocyclic lactones combined with 1 month doxycycline/minocycline therapy should eliminate microfilaria in 1–3 months.
- Due to recent increase in number of lack of efficacy reports and concern of possible heartworm resistance to current heartworm preventatives, dogs should be rendered microfilaria free 3–4 months post diagnosis.

POSSIBLE COMPLICATIONS

- Post-adulticide PTE—may occur up to 4–6 weeks after treatment; more likely in dogs with severe disease and those not properly confined.
- Thrombocytopenia and disseminated intravascular coagulation.
- Melarsomine adverse effects—PTE (usually 7–30 days post therapy); anorexia; injection site reaction: myositis; lethargy or depression; elevation of hepatic enzymes; paresis/paralysis/ altered mentation; lack of efficacy.

EXPECTED COURSE AND PROGNOSIS

- Mild—usually uneventful with excellent prognosis.
- Severe or caval syndrome—guarded prognosis with higher risk of complications.



MISCELLANEOUS

When anesthesia/surgery required, delay heartworm treatment until after procedure.

ASSOCIATED CONDITIONS

Wolbachia

PREGNANCY/FERTILITY/BREEDING

- Delay adulticide treatment.
- Transplacental infestation by microfilaria can occur.

SEE ALSO

- Congestive Heart Failure, Right-Sided.
- Disseminated Intravascular Coagulation.
- Hypertension, Pulmonary.
- Nephrotic Syndrome.
- Pulmonary Thromboembolism.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- APTT = activated partial thromboplastin time.
- PH = pulmonary hypertension.
- PTE = pulmonary thromboembolism.
- rCHF = right-sided congestive heart failure.

INTERNET RESOURCES

www.heartwormssociety.org

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Acknowledgment The author and book editors acknowledge the prior contribution of Clay A. Calvert



Client Education Handout
available online

HEMATURIA



BASICS

DEFINITION

Blood in urine.

PATHOPHYSIOLOGY

Secondary to loss of endothelial integrity in urinary tract, clotting factor deficiency, or thrombocytopenia/cytopathia.

H

SYSTEMS AFFECTED

- Renal/urologic.
- Reproductive.
- Hemic/lymphatic/immune.

SIGNALMENT

- Dog and cat.
- Familial hematuria in young animals; neoplasia in older animals.
- Females at greater risk for urinary tract infection (UTI).

SIGNS

Historical Findings

Red-tinged urine with or without pollakiuria.

Physical Examination Findings

- Palpable mass in patients with neoplasia.
- Abdominal pain in some patients.
- Enlarged and/or painful prostate gland in males.
- Petechiae or ecchymoses in patients with coagulopathy.

CAUSES

Systemic

- Coagulopathy.
- Thrombocytopenia.
- Vasculitis.

Upper Urinary Tract

- Anatomic—cystic kidney disease and familial malformations.
- Metabolic—nephrolithiasis.
- Neoplastic—renal lymphoma, adenocarcinoma, and hemangiosarcoma.
- Infectious—leptospirosis, feline infectious peritonitis (FIP), and bacterial or fungal UTI.
- Inflammatory—glomerulonephritis.
- Idiopathic renal hematuria.
- Trauma.

Lower Urinary Tract

- Anatomic—bladder malformations.
- Metabolic—uroliths.
- Neoplastic—transitional cell carcinoma and lymphosarcoma.
- Infectious—bacterial, fungal, and viral UTI.
- Idiopathic—cats (idiopathic cystitis).
- Traumatic.
- Cyclophosphamide-induced hemorrhagic cystitis.

Genitalia

- Metabolic—estrus, benign prostatic hyperplasia.
- Neoplastic—transmissible venereal tumor (TVT), leiomyoma, and prostatic adenocarcinoma.
- Infectious—bacterial and fungal disease.
- Inflammatory—prostatitis.
- Trauma.

RISK FACTORS

Breed predisposed to urolithiasis, coagulopathy, or neoplasia.



DIAGNOSIS

See Figure 1.

DIFFERENTIAL DIAGNOSIS

Other causes of discolored urine (myoglobinuria, hemoglobinuria, and bilirubinuria).

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Substantial doses of vitamin C (ascorbic acid) may cause false-negative reagent test strip results; newer generations of reagent strips are more resistant to interference by reducing substances such as ascorbic acid.

Disorders That May Alter Laboratory Results

- Common urine reagent strip tests for blood are designed to detect red blood cells, hemoglobin, or myoglobin.
- Low urine specific gravity (polyuric syndromes) lyses red blood cells (RBCs).
- Bacteriuria (bacterial peroxidase) causes false-positive reagent test strip results.
- Formalin preservative causes false-negative reagent test strip results.

Valid if Run in a Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Thrombocytopenia and severe anemia in some patients.
- Azotemia in some patients with bilateral renal disease.
- RBCs (>5–10 RBC/hpf) and possibly infectious agents seen in urine sediment.
- Crystalluria in some patients with urolithiasis.

OTHER LABORATORY TESTS

- Coagulation testing to rule out coagulopathy.
- Bacterial culture of urine to identify UTI.
- Examination of ejaculate to identify prostatic disease.

IMAGING

Ultrasonography, radiography, and possibly contrast radiography are useful in localizing the underlying cause. Cystoscopy often required to diagnose renal hematuria.

DIAGNOSTIC PROCEDURES

- Biopsy of mass lesion.
- Vaginourethroscopy in females or urethroscopy in males and females.



TREATMENT

- Hematuria may indicate a serious disease process.
- Urolithiasis and renal failure may require diet modification.
- UTI may be associated with another disease that also requires treatment—local (e.g., neoplasia and urolithiasis) or systemic (e.g., hyperadrenocorticism and diabetes mellitus).
- Renal hematuria may be treated via endoscopic sclerotherapy; nephrectomy should not be performed.



MEDICATIONS

DRUG(S) OF CHOICE

- Blood transfusion if patient is severely anemic.
- Antibiotics to treat UTI and septicemia.
- Heparin for disseminated intravascular coagulation (DIC).

CONTRAINDICATIONS

Immunosuppressive drugs, except to treat immune-mediated disease.

POSSIBLE INTERACTIONS

Intravenous contrast media may cause acute kidney injury.



FOLLOW-UP

PATIENT MONITORING

Depends on primary or associated diseases.

POSSIBLE COMPLICATIONS

- Anemia.
- Hypovolemia if severe hemorrhage.
- Ureteral or urethral obstruction due to blood clots.



MISCELLANEOUS

AGE-RELATED FACTORS

- Neoplasia tends to occur in older animals.
- Immune-mediated diseases tend to occur in young adult animals.

ZOONOTIC POTENTIAL

Leptospirosis

SEE ALSO

- Coagulation Factor Deficiency.
- Crystalluria.
- Cylindruria.
- Dysuria, Pollakiuria, and Stranguria.
- Feline Idiopathic Lower Urinary Tract Disease.
- Glomerulonephritis.
- Hemoglobinuria and Myoglobinuria.
- Lower Urinary Tract Infection, Bacterial.
- Lower Urinary Tract Infection, Fungal.
- Nephrolithiasis.
- Prostatitis and Prostatic Abscess.
- Prostatomegaly.
- Proteinuria.
- Pyelonephritis.
- Thrombocytopenia.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation.
- FIP = feline infectious peritonitis.
- RBC = red blood cell.
- TVT = transmissible venereal tumor.
- UTI = urinary tract infection.

Suggested Reading

Bartges JW. Discolored urine. In: Ettinger SJ, Feldman EC, eds., Textbook of Veterinary Internal Medicine, 7th ed. St. Louis, MO: Elsevier, 2008, pp. 164–168.

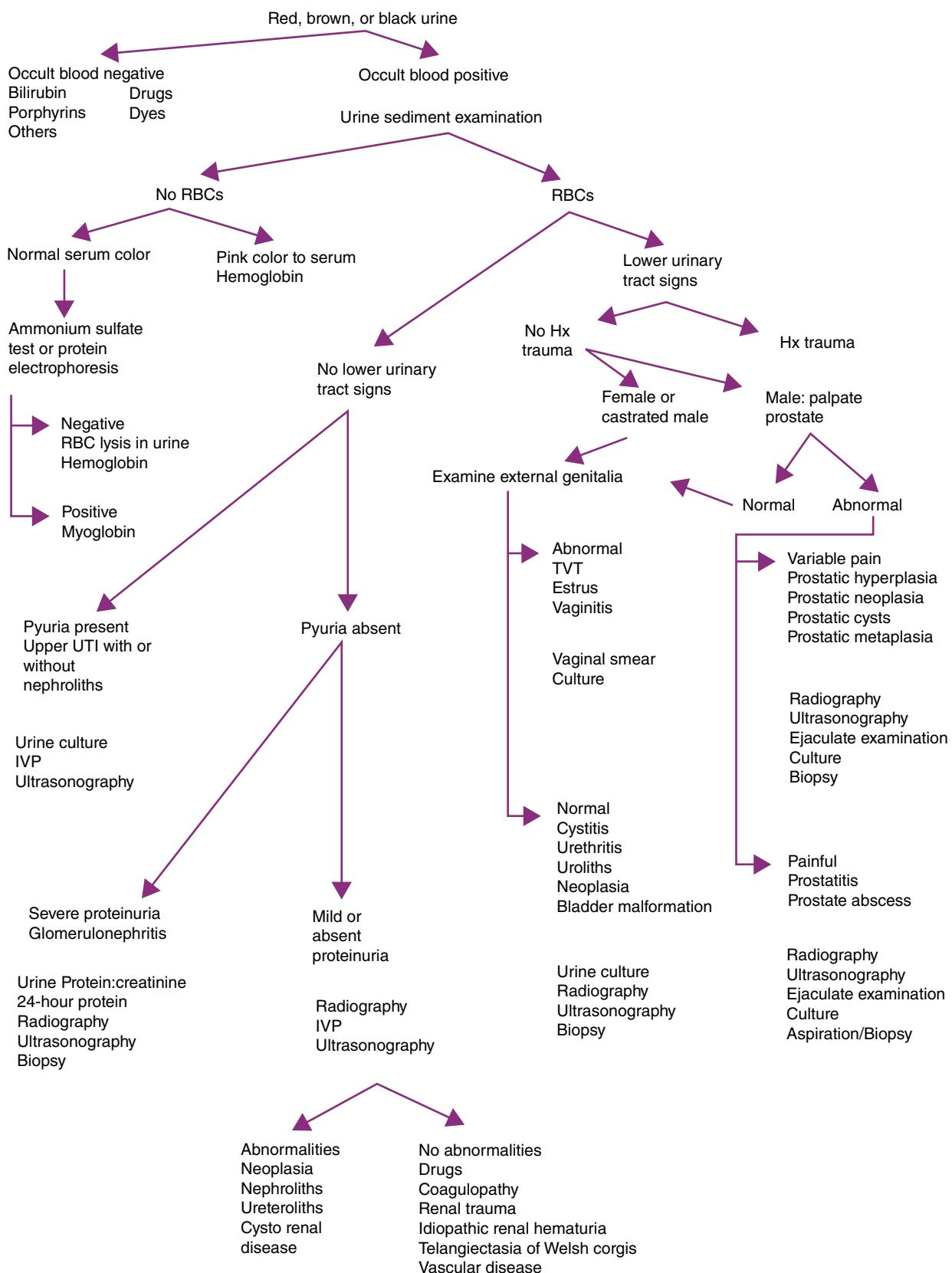
Author Joseph W. Bartges

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(CONTINUED)

HEMATURIAFigure 1.
Algorithm for the diagnosis of red, brown, or black urine.

HEPATIC LIPIDOSIS

H



BASICS

DEFINITION

- Feline hepatic lipidosis (HL)—lipid vacuolation distends the cytosolic compartment in >80% of hepatocytes.
- Untreated—leads to progressive metabolic dysregulation, hepatic failure, and death.
- Develops secondary to a primary disease or condition causing anorexia or catabolism; idiopathic HL is uncommon: a cause is usually discoverable.

PATOPHYSIOLOGY

- Cats have a unique propensity to accumulate triglyceride-filled hepatocellular vacuoles.
- Causal factors—negative energy and protein balance with increased peripheral fat mobilization.
- Cytosolic triglyceride vacuoles cause severe cholestasis and jaundice via canalicular compression and associated hepatic organelle dysfunction.
- Hepatic failure—with rare evidence of hepatic encephalopathy (HE).

SYSTEMS AFFECTED

- Hepatobiliary.
- Gastrointestinal—anorexia; vomiting.
- Musculoskeletal—peripheral muscle wasting (sarcopenia) and fat mobilization.
- Nervous—HE, ptalism, moribund status.
- Hemic/lymphatic/immune—abnormal red blood cell (RBC) shapes (poikilocytes), Heinz body hemolysis.
- Renal/urologic—potassium wasting; renal tubule triglyceride accumulation.

INCIDENCE/PREVALENCE

Most common severe hepatopathy in North America causing jaundice in pet cats.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cats, rarely dogs (toy-breed failure-to-thrive puppies), juveniles with lysosomal or glycogen storage disease; may develop in small-breed puppies with portosystemic vascular anomaly (PSVA).

Breed Predilection

N/A

Mean Age and Range

Middle-aged adult cats—median age 8 (range: 1–16 years).

Predominant Sex

N/A

SIGNS

Historical Findings

- Anorexia or hyporexia, weight loss, sarcopenia.
- Vomiting, diarrhea or constipation, jaundice.

- Lethargy, with gradual onset of weakness progressing to collapse.
- Ptyalism.
- Neck ventriflexion—weakness, electrolyte depletions (potassium, phosphate), thiamine deficiency.
- Underlying disease or illness causing hyporexia/anorexia → hepatic lipidosis.

Physical Examination Findings

- Jaundice.
- Hepatomegaly.
- Dehydration.
- Weakness—neck ventriflexion, recumbency.
- Ptyalism.
- Collapse ↔ obtunded (signs of HE).
- Others, depending on underlying primary disease.

CAUSES

"Idiopathic" Hepatic Lipidosis

Idiopathic = uncommon; antecedent health problems discoverable in >85% of cases causing anorexia or malassimilation; remainder have food deprivation often attributable to adverse social interactions, environmental cause.

Secondary Hepatic Lipidosis

- Primary liver disease—PSVA; cholangitis/cholangiohepatitis syndrome (CCHS); extrahepatic bile duct obstruction (EHBD); cholelithiasis; neoplasia.
- Gastrointestinal—obstruction; neoplasia; inflammatory bowel disease (IBD); pancreatitis.
- Urogenital disease—renal failure, chronic interstitial nephritis (CIN), lower urinary tract syndromes.
- Neurologic conditions—cannot eat.
- Infectious diseases—toxoplasmosis; feline infectious peritonitis (FIP); feline immunodeficiency virus (FIV)—or feline leukemia virus (FeLV)—related disorders.
- Hyperthyroidism.
- Vitamin B₁₂ deficiency and deficiency of other water-soluble vitamins may predispose cats to HL as a result of disrupted metabolism as one factor.
- Many other systemic conditions or toxins can provoke anorexia and lead to HL.
- Rapid weight loss protocols or change to restricted-calorie diet the cat refuses to eat.

RISK FACTORS

- Obesity.
- Anorexia, negative nitrogen balance.
- Catabolism or rapid weight loss.
- Water-soluble vitamin deficiency.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary liver disease—CCHS, cholelithiasis, EHBD, or neoplasia (esp.

lymphosarcoma) differentiated by abdominal US, liver aspiration, and liver biopsy.

- PSVA—diagnosis by US or colorectal scintigraphy, lab testing.
- Hepatic toxoplasmosis or FIP—liver biopsy, serology, immunohistochemistry.
- Pancreatitis—differentiated by US, serum tests, pancreatic aspiration cytology, gross inspection, biopsy.
- Gastrointestinal disease—IBD differentiated by bowel biopsies; obstruction differentiated by abdominal survey or contrast radiography and US.
- Toxicities—suspected based on history (e.g., oral diazepam, acetaminophen, methimazole).
- Hyperthyroidism—serum thyroid panel, absence of jaundice.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematology—poikilocytes common; nonregenerative anemia; hemolytic anemia (severe hypophosphatemia or Heinz bodies).
- Biochemistry—hyperbilirubinemia; high alkaline phosphatase (ALP), alanine aminotransferase (ALT), ± aspartate aminotransferase (AST) activity; normal or mild increase in γ-glutamyltransferase (GGT) if no primary necro-inflammatory ductal disorder (i.e., biliary, pancreatic); low blood urea nitrogen (BUN); normal creatinine; variable glucose (hypoglycemia rare); variable cholesterol, albumin, globulins; hypokalemia; hypophosphatemia, increased ketones (beta-hydroxybutyrate); lactic acidosis.
- Urinalysis—bilirubinuria, lipiduria, and unconcentrated urine common.

OTHER LABORATORY TESTS

- Prolonged coagulation times—prothrombin time (PT), activated partial thromboplastin time (APTT), activated clotting time (ACT); fibrinogen usually normal.
- Hyperammonemia—uncommon.
- Serum bile acids—high before hyperbilirubinemic; redundant test if hepatobiliary jaundice.
- B₁₂ deficiency.

IMAGING

Survey Abdominal Radiography

- Hepatomegaly.
- May note features of underlying disorder.

Abdominal US

- Diffuse hyperechoic hepatic parenchyma, hepatomegaly.
- Look for primary disease causing HL.

DIAGNOSTIC PROCEDURES

- Fine-needle liver aspiration cytology—>80% hepatocytes display severe cytosolic lipid vacuolation; biopsy rarely needed to confirm HL.
- Definitive diagnosis HL—based on history, clinical features, high ALP, diffuse hyperechoic hepatic parenchyma, severe hepatocyte lipid

HEPATIC LIPIDOSIS

vacuolation on aspiration cytology; however, cannot rule out primary hepatic disorders (e.g., CCHS, EHBD, PSVA) with these tests.

- Liver biopsy—definitive diagnosis of underlying “primary” liver disorders; *done only if poor response to therapy or high GGT; caution:* stabilize cat before anesthesia and liver biopsy.
- Vitamin K₁ (0.5–1.5 mg/kg SC/IM) three doses at 12h intervals, *before* aspiration sampling, liver biopsy, jugular vein catheterization, cystocentesis, or feeding appliance insertion.

PATHOLOGIC FINDINGS

- Gross—diffuse hepatomegaly, smooth surface, friable greasy consistency, yellow/pale color with reticulated appearance; sample floats in formalin.
- Microscopic—diffuse, severe hepatocellular lipid vacuolation; large (macrovesicular) or small (microvesicular) vacuolation; type of vacuolation lacks prognostic value.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—recumbent cats or those with neck ventriflexion and anorectic.
- Discharge for home care—see Patient Monitoring.
- Frequent reevaluations imperative.
- Outpatient—reduces stress and thereby facilitates recovery in some cats.

NURSING CARE

- Balanced polyionic fluids—*avoid* lactate and dextrose supplementation; 0.9% NaCl preferred.
- Potassium chloride supplementation essential (see Hypokalemia).
- Phosphate supplements usually needed (see Hypophosphatemia) at initial feeding; often started prophylactically, see below.
- Magnesium supplements rarely needed.

Correct Hypophosphatemia

- Serum phosphate <2.0 mg/dL reflects refeeding syndrome; may provoke anorexia, vomiting, weakness, myonecrosis, ileus, hemolysis, coagulopathy, neurologic signs confused with HE.
- Treatment—potassium phosphate initial dose 0.01–0.03 mmol/kg/h IV; monitor serum phosphate q6h; discontinue when stable phosphate >2 mg/dL; *caution:* judiciously reduce IV potassium chloride supplements concurrently given in fluids; monitor potassium.

Correct Hepatic and Circulating GSH Depletion

- Low liver glutathione (GSH) confirmed in HL; routine GSH measurements not available.

- Crisis intervention for low hepatic GSH or Heinz body anemia—N-acetylcysteine (NAC) 140 mg/kg IV, then 70 mg/kg IV, 10% solution diluted 1 : 2 in saline; administered over 20 min otherwise may provoke hyperammonemias.
- When enteral feeding established, change to S-adenosylmethionine (SAMe) 200 mg/cat PO q24h; need for dosing on empty stomach complicates use.

ACTIVITY

Physical activity (walking), when possible, may increase gastric motility when gastroparesis complicates feeding (chronic vomiting).

DIET

- Nutritional support—cornerstone of recovery.
- High-protein, high-calorie balanced feline diet essential.
- Energy—50–60 kcal/kg ideal weight/day; gradual transition to full energy requirement over 3–7 days; feed multiple small meals/day or trickle feed through esophageal feeding tube (E-tube).
- Forced alimentation usually required; *caution:* oral forced feeding may provoke food aversion syndrome.
- Correct hypokalemia and hydration before commencing feeding; associated gastroparesis may lead to vomiting and potential for aspiration pneumonia.
- Tube feeding—initially by nasogastric tube (first 1–2 days *after* electrolyte and vitamin deficiency improved), transition to E-tube after hydration and electrolyte status improves, and vitamin K₁ protocol administered.
- Avoid laparotomy for gastric feeding tube insertion; cats with HL have high risk for mortality with general anesthesia and surgery; E-tube preferable.
- Cautiously offer PO food daily to assess interest.
- Human stress formula enteral diets (not recommended)—require supplemental arginine (or citrulline), and taurine; use feline formulated liquified diet with vitamin supplements.

Supplements

- Supplements improve survival in severely affected cats.
- Water-soluble vitamins—in IV fluids; generally 2 mL/L.
- Thiamin—50–100 mg/day, give PO rather than SC/IM, also add via water-soluble vitamins mixed in IV fluids.
- Vitamin B₁₂—initially 0.25–1 mg IM/SC once); determine chronic vitamin B₁₂ needs by sequential B₁₂ values (weekly, q2 weeks, to monthly then quarterly intervals).
- Medical-grade L-carnitine (250–500 mg/day); over-the-counter carnitine supplements have wide variability in bioavailability; Carnitor® (liquid medical-grade carnitine) recommended.

- Taurine 250–500 mg/day PO.
- Vitamin E 10 IU/kg/day PO in food—use water-soluble form initially.
- Thiol donors IV NAC, PO SAMe—as above.
- Potassium gluconate (for hypokalemia) PO, reduce fluid potassium supplements.
- Marine oil in food 2000 mg q24h.

CLIENT EDUCATION

- Warn client—sequential biochemical assessments needed to monitor recovery.
- Educate client about feeding tube use/care and need for chronic use (up to 4–6 months).
- Advise client—recurrence unlikely; liver function will not be chronically compromised.

SURGICAL CONSIDERATIONS

- Avoid surgical interventions until normalization of hydration, electrolyte depletions, and supplements of vitamins provided, Heinz body anemia alleviated.
- Exploratory laparotomy and liver biopsy—*only* indicated if failure to improve on described interventions or marked increase in GGT activity to identify underlying disorders; biopsy liver, pancreas, stomach, and small bowel if explored; lymph nodes if enlarged.



MEDICATIONS

DRUG(S) OF CHOICE

- Vitamin K₁—recommended for all cats with suspected HL; see above, avoid overdosage.
- Drugs to ameliorate HE (see Hepatic Encephalopathy), rarely.
- Emesis control—metoclopramide: for vomiting, nausea, gastroparesis (0.2–0.5 mg/kg SC q8h 30 min before feeding, or as CRI IV drip at 0.01–0.02 mg/kg/h or 1–2 mg/kg/day); dolasetron or ondansetron; or maropitant (1 mg/kg IV/SC/PO q24h 5 days max); pantoprazole to avert esophageal damage secondary to vomiting (0.5–1.0 mg/kg q12–24h).
- Systemic antibiotics—as appropriate for suspected infection.

CONTRAINdications/PRECAUTIONS

- Downward adjust dosages of medications relying on hepatic metabolism or excretion.
- Avoid benzodiazepines and barbiturates—may provoke HE.
- Appetite stimulants do not provide dependable energy intake in cats with HL; some produce sedation; diazepam may cause rare fulminant hepatic failure.
- Avoid injectable medications with propylene glycol carrier; may lead to hemolysis in cats with low GSH.
- Ursodeoxycholic acid—likely not beneficial; may promote taurine deficiency.
- Dextrose supplements—may provoke hepatic triglyceride accumulation.

(CONTINUED)

- Avoid tetracyclines or stanozolol—promote hepatocyte triglyceride vacuolation.
- Avoid recurrent or prolonged use of propofol—may provoke hemolysis (12h after infusion) esp. in cats with Heinz body anemia; HL cats may recover slowly; alternatively use gas anesthesia.



FOLLOW-UP

PATIENT MONITORING

- Bodyweight and condition, hydration, electrolytes; judicious adjustment of energy, fluid, electrolyte, and vitamin provisions essential.
- Serum bilirubin—predicts recovery.
- Reduced lactate and ketones reconcile with metabolic improvement.
- Liver enzyme activity—do not predict recovery.
- Discharge for home care—when vomiting controlled, gastroparesis resolved, bilirubin declining, patient ambulatory, and tube-feeding apparatus problem-free.
- Tube feeding—discontinued only after confirmed voluntary food consumption.

PREVENTION/AVOIDANCE

- Obesity—prevent; weight reduction must not exceed 2% bodyweight per week.
- Caution owner to verify food intake during weight loss regimens and at-home stress.

POSSIBLE COMPLICATIONS

- Feeding tube malfunction or obstruction—tube obstructions relieved with papaya juice, carbonated soft drink, or pancreatic enzyme slurry; 15 min dwell time, warm water flush.
- Rare HE after dietary support introduced.
- Unremitting HL can lead to lethal hepatic failure.

- Untreatable underlying causal disorder.

EXPECTED COURSE AND PROGNOSIS

- Optimal response to tube feeding and nutritional supplements—recovery in 3–6 weeks.
- Therapy as described—85% recovery in severely affected animals with controllable primary disease process that provoked HL.
- Underlying disease influences outcome.
- HL rarely recurs.
- HL does not cause chronic liver dysfunction, hepatitis, persistent remodeling.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Primary liver disorders.
- Pancreatitis.
- Malassimilation—various causes but IBD predominant.
- Diabetes mellitus—relatively uncommon.
- Neoplasia—hepatic and systemic.
- HE (rare).
- Systemic illness limiting food intake.

SYNOMYS

- Fatty liver syndrome.
- Hepatosteatosis.
- Feline hepatic vacuolation.
- Vacuolar hepatopathy.
- Vacuolar degeneration.

SEE ALSO

- Cholangitis/Cholangiohepatitis Syndrome.
- Hepatic Encephalopathy.

ABBREVIATIONS

- ACT = activated clotting time.
- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- APTT = activated partial thromboplastin time.

HEPATIC LIPIDOSIS

H

- AST = aspartate aminotransferase.
- BUN = blood urea nitrogen.
- CCHS = cholangitis/cholangiohepatitis syndrome.
- CIN = chronic interstitial nephritis.
- EHBDO = extrahepatic bile duct obstruction.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- GGT = gamma glutamyltransferase.
- GSH = glutathione.
- HE = hepatic encephalopathy.
- HL = hepatic lipidosis.
- IBD = inflammatory bowel disease.
- NAC = *N*-acetylcysteine.
- PSVA = portosystemic vascular anomaly.
- PT = prothrombin time.
- RBC = red blood cell.
- SAME = *S*-adenosylmethionine.

Suggested Reading

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Consulting Editor Kate Holan



Client Education Handout
available online

HEPATITIS, CHRONIC



BASICS

DEFINITION

- Hepatic injury associated with active chronic necroinflammatory liver injury; “chronic active hepatitis” should not be used.
- Nonsuppurative inflammation—most common; lymphocytes, plasma cells, macrophages, occasional neutrophils.
- Chronicity—progressive remodeling, regenerative nodule formation, evolving sinusoidal fibrosis with location dependent on zonal tropism of inflammation; changes eventuate in cirrhosis.

PATHOPHYSIOLOGY

- A multitude of initiating events or agents cause hepatic injury; damage to cell and/or organelle membranes usually involves oxidative injury; activated cytokines and cell-mediated immune responses widen and perpetuate inflammation; hepatic neoepitopes may become targeted foci.
- Initial injury may include infectious agents, toxins, xenobiotics, or pathologic Cu accumulation; with exception of Cu-mediated injury, cause often remains undetermined.
- Inflammatory cells—predominantly lymphocytes, fewer Kupffer cells (resident hepatic sinusoidal macrophages), and variable neutrophils are initial effectors.
- Injury zone demarcates area of predominant necroinflammatory damage—zone 1 (periportal) common to idiopathic hepatitis or inflammation involving portal tract structures; zone 3 incriminates Cu, nonsteroidal anti-inflammatory drug (NSAID), other xenobiotic or toxin-mediated injury, or repeated ischemic/hypoxic insult; panlobular inflammation common.
- Lesion progression—variable, may include portal and periportal lymphoplasmacytic infiltrates with interface hepatitis (inflammation breaching limiting plate of portal tract), and otherwise variable lobular injury; chronic inflammation: leads to progressive fibrosis with bridging of involved zones.
- Bridging fibrosis and regenerative nodules distort lobular architecture; fibrosis, intrahepatic sinusoidal hypertension, neovascularization, and impaired hepatic function evolve into cirrhosis.
- Progressive cholestasis due to mechanical compression/distortion of bile ducts may occur.
- Cirrhosis and hepatic failure—late stage.
- Fibrosis—usually reflects chronic injury from sustained inflammation.
- Cirrhosis—associated with hepatic dysfunction, sinusoidal hypertension; intrahepatic shunting through collagenized sinusoids or neovascular pathways in fibrotic partitions that segregate regenerative nodules.

H

- Sinusoidal hypertension—leads to hepatofugal portal circulation (flow away from liver); mesenteric splanchnic hypertension; development of acquired portosystemic shunt(s) (APSS); episodic hepatic encephalopathy (HE); ascites; portal hypertensive enteric vasculopathy predisposes to enteric bleeding.

SYSTEMS AFFECTED

- Hepatobiliary—inflammation; necrosis; cholestasis; fibrosis.
- Gastrointestinal (GI)—emesis; diarrhea; anorexia, portal hypertension, ascites, and propensity for enteric bleeding.
- Neurologic—HE (advanced stage, associated with APSS).
- Hemic—red blood cell (RBC) microcytosis reflects APSS; bleeding or thrombotic tendencies: failed factor or anticoagulant synthesis or activation, thrombocytopenia or thrombopathia; coagulopathies typically observed with advanced injury or severe diffuse hepatic necrosis.
- Renal/urologic—polyuria/polydipsia (PU/PD); isosthenuria; ammonium biurate crystalluria (advanced stage with APSS and HE).
- Endocrine/metabolic—hypoglycemia if end-stage liver failure.
- Respiratory—tachypnea if tense ascites; bicavitory effusion or pulmonary edema.

GENETICS

- Breed or familial predisposition for chronic hepatitis—Doberman pinscher, Labrador retriever, West Highland white terrier, and Dalmatian may develop chronic hepatitis secondary to pathologic Cu accumulation; cocker spaniel hepatopathy, anecdotal in other breeds or breeding lines.
- Inherited Cu associated hepatopathy only proven in Bedlington terrier—autosomal recessive, genetic test available.

SIGNALMENT

Species

Dog

Breed Predilection

See Genetics.

Mean Age and Range

Average age 6–8 years (range: 2–14 years).

Predominant Gender

Inconsistent among reports for any breed.

SIGNS

General Comments

- Initially—vague and nonspecific, often includes lethargy and inappetence.
- Later—relate to complications of portal hypertension; impaired hepatic function including cholestasis.

Historical Findings

- May be no signs in early disease or mild lethargy.
- Anorexia, vomiting, weight loss, reduced body condition.

- PU/PD.

- Jaundice—later stage unless portal hepatitis involves bile duct injury.
- Ascites—late stage.
- HE—late stage, infers APSS with cirrhosis.

Physical Examination Findings

- May be no signs in early disease.
- Lethargy, poor coat, declining body condition.
- Variable jaundice.
- Liver size—normal to small, depends on chronicity.

Late-Stage Physical Findings

- Ascites.
- HE.
- Obstructive uropathy—ammonium biurates.
- Bleeding or thrombotic tendencies.

CAUSES

- Chronic necroinflammatory, oxidant, and immune-mediated liver injury has many causes.
- Infectious—canine hepatitis virus; leptospirosis, enteric-portal bacteremia or endotoxemia affiliated with inflammatory bowel disease; accidental parenteral administration of intranasal *Bordetella* vaccine.
- Immune-mediated—autoimmune with positive antinuclear antibody (ANA); acquired immune sensitization, nonsuppurative inflammation.
- Toxic—Cu associated hepatopathy; acute or chronic exposure to drugs—predictable or idiosyncratic toxicity: e.g., azole antifungals, trimethoprim-sulfa, zonisamide, phenobarbital, primidone, phenytoin, CCNU, NSAIDs (esp. carprofen); repeat exposure to environmental or food-borne toxins, e.g., dimethylnitrosamine, aflatoxin, cycad, cyanobacteria.

RISK FACTORS

- Immunostimulants (vaccinations?) and molecular mimicry of cell epitopes by infectious agents or infection of sinusoidal endothelium.
- Cu associated hepatopathy.
- Hepatic iron accumulation—from inappropriate supplementation.
- Xenobiotics (drugs, herbal, holistic, or Chinese remedies), inducers or inhibitors of microsomal enzymes, impaired hepatic antioxidant status; xenobiotic metabolites foster inflammation or augment direct initial liver injury.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Acute hepatitis—history, sequential biochemistry profiles or liver biopsy.
- Congenital portosystemic shunt (portosystemic vascular anomaly [PSVA]).

(CONTINUED)

- Primary hepatic neoplasia.
- Metastatic neoplasia or carcinomatosis.
- Chronic pancreatitis.
- Other causes of abdominal effusion— hypoalbuminemia; passive congestion; carcinomatosis; chemical peritonitis (bile, urine, pancreatitis), hepatic or nonhepatic causes of portal hypertension: see Hypertension, Portal.
- Jaundice—extrahepatic bile duct occlusion (EHBD); bile peritonitis, cholangitis/ cholangiohepatitis syndrome, ductopenia, hemolysis.

CBC/BIOCHEMISTRY/URINALYSIS

Hemogram

CBC—nonregenerative anemia; RBC microcytosis if APSS; variable leukogram, occasional thrombocytopenia; low total protein if chronic disease with synthetic failure and portal hypertension causing enteric protein loss.

Biochemistry

High liver enzymes; variable bilirubin, albumin, blood urea nitrogen (BUN), glucose, cholesterol; hepatic failure—suggested by low albumin, BUN, glucose, and cholesterol in absence of alternative causes.

Urinalysis

Variable urine concentration; escalated bilirubinuria; ammonium biurate crystalluria if APSS.

OTHER LABORATORY TESTS

- Total serum bile acids (TSBA)—variable; depends on extent of hepatic remodeling, sinusoidal hypertension, and cholestasis; *superfluous test if hepatic hyperbilirubinemia*.
- Ammonia intolerance—reflects APSS; insensitive to cholestasis, lability impairs accuracy.
- Coagulation tests—reflect panlobular injury, chronicity, vascular injury, impaired synthetic capacity or vitamin K adequacy; early disease: few abnormalities except possible high fibrinogen; advanced stage or severe panlobular injury: single or multiple abnormalities including prolonged prothrombin, activated partial thromboplastin time, low fibrinogen, increased D-dimers.
- Low protein C or antithrombin activity—may reflect PSVA, APSS, hepatic failure, or consumptive coagulopathy.
- Abdominal effusion—chronic liver disease portal hypertension: pure or modified transudate.
- Liver tissue zinc—low with chronic disease and APSS.
- Serologic or PCR tests—possible infectious agents, e.g., leptospirosis, rickettsial diseases, *Borrelia*, *Bartonella*, endemic fungal agents.
- ANA titer—if potential for autoimmune disease; *note*: low-level positive titers nonspecific and more common with advanced age.

- Immunohistochemical staining of liver biopsy—can confirm infectious agents or phenotype of infiltrating cells (inflammatory or neoplastic).

IMAGING

Abdominal Radiography

- Microhepatia—suggests late-stage disease or APSS causing lobular atrophy.
- Abdominal effusion—obscures image.
- Ammonium biurate calculi—radiolucent unless combined with radiodense minerals.

US

- Liver size depends on disease stage.
- Normal to variable parenchymal and biliary tract echogenicity; may note nodularity and irregular liver margins with chronicity due to regenerative nodules.
- APSS—tortuous vessels most commonly identified caudal to left kidney or near splenic vein.
- Abdominal effusion—US facilitates fluid sampling.
- Uroliths—renal pelvis or urinary bladder; may signify ammonium biurate urolithiasis but cannot differentiate mineral composition without stone analysis.
- Rule out—EHBD; identify mass lesions; cholelithiasis; gallbladder mucocele (GBM); cholecystitis; choledochitis; cystic lesions (abscess or ductal plate malformation-related).
- Enables fine-needle aspiration—cytology and cholecystocentesis for bile collection.

Colorectal/Splenoportal Scintigraphy (CRS/SPS)

- ^{99m}Technetium pertechnetate isotope time activity curve displays chronologic isotope distribution: delivery to liver first = no shunting, delivery to heart first = shunting.
- CRS—sensitive, noninvasive; cannot differentiate PSVA from APSS.
- SPS—no diagnostic advantage, US-guided splenic injection, uses a lower isotope dose and therefore has faster discharge from hospital.

DIAGNOSTIC PROCEDURES

Aspiration Cytology

- Fine-needle aspiration cytology—*cannot define* fibrosis or nonsuppurative inflammation; *cannot recommend* therapy.
- Cannot definitively diagnose chronic hepatitis, hepatic fibrosis, or Cu associated hepatopathy.

Liver Biopsy

- Liver biopsy—needed for definitive diagnosis; acquire biopsies from multiple liver lobes.
- Tru-Cut® needle biopsy—use 14–16 G.
- Laparoscopy—best biopsy method; lower morbidity and faster recovery vs. exploratory laparotomy.

Bacterial Culture

Aerobic and anaerobic bacterial culture and sensitivity of liver and bile; use particulate biliary debris if possible.

HEPATITIS, CHRONIC

H

Metal Analyses

- Measure Cu, iron, and zinc concentrations in liver (dry matter basis).
- Low hepatic zinc associated with portosystemic shunting requires supplementation.
- Iron commonly accumulates in necroinflammatory disorders; must be reconciled with distribution for relevance: e.g., Prussian blue staining defines distribution in macrophages (chronic inflammation) vs. predominantly in hepatocytes (hemochromatosis).
- Cu quantification and rhodanine staining—ascertains relevance to parenchymal injury.

PATHOLOGIC FINDINGS

- Gross—early: no gross change; late stage: irregular surface contours, microhepatica, ± tortuous APSS varices.
- Microscopic—nonsuppurative inflammation in zone(s) of necroinflammatory injury; variable cholestasis and biliary hyperplasia; interface hepatitis: invasion of limiting plate; late-stage disease: fibrotic bridging partitions between or within involved zones and marginating regenerative nodules, sinusoidal dissecting fibrosis; final transition to cirrhosis.

Histopathology

- Immune-mediated hepatitis—periportal, lobular, centrilobular, or panlobular with lymphoplasmacytic infiltrates, hepatic cord injury causing disorganization, sinusoidal fibrosis, biliary hyperplasia.
- Cu associated hepatopathy—initially centrilobular, may evolve panlobular immune-mediated hepatitis.
- Cirrhosis—diffuse, unresolvable; fibrosis, nodular regeneration distorting lobular architecture.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—for diagnostic testing, supportive care, treatment initiation in severe illness.
- Outpatient—if condition stable at diagnosis; slowly titrated onto medical therapy.

NURSING CARE

- Depends on underlying condition.
- Fluid therapy—balanced polyionic fluids supplemented to correct hydration, electrolyte aberrations, or hypoglycemia; restricted sodium if ascites, may require fresh frozen plasma, avoid synthetic colloids.
- Water-soluble vitamins—2 mL/L fluids.
- Ascites (see Cirrhosis and Fibrosis of the Liver).

ACTIVITY

Keep patient warm and hydrated; restricted activity may improve hepatic regeneration, euglycemia, and ascites mobilization.

HEPATITIS, CHRONIC

(CONTINUED)

DIET

- Conserve body condition and muscle mass.
- Adequate calories and protein—to avoid negative nitrogen balance and catabolism.
- Dietary protein—restrict protein quantity *only* if signs of HE or observe ammonium biurate crystalluria; feed balanced species-specific diet; if HE, avoid fish and red meat source protein (dogs).
- Fat restriction rarely needed.
- If Cu associated liver injury, see Copper Associated Hepatopathy.
- Meal frequency—feed several small meals per day.
- Sodium restriction—with ascites or severe hypoalbuminemia: <100 mg/100 kcal or <0.2% dry matter basis formula.
- Balanced vitamin supplements (water soluble, fat soluble)—increased urinary water-soluble vitamin loss if PU/PD or diuretic therapy.
- Thiamin—ensure repletion to avoid metabolic complications and neurologic signs; 50–100 mg PO q24h; *caution:* anaphylactoid reactions may occur with injectable thiamin.
- Partial parenteral nutrition—may consider, insufficient to meet energy requirements.
- Total parenteral nutrition—if inappetence >7 days; branched-chain amino acids remain controversial in dogs with liver dysfunction.

CLIENT EDUCATION

- Control rather than cure is expected goal; medications usually required for life; chronic hepatitis is cyclic and will minimally require reevaluations q4–6 months after initial control.
- Antifibrotics—best control of fibrosis through control of inflammation and underlying primary process.
- Attenuate factors provoking HE—dehydration; azotemia, infection; catabolism; constipation; hypokalemia; alkalemia; high-protein meals; endoparasitism; enteric bleeding; certain drugs.

SURGICAL CONSIDERATIONS

- APSS—do not ligate APSS or band vena cava.
- Cirrhosis—high anesthetic risk; gas anesthesia preferred: isoflurane or sevoflurane.



MEDICATIONS

DRUG(S) OF CHOICE

- Treatments for specific etiologies.
- Withdraw plausible hepatotoxic drugs.
- No clinical trials prove efficacy of specific therapeutic regimens at this time.

Immunomodulation

- *Prednisolone/prednisone*—1–2 mg/kg daily PO; taper to lowest effective dose (0.25–0.5 mg/kg PO q48h); if ascites: use

dexamethasone to avoid mineralocorticoid effects (divide prednisone dose by 7–10 for dexamethasone dose), SID q2–3 days.

- *Azathioprine*—dogs: 2 mg/kg (50 mg/m²) PO q24h × 14 days *then* titrate to q48h; contraindicated in cats (toxic); dogs: combine with prednisone, antioxidants, antifibrotic polyunsaturated phosphatidylcholine (PPC); during chronic therapy, titrate by 25–50% dose reduction after 2–6 months based on sequential biochemistries showing improvements (e.g., normalization of total bilirubin and marked decline in liver enzyme activity); monitor CBC and biochemistry profile q7–14 days for first 2 months to ensure absence of hematopoietic, hepatic, or pancreatic toxicity; if acute hematopoietic toxicity, stop therapy, allow recovery, then reintroduce with 25% dose reduction; if insidious chronic hematopoietic toxicity (after months) or acute cholestatic liver or pancreatic injury, discontinue therapy and change to different drug (e.g., mycophenolate or cyclosporin); risk for neoplasia with chronic use.

- *Mycophenolate mofetil*—10–15 mg/kg PO q12h; doses ≥10 mg/kg PO BID may lead to diarrhea' start lower initial dose and/or divide total daily dose into 3–4 doses to reduce toxic effects; monitor as for azathioprine and adjust similarly; fewer bone marrow side effects than azathioprine but more GI toxicity; avoid dosing with food or after administration of proton pump inhibitor as these factors reduce drug bioavailability; if failure to respond to azathioprine go to cyclosporin vs. mycophenolate; if azathioprine toxicity go to mycophenolate.

- *Microemulsified cyclosporine* (Atopica®)—2.5–5 mg/kg PO q24h; use with glucocorticoids may increase drug efficacy and permit lower dose; side effects: gingival hyperplasia (managed with azithromycin), rare cholestatic liver injury, hyperlipidemia, hypercholesterolemia, worsening preexistent hypertension, risk for GB disease, risk for opportunistic infections; high dose can lead to nephrotoxicity; risk for neoplasia with chronic use; avoid concurrent use of p450 inhibitors unless cyclosporin dose substantially reduced.

Ursodeoxycholic Acid

Hepatomembranoprotectant, immuno-modulatory, antifibrotic, choleretic, anti-endotoxic, and antioxidant effects; 10–15 mg/kg PO SID or divided q12h; administer with food for best bioavailability; may use as aqueous solution; no deleterious side effects; maintain indefinitely.

Antifibrotics

- Immunomodulators, S-adenosylmethionine (SAMe), vitamin E.
- *Polyunsaturated phosphatidylcholine* (PPC, dilinolylphosphatidylcholine [DLPC])—PPC containing DLPC antifibrotic, has immuno-modulatory, antioxidant, hepatoprotective

effects, and improves membrane fluidity; 25–50 mg/kg/day PO with food; PhosChol® with preformed DLPC (52%) has benefit in some forms of liver disease (humans, animal models); may have corticosteroid-sparing effect (allows reduced glucocorticoid dosing); safely prescribed without liver biopsy.

- *Colchicine*—not recommended.
- *Silybin with PPC* (milk thistle)—experimental studies suggest potential hepatoprotectant (against numerous toxins), antifibrotic, antioxidant effects, and possibly promoting hepatocyte regeneration; low bioavailability of oral forms significantly limits biologic effect at traditional oral dosing: 2–5 mg/kg/day PO (PPC complexed form); only bioavailable form IV formulation (Legalon® SIL) used for *Amanita* death cap mushroom toxicity with high dose protocol; orphan drug.

Antioxidants

- Vitamin E—α-tocopherol, 10 IU/kg PO q24h with food.
- SAMe—20 mg/kg/day enteric-coated tablet PO, give on empty stomach for best bioavailability, 1–2h before feeding.
- Avoid vitamin C (ascorbate).
- Zinc (zinc acetate)—has antioxidant and antifibrotic benefits, supplementation may improve control of HE if low liver zinc concentration documented, unreliable for limiting enteric Cu uptake; elemental zinc 1.5–3 mg/kg PO daily as supplement if low liver zinc concentration (<120 µg/g dry weight liver); adjust dose using sequential plasma zinc concentrations that show increased concentrations; avoid plasma concentrations ≥800 µg/dL to prevent hemolysis; plasma zinc levels do not correlate with tissue levels.

Hepatoprotectants

- Ursodeoxycholate, vitamin E, SAMe, PPC—provide hepatoprotectant effects in addition to other benefits.
- Silybin—see above.

Bleeding Tendencies

See Coagulopathy of Liver Disease.

GI Signs/Vomiting/Hematemesis

- HCl pump inhibitors—omeprazole 0.5–1.0 mg/kg q12–24h PO or pantoprazole 0.7–1 mg/kg q12h IV, better long-term control vs. famotidine.
- Sucralfate—gastroprotectant dose 0.25–1.0 g/10 kg PO q8–12h; titrated to effect; beware of drug interactions as sucralfate may bind other medications, reducing bioavailability.
- Eliminate endoparasitism.

CONTRAINDICATIONS

- NSAIDs—avoid; may provoke enteric ulceration and bleeding; may worsen ascites; metabolites cause centrilobular hepatocyte injury.

(CONTINUED)

HEPATITIS, CHRONIC**H**

- Avoid drugs requiring extensive hepatic metabolism or judiciously adjust dose if APSS, HE, jaundice, or hepatic failure evident.

PRECAUTIONS

- Diuretics—dehydration, hypokalemia, alkalosis, constipation: provoke or worsen HE.
- Glucocorticoids—increase susceptibility to infection, enteric bleeding, sodium and water retention (those with mineralocorticoid effects), PU/PD, protein catabolism, HE.
- Avoid drugs or reduce dose for those dependent on first-pass hepatic extraction if APSS or those requiring hepatic conjugation or biotransformation for detoxification, e.g., metronidazole—reduce conventional dose to 7.5 mg/kg PO q12h (often used for HE).
- Zinc overdose may cause hemolysis.

POSSIBLE INTERACTIONS

- Avoid medications altering hepatic p450 cytochrome biotransformation/elimination pathways (cimetidine, quinidine, ketoconazole).
- Avoid concurrent treatment with metoclopramide if spironolactone used for diuresis (causes aldosterone release).
- Adjust dose of immunomodulators if used in combination to avoid immunodeficiency.

ALTERNATIVE DRUG(S)

- Dexamethasone—if ascites, replace prednisone or prednisolone with this drug to avoid mineralocorticoid effect; divide dose by 7–10, administer q3 days.
- Mycophenolate—alternative if azathioprine intolerance, see above.

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

- At-home behavior/cognitive function, bodyweight, body condition, and muscle mass scores monitored.
- CBC, biochemistry, urinalysis—depending on immunosuppressive medications (see above), initially q2 weeks for 2 months, then monthly or quarterly; depends on patient status and drugs administered; monitor for opportunistic infections.
- Serial monitoring of TSBA—usually does not add prognostic or diagnostic information.

- Abdominal girth—reflects ascites volume; important to standardize measurement site, method, and operator determining circumference.

- Azathioprine—monitor for possible bone marrow toxicity (serial CBCs q2 weeks for 2 months then quarterly); leukopenia may develop acutely or after chronic use; GI or pancreatic toxicity; hepatotoxicity (alanine aminotransferase activity), other effects and opportunistic infectious complications.
- Mycophenolate—monitor for GI toxicity, rare bone marrow toxicity, opportunistic infectious complications; diarrhea most common complication, manage by dividing daily drug dose into 3–4.
- Cyclosporine—renal function, infectious complications, avoid cytochrome p450 inhibitor drugs; remain aware of possible drug-provoked hyperlipidemia, hypercholesterolemia, related GB disease (dysmotility, GBM, cholelithiasis).

POSSIBLE COMPLICATIONS

HE, septicemia, bleeding—may be life-threatening; disseminated intravascular coagulation—may be terminal event.

EXPECTED COURSE AND PROGNOSIS

- Chronic hepatitis often cyclic; occasional flare-ups inconsistently associated with clinical illness, more consistently associated with vacillating liver enzymes or hyperbilirubinemia.
- Some dogs achieve solid long-term remission.
- Some dogs with Cu associated hepatopathy achieve permanent remission of apparent “immune-mediated” inflammation with Cu chelation and lifelong dietary Cu restriction.
- Development of ascites—severe liver injury, APSS, potential for HE, shorter survival.
- Severe disease—with APSS, HE, and ascites may require occasional hospitalizations to adjust nutritional and medical interventions.

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

- Dogs with leptospirosis-associated chronic liver disease (rare) may shed organisms.
- *Bartonella* and rickettsial infections are sentinels for endemic vectors.

SEE ALSO

- Ascites.
- Cirrhosis and Fibrosis of the Liver.
- Copper Associated Hepatopathy.
- Glycogen-Type Vacuolar Hepatopathy.
- Hepatic Encephalopathy.
- Hepatic Failure, Acute.
- Hypertension, Portal.
- Portosystemic Shunting, Acquired.

ABBREVIATIONS

- ANA = antinuclear antibody.
- APSS = acquired portosystemic shunt.
- BUN = blood urea nitrogen.
- CRS = colorectal scintigraphy.
- DLPC = diltinolylphosphatidylcholine.
- EHBDO = extrahepatic bile duct occlusion.
- GBM = gallbladder mucocele.
- GI = gastrointestinal.
- HE = hepatic encephalopathy.
- NSAID = nonsteroidal anti-inflammatory drug.
- PPC = polyunsaturated phosphatidylcholine.
- PSVA = portosystemic vascular anomaly.
- PU/PD = polyuria/polydipsia.
- RBC = red blood cell.
- SAME = S-adenosylmethionine.
- SPS = splenoportal scintigraphy.
- TSBA = total serum bile acids.

Suggested Reading

Webster CRL, Center SA, Cullen JM, et al. ACVIM consensus statement on the diagnosis and treatment of chronic hepatitis in dogs. J Vet Intern Med 2019, 33(3):1173–1200.

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Acknowledgment The author and book editors acknowledge the prior contribution of Sean P. McDonough.



**Client Education Handout
available online**

HEPATITIS, INFECTIOUS (VIRAL) CANINE



BASICS

OVERVIEW

- Viral disease of dogs (*Canidae*) caused by canine adenovirus-1 (CAV-1). It is serologically homogeneous and antigenically distinct from respiratory CAV-2, the causative agent of canine infectious laryngotracheitis.
- CAV-1 has worldwide geographic distribution and it also causes disease in wolves, coyotes, skunks, and bears. It causes encephalitis in foxes.
- Virus is spread via direct dog-to-dog oronasal contact or via contact of contaminated fomites. Airborne transmission is not an important means of contracting the virus.
- Virus initially replicates in tonsils, then spreads to regional lymph nodes and bloodstream via lymphatics.
- Infection—targets parenchymal organs (especially liver), eyes, endothelium, lung, spleen, kidneys, and brain.
- Oronasal exposure—viremia (4–8 days); virus shed in saliva and feces; initial dispersal to hepatic macrophages (hepatic Kupffer cells) and endothelium; replicates in Kupffer cells; damages adjacent hepatocytes producing massive viremia when released.
- Adequate antibody response clears organs in 10–14 days; virus can persist in renal tubules, glomeruli, iris, ciliary body, and cornea. Virus can be shed in urine for 6–9 months.
- Chronic hepatitis—after infection in dogs with only partial neutralizing antibody response.
- Cytotoxic ocular injury—anterior uveitis; leads to classic “hepatitis blue eye” and can cause glaucoma. Develops in ~1% of dogs after modified live virus (MLV) vaccine.
- Glomerulonephritis can develop 1–2 weeks after acute signs resolve and produce proteinuria and interstitial nephritis; chronic renal failure has not been described.

SIGNALMENT

- Dogs and other *Canidae*.
- No breed or sex predilections.
- Most common in dogs <1 year of age.
- Any dog not vaccinated is susceptible.

SIGNS

- Depend on immunologic status of host and degree of initial cytotoxic injury.
- Peracute—fever; CNS signs; vascular collapse; disseminated intravascular coagulation (DIC); death within hours.
- Acute—fever; anorexia; lethargy; vomiting; diarrhea; hepatomegaly; abdominal pain; abdominal effusion; vasculitis (petechia, bruising); DIC; lymphadenopathy; rarely, nonsuppurative encephalitis.
- Uncomplicated—lethargy; anorexia; transient fever; tonsillitis; vomiting;

diarrhea; lymphadenopathy; hepatomegaly; abdominal pain.

- Late—20% of cases develop anterior uveitis and corneal edema 4–6 days post infection; recover within 21 days; may progress to glaucoma and corneal ulceration. May be the only clinical feature of inapparent infection.

CAUSES & RISK FACTORS

- CAV-1.
- Unvaccinated dogs susceptible.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Canine herpesvirus (neonatal).
- Other infectious hepatopathies.
- Leptospirosis.
- Granulomatous hepatitis.
- Toxic hepatitis.
- Fulminant infectious disease—e.g., parvovirus, canine distemper.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—schistocytes; leukopenia during acute viremia, followed by leukocytosis with reactive lymphocytosis and nucleated red blood cells (RBCs); thrombocytopenia.
- Biochemistry—liver enzyme activity high initially, begins to decline within 14 days; low glucose and albumin reflect fulminant hepatic failure, vasculitis, and endotoxemia; low sodium and potassium levels reflect GI losses; hyperbilirubinemia if survive several days.
- Urinalysis—proteinuria (glomerular injury); granular casts (renal tubule damage); bilirubinuria consistent with jaundice.

OTHER LABORATORY TESTS

- Coagulation tests—reflect severity of liver injury and DIC.
- Serology for antibodies to CAV-1—fourfold rise in immunoglobulin IgM and IgG; recent vaccine-induced antibodies confuse interpretation.
- PCR—real-time PCR not currently available; conventional PCR is able to differentiate between virulent CAV-1 and vaccine virus, which is CAV-2 in all current vaccines. Nasal, rectal, or ocular swabs or blood can be submitted as well as tissue at necropsy; positive results from urine can be difficult to interpret due to potential shedding from asymptomatic dogs.
- Viral isolation—anterior segment of eye, kidney, tonsil, and urine; difficult in parenchymal organs (especially liver) unless first week of infection.

IMAGING

- Abdominal radiography—normal or large liver; poor detail due to effusion.
- Abdominal ultrasonography—may observe hepatomegaly, hypoechoic

parenchyma (multifocal or diffuse pattern), and effusion.

DIAGNOSTIC PROCEDURES

- Liver cytology via aspiration or biopsy may identify intranuclear hepatocyte inclusions.
- Viral culture.
- Acute and convalescent serology.
- Necropsy.

PATHOLOGIC FINDINGS

- Acute—edema and hemorrhage of lymph nodes; serosal visceral hemorrhages; liver large, dark-mottled; edematous gallbladder; fibrinous exudate on liver, gallbladder, and other viscera; splenomegaly; renal infarcts; abdominal effusion. Perivasculär necrosis in liver and other organs; widespread centrilobular to panlobular necrosis. Liver is discolored; abdominal effusion also observed in canine herpesvirus in neonates.
- Chronic—small, fibrotic or cirrhotic liver.



TREATMENT

- Usually inpatient.
- Fluid therapy—balanced polyionic fluids; avoid lactate if fulminant hepatic failure; carefully monitor fluids to avoid overhydration in context of increased vascular permeability.
- Judicious potassium (and other electrolyte) supplementation since electrolyte depletion may augment hepatic encephalopathy (HE).
- Avoid neuroglycopenia—supplement fluids with dextrose (2.5–5.0%) as necessary.
- Blood component therapy for coagulopathy; blood component preferred to synthetic colloids for support of colloidal osmotic pressure; widespread vasculitis and DIC allow rapid systemic third-space colloid dispersal.
- Overt DIC—fresh blood products and low molecular weight heparin, e.g., enoxaparin 100 U/kg (1 mg/kg) q24h. See Coagulopathy of Liver Disease.
- Nutritional support—frequent small meals as tolerated; optimize nitrogen intake; inappropriate protein restriction may impair tissue repair and regeneration; nitrogen restriction advised only if overt signs of HE. A feeding tube may be necessary initially.
- If oral feeding not tolerated, provide partial parenteral nutrition (maximum 5 days) or, preferably, total parenteral nutrition.



MEDICATIONS

DRUG(S) OF CHOICE

- Prophylactic antimicrobials—transmural passage of enteric bacteria and endotoxemia

(CONTINUED)

HEPATITIS, INFECTIOUS (VIRAL) CANINE

with hepatic failure; e.g., ticarcillin (33–50 mg/kg q6–8h) combined with metronidazole (reduce conventional dose to 7.5 mg/kg IV q8–12h) and fluoroquinolone.

- Antiemetics—metoclopramide (0.2–0.5 mg/kg PO/SC q6–8h or CRI); ondansetron (0.5–1.0 mg/kg PO q12h); maropitant (1 mg/kg/day SC).
- Gastroprotection—proton pump inhibitors (omeprazole 0.5–1.0 mg/kg PO q12–24h, pantoprazole 0.7–1.0 mg/kg IV q12–24h); H₂ receptor antagonists (e.g., famotidine 0.5 mg/kg PO/IV/SC q12–24h) and sucralfate (0.25–1.0 g PO q8–12h).
- Manage HE (see Hepatic Encephalopathy).
- Ursodeoxycholic acid—choleretic and hepatoprotectant (10–15 mg/kg daily in two divided doses, with food); give indefinitely if chronic hepatitis.
- Antioxidants—vitamin E (10 IU/kg/day PO), *N*-acetylcysteine IV (140 mg/kg load, then 70 mg/kg q8h) until PO route possible; transition to *S*-adenosylmethionine (20 mg/kg/day PO, dose on empty stomach) when patient can tolerate oral medications until liver enzymes normalize or indefinitely if chronic hepatitis.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Consider severity of liver injury, protein depletion, and age in calculating drug dosages.
- Sucralfate may impair oral absorption of certain medications (fluoroquinolones, tetracycline, doxycycline, and fat-soluble vitamins, e.g., vitamin E).

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

- Monitor fluid, electrolyte, acid-base, and coagulation status to adjust supportive measures.
- Monitor for acute renal failure.

PREVENTION/AVOIDANCE

MLV vaccination—at 6–8 weeks of age; two boosters 3–4 weeks apart until 16 weeks of age; booster at 1 year; highly effective vaccine; boosters may not be needed.

POSSIBLE COMPLICATIONS

- Fulminant hepatic failure.
- HE.
- Septicemia.
- Acute renal failure.
- Glomerulonephritis.
- DIC.
- Glaucoma.
- Chronic hepatitis.

EXPECTED COURSE AND PROGNOSIS

- Peracute—poor prognosis; death within hours.
- Acute—variable: guarded to good prognosis.
- Poor antibody response (titer 1 : 16–1 : 50)—chronic hepatitis may develop.
- Good antibody response (titer >1 : 500 IgG)—complete recovery in 5–7 days possible.
- Recovered patients—may develop chronic liver or renal disease.

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

- Maternal antibody—may protect some pups for first 8 weeks; depends on maternal antibody concentration and efficacy of passive transfer.
- Vaccination of pups with high levels of passively acquired antibodies—successful at 14–16 weeks of age.

SEE ALSO

- Acute Kidney Injury.
- Anterior Uveitis—Dogs.
- Disseminated Intravascular Coagulation.
- Hepatic Encephalopathy.
- Hepatic Failure, Acute.
- Hepatitis, Chronic.

ABBREVIATIONS

- CAV-1 = canine adenovirus-1.
- DIC = disseminated intravascular coagulation.
- HE = hepatic encephalopathy.
- Ig = immunoglobulin.
- MLV = modified live virus.
- RBC = red blood cells.

Suggested Reading

Greene, CE. Infectious canine hepatitis and canine acidophil cell hepatitis. In: Greene CE, ed. Infectious Diseases of the Dog and Cat, 3rd ed. Philadelphia, PA: Saunders, 2012, pp. 42–47.

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Acknowledgment The author and book editors acknowledge the prior contribution of Sharon A. Center.

HEPATOMEGLY



BASICS

DEFINITION

Large liver detected on physical examination, abdominal radiography, US, or direct visualization.

PATHOPHYSIOLOGY

- Liver size— influenced by hepatotropic factors produced by splanchnic viscera (insulin dominates); delivered in portal blood. • Enlargement may reflect sinusoidal capacitance (blood pooling), parenchymal or sinusoidal accumulation of cells or substrates, or storage products expanding hepatocytes.

Diffuse or Generalized

- Inflammatory—immune-mediated, infectious, pyogranulomatous hepatitis; classified by infiltrative cell type. • Lymphoreticular hyperplasia—response to antigens or accelerated erythrocyte destruction.
- Congestion—impaired drainage through hepatic vein (cardiac, pericardial, thrombotic, neoplastic causes); sinusoidal occlusion syndrome or Budd Chiari syndrome.
- Infiltration—cellular (neoplastic: primary hepatocellular, metastatic); excessive glycogen, lipid, or, rarely, metabolic products (genetic diseases) expanding hepatocytes or space of Disse (amyloid). • Cystic lesions as observed in ductal plate malformations (DPMs).
- Cholestasis—most commonly with extrahepatic bile duct obstruction (EHBDO); rarely, intrahepatic cholestasis causing bile duct distention. • Extramedullary hematopoiesis (EMH)—diffuse, severe, or obstructing perfusion.

Nodular, Focal, or Asymmetric Hepatic Enlargement

- Neoplasia—hepatocellular carcinoma (HCA), hemangiosarcoma, lymphoma, metastatic carcinoma, other. • Hemorrhage.
- Infection or inflammation. • Hepatic nodular hyperplasia (uncommon cause).
- Nodular regeneration (uncommonly associated with hepatomegaly). • Arteriovenous malformation—involved lobe larger than other lobes; other lobes atrophied. • Asymmetric regeneration after large-volume resection or panlobular necrosis. • Biliary cystic lesions (DPM). • Other DPM malformations—large liver lobes usually with some atretic liver lobes or even atretic gallbladder; proliferative-like biliary epithelium with fibrotic bridging portal trabeculae (congenital hepatic fibrosis: DPM phenotype). • Liver lobe torsion—acute venous congestion.

SYSTEMS AFFECTED

- Gastrointestinal—gastric compression or displacement by large liver. • Peritoneal effusion—sinusoidal or postsinusoidal hepatic hypertension weeping lymph. • Pulmonary—

reduced ventilatory space from diaphragmatic compression. • General/vague pain—stretching of liver capsule, compression of adjacent viscera.

SIGNALMENT

- Dog and cat. • Old animals more commonly; younger if DPM related.

SIGNS

Historical Findings

- Abdominal distention or palpable mass.
- Abdominal discomfort—vague location.
- Depends on underlying cause.

Physical Examination Findings

- Dogs—liver palpable beyond costal margin (normal liver palpable in some breeds).
- Cats—liver palpable >1.5 cm beyond costal margin (normal liver palpable in some cats). • May be undetected in obese animals.

CAUSES

Inflammation

- Infectious or chronic (early) hepatitis.
- Acute toxic hepatopathy. • Feline cholangitis/cholangiohepatitis syndrome (CCHS). • EHBDO. • Lymphoreticular/pyogranulomatous—immune-mediated disease (hemolytic anemia, hemophagocytic syndrome, systemic lupus erythematosus, idiopathic), infectious disorders. • Venous outflow obstruction—sinusoidal occlusion syndrome or Budd Chiari syndrome.

Congestive Hepatopathy

- Increased central venous pressure—right-sided congestive heart failure: tricuspid valve disease; cardiomyopathy; congenital anomaly (cor triatriatum dexter); neoplasia; pericardial disease; heartworm disease; pulmonary hypertension; severe arrhythmias or bradycardia reducing cardiac output. • Vena caval or hepatic vein occlusion—thrombosis; tumor invasion or extramural caval occlusion; heartworm vena cava syndrome; vena caval stenosis or congenital kink (rare); diaphragmatic hernia; vena caval or large hepatic vein thrombosis (Budd Chiari syndrome); intrahepatic hepatic vein occlusion (thrombi, neoplasia, centrilobular parenchymal collapse causing sinusoidal occlusion syndrome).
- Sinusoidal occlusion syndrome—collapsed centrilobular parenchyma and/or damage to hepatic venules impairing circulatory egress; causes include xenobiotic or herbal toxicity (e.g., pyrrolizidine alkaloids), severe non-steroidal inflammatory drug-induced injury, severe copper hepatopathy. • Liver lobe torsion (acute).

Infiltration

- Neoplasia. • Metabolic abnormalities—amyloid; lipid (see Hepatic Lipidosis [cats]), glycogen (see Glycogen-Type Vacuolar Hepatopathy [dogs]); cats and dogs: diabetes mellitus (DM), hyperlipidemic syndromes; neonatal metabolic storage disorders.
- Lymphohistiocytic/pyogranulomatous—

infectious disease, immune response, antigen stimulation, neoplasia (histiocytic/dendritic cells: histiocytic sarcoma), hemophagocytic syndrome.

Extramedullary Hematopoiesis

Regenerative anemias—hemolytic (immune-mediated, congenital, metabolic, infectious); oxidant injury; erythroparasitism; severe blood loss, bone marrow failure; idiopathic.

Neoplasia

- Infiltrative, diffuse, or large focal tumors—primary or metastatic. • Primary hepatic—lymphoma; massive HCA; cholangiocarcinoma (bile duct carcinoma ± EHBDO); hemangiosarcoma. • Metastatic—lymphosarcoma, hemangiosarcoma, histiocytic sarcoma, fibrosarcoma, leiomyoma/sarcoma, neuroendocrine, osteosarcoma, others.

Major Bile Duct Obstruction

- Pancreatitis; pancreatic neoplasia. • Neoplasms in porta hepatis—bile duct carcinoma, lymphoma. • Granuloma/fibrosis of common bile duct. • Insipidated bile syndrome, choledochal cyst (DPM phenotype), or gallbladder mucocele. • Cholelithiasis.
- Proximal duodenitis; duodenal foreign body.
- Fluke migration (cats).

Cystic Lesions

- Primary single hepatic or biliary cysts.
- Acquired cysts within neoplastic masses.
- DPM—may associate with renal cysts (common in Persian cats). • Biliary cystadenoma (cats; DPM phenotype).
- Hepatic abscesses (cystic cavitation); hepatocellular carcinoma housing abscess.
- Parasitic—echinococcus (hydatid cyst).

Other

- Drugs—corticosteroids (see Glycogen-Type Vacuolar Hepatopathy), phenobarbital (dogs).
- Hepatic nodular hyperplasia (rare cause).
- Acromegaly—cats.

RISK FACTORS

- Cardiac disease. • Heartworm disease.
- Neoplasia. • Primary hepatic disease—-inflammatory, neoplastic, cystic, or other DPM phenotypes. • Corticosteroids—exogenous or endogenous. • Phenobarbital treatment. • Poorly controlled DM.
- Anorexia in obese cats—hepatic lipidosis.
- EHBDO. • Cystic malformations—DPM. • Certain anemias—diffuse hepatic EMH.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Similar Signs

Distinguish from other disorders causing visceromegaly (gastric, splenic), cranial abdominal masses, or effusions via radiography and US.

(CONTINUED)

HEPATOMEGLALY**H****Differential Causes**

- Cardiac disorders—heart murmur, weak femoral pulses, hepatojugular reflex, jugular distention and jugular pulses, muffled heart sounds, arrhythmias, cough, dyspnea/tachypnea. • Symptomatic anemia—pallor ± jaundice; tachycardia; tachypnea; exercise intolerance; bounding pulses. • Parenchymal liver disease—lethargy, anorexia, vomiting, diarrhea, weight loss, variable liver enzymes ± jaundice, coagulopathies, polyuria/polydipsia (PU/PD), if advanced may see hepatic encephalopathy (HE) or ascites. • Glycogen-type vacuolar hepatopathy (VH; dog)—signs of hyperadrenocorticism or adrenal hyperplasia or other chronic disease imposing stress; DM—persistent hyperglycemia; PU/PD, signs of underlying endocrinopathy.
- Hepatic lipidosis—jaundice in obese hyporexic cat; poorly controlled DM (dog or cat); failure-to-thrive puppies or kittens; congenital lysosomal or glycogen storage disorders.

CBC/BIOCHEMISTRY/URINALYSIS**CBC**

- Identify anemia and cause; spherocytes (immune-mediated hemolytic anemia, microangiopathic anemia); schistocytes (vascular shearing-microangiopathic, vena cava syndrome, hemangiosarcoma, disseminated intravascular coagulation (DIC), Heinz bodies (oxidant injury); erythroparasitism (*Mycoplasma haemofelis* or *haemominutum*, *Babesia*).
- Circulating blast cells—myeloproliferative or lymphoproliferative disorders. • Nucleated red cells—EMH, splenic disease, regenerative anemia. • Macrocytosis and nonregenerative anemia—feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), myelophthisis.
- Thrombocytopenia—increased consumption, destruction, or reduced platelet production.
- Thrombocytosis—neoplasia; inflammation; hyperadrenocorticism; splenic disease.

Biochemistry

- Inflammatory hepatic disorders—usually high liver enzyme activity; variable hyperglobulinemia, bilirubin, and albumin concentrations. • Reticuloendothelial hyperplasia—variable liver enzyme activity.
- Primary hepatic neoplasia—moderate to marked increases in liver enzyme activity (alkaline phosphatase [ALP] and γ -glutamyltransferase [GGT] usually predominate with HCA, variable alanine aminotransferase [ALT]). • Metastatic neoplasia—variable liver enzymes; occasional high calcium or globulin. • Infiltrative disorders—minor liver enzyme change; variable bilirubin concentration. • Glycogen-type VH (dogs)—markedly high ALP; high cholesterol ± triglycerides with increased glucocorticoids or sex steroids; DM—high

ALP, cholesterol, hyperglycemia. • Hepatic lipidosis (cats)—high ALP, aspartate aminotransferase (AST), ALT; minor increase in GGT unless concurrent pancreatitis, CCHS, or EHBDO. • Storage diseases—may display few abnormalities. • EHBDO—markedly high ALP, GGT, other enzymes; high bilirubin and cholesterol. • Cystic lesions—normal, except with hepatic abscess (markedly high ALT and AST) or CCHS (high ALP, ALT, GGT, variable bilirubin); DPM often presents with suppurative CCHS. • Phenobarbital-associated—high liver enzymes (especially ALP in dogs). • Nodular hyperplasia—normal to moderately high ALP, elderly dogs: rare cause of hepatomegaly.

OTHER LABORATORY TESTS

- FeLV and FIV testing—cats. • Buffy coat—circulating blasts with neoplasia or uncommon cell type observed. • Coagulation panel—DIC common with hemangiosarcoma or diffuse lymphoma; prolonged coagulation times common with EHBDO >5 days esp. in cats.
- Total serum bile acids (TSBA)—high in diffuse disorders or EHBDO; *redundant test if nonhemolytic jaundice*. • Pituitary-adrenal axis testing (dogs)—see Glycogen-Type Vacuolar Hepatopathy; Hyperadrenocorticism (Cushing's Syndrome)—Dogs. • Insulin-like growth factor-1 (IGF-1) in acromegalic cats; typically males with DM. • Heartworm testing—in endemic areas. • Fungal serology—in endemic areas. • Other serology—e.g., Rickettsial, *Bartonella*, *Leishmania*, *Toxoplasmosis*.

IMAGING**Abdominal Radiography**

- Hepatomegaly—rounded margins extending beyond costal arch; caudal-dorsal gastric displacement; caudal displacement: cranial duodenal flexure, right kidney, transverse colon. • May suggest cause.

Thoracic Radiography

- Three views (lateral [right, left], dorsal-ventral)—metastasis, other disorders, cranial displacement of diaphragm, wide vena cava if passive congestion. • Cardiac, pulmonary, pericardial, and vena caval disorders usually need US imaging. • Sternal lymphadenopathy—reflects abdominal inflammation or neoplasia.
- Puppies, kittens, deep inspiration, and certain canine breeds—spurious hepatomegaly.

Abdominal US

- Liver size and surface contour. • Diffuse enlargement with normal echogenicity—congestion; cellular infiltration (lymphoma); inflammation; EMH; reticuloendothelial hyperplasia, diffuse amyloid deposition expanding space of Disse. • Diffuse enlargement with hypoechoic parenchyma—normal variation; congestion, lymphoma, diffuse sarcoma; amyloidosis expanding space of

Disse. • Diffuse enlargement with hyper-echoic parenchymal (minor nodularity)—lipid or glycogen; inflammation; fibrosis; lymphoma; DPM fibrotic bridging portal trabeculae. • Diffuse enlargement with hypoechoic nodules—neoplasia; abscess; degenerative glycogen-type VH (dog); HCS, cystic lesions (DPM). • Identify EHBDO. • Identify concurrent abdominal diseases—kidneys; intestines; lymph nodes; effusion; interrogation of porta hepatis for obstructions and lymphadenopathy. • Identify portal or vena caval thrombi. • Identify abdominal effusion—distribution and echogenic patterns. • Cannot distinguish benign from malignant disease.

DIAGNOSTIC PROCEDURES**ECG/Echocardiography**

Characterize cardiac rhythm, structure, function, pulmonary pressure gradient.

Fine-Needle Aspiration

- Procedure—22-G, 2.5–3.75 cm (1–1.5 in) needle; diffusely large liver directly aspirated without US; focal lesions aspirated under US guidance. • Cytology—may disclose infectious agents, vacuolar change, neoplasia, inflammation, or EMH; definitive diagnosis seldom confidently confirmed (false-positive and -negative results). • Hepatic biopsy—if US rules out EHBDO, cytology does not indicate septic inflammation or neoplasia, and no obvious diagnoses made; percutaneous ultrasound-guided Tru-Cut® needle biopsy for suspected neoplasia or amyloid (avoid if abscess or EHBDO possible); otherwise, best sampling with laparoscopic or surgical exploratory approaches. • Microbial culture—aerobic and anaerobic bacterial; fungal as appropriate. • Staining—H&E (routine); reticulin (architectural substructural remodeling, infiltration, compression), Masson's trichrome (collagen deposition, amyloid detection); rhodanine (copper); periodic acid-Schiff (glycogen ± amylose predigestion); acid-fast stain (mycobacteria if granulomatous inflammation); Congo red (amyloid); Oil Red O (lipid, requires frozen section), infectious disease stains (see Hepatitis, Granulomatous). • Coagulation testing—before liver sampling, consider measurement of prothrombin time, activated partial thromboplastin time, fibrinogen, buccal mucosal bleeding time (BMBT); prediction of iatrogenic hemorrhage poor with bench tests; BMBT may be more relevant. • Abdominal effusion—cytology; protein content; culture; evaluate before tissue sampling. • Pericardiocentesis—if pericardial tamponade. • Cyst aspiration sampling—if possible infectious cause when plausible treatment might be recommended; risk for abdominal contamination if hepatic abscess.

HEPATOMEGLALY



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—except cardiac/pericardial causes or hepatic failure.
- General supportive goals—eliminate or manage inciting cause; prevent complications; palliate derangements reflecting hepatic failure.
- Important derangements—dehydration and hypovolemia; HE; hypoglycemia; acid-base and electrolyte abnormalities; coagulopathies; enteric hemorrhage; sepsis; endotoxemia.

NURSING CARE

- Heart failure or ascites—impose sodium restriction: fluids and food (<100 mg/100 kcal, <0.2% dry matter basis food), prescribe appropriate cardiac medications or diuretics.
- Supplement potassium chloride if IV fluids—sliding scale (maintenance = 20 mEq/L fluid).
- Supplement B-soluble vitamins in IV fluids.
- If jaundiced—parenteral vitamin K before invasive procedures.

ACTIVITY

Restricted; initial cage rest in some disorders.

DIET

- Dietary protein—restrict only if evidence of HE.
- Well-balanced, adequate energy, positive nitrogen balance essential; adequate vitamins and micronutrients for most disorders; fat restriction only if hypertriglyceridemia or steatorrhea.
- May need feeding tube (e.g., esophagostomy tube) in cats with HL (see Hepatic Lipidosis).
- Sodium—restrict if cardiac failure or ascites.

CLIENT EDUCATION

- Treatment depends on underlying cause.
- Many causes life-threatening; some less serious and amenable to treatment.
- Thorough diagnostic evaluations essential for determining definitive cause and interventions.

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SURGICAL CONSIDERATIONS

- Resection of primary or focal hepatic mass lesions (neoplasia, abscess, compromising cyst)—biliary decompression if EHBDO.
- Pericardiectomy (thoracoscopic procedure)—if effusion recurs after initial pericardiocentesis.



MEDICATIONS

DRUG(S) OF CHOICE

Vary with underlying cause.

CONTRAINDICATIONS

- Avoid hepatotoxic drugs.
- Glycogen-type VH (dogs)—avoid glucocorticoids.
- Hepatic lipidosis (cats)—avoid catabolism or drugs that promote it; avoid fasting.



FOLLOW-UP

PATIENT MONITORING

- Physical assessment and hepatic imaging—reassess liver size.
- CBC, biochemistry, TSBA—serial assessments of lab abnormalities and liver function; packed cell volume and reticulocyte count with anemia.
- Thoracic radiography, ECG, and echocardiography—reassess status.
- Pituitary-adrenal axis—adrenal disorders.
- Adjust drug dosages according to status of liver function, body condition, and weight.

POSSIBLE COMPLICATIONS

Many causes are life-threatening.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Certain infectious agents of concern.

(CONTINUED)

SEE ALSO

- Amyloidosis.
- Anemia, Immune-Mediated.
- Bile Duct Obstruction (Extrahepatic).
- Cholangitis/Cholangiohepatitis Syndrome.
- Congestive Heart Failure, Right-Sided.
- Ductal Plate Malformation (Congenital Hepatic Fibrosis).
- Glycogen Storage Disease.
- Glycogen-Type Vacuolar Hepatopathy.
- Hepatic Lipidosis.
- Hepatitis, Granulomatous.
- Hepatitis, Suppurative and Hepatic Abscess.
- Hepatocellular Carcinoma.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- AST = aspartate aminotransferase.
- BMBT = buccal mucosal bleeding time.
- CCHS = cholangitis/cholangiohepatitis syndrome.
- DIC = disseminated intravascular coagulation.
- DM = diabetes mellitus.
- DPM = ductal plate malformation.
- EHBDO = extrahepatic bile duct obstruction.
- EMH = extramedullary hematopoiesis.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- GGT = γ -glutamyltransferase.
- IGF-1 = Insulin-like growth factor-1.
- HCA = hepatocellular carcinoma.
- HE = hepatic encephalopathy.
- PU/PD = polyuria/polydipsia.
- TSBA = total serum bile acids.
- VH = vacuolar hepatopathy.

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HIP DYSPLASIA

H



BASICS

DEFINITION

A developmental syndrome characterized in growing animals by excessive laxity of the coxofemoral joint that results in secondary osteoarthritis (OA) of the coxofemoral joints in the adult animal.

PATHOPHYSIOLOGY

- Developmental defect initiated by genetic predisposition to subluxation of immature hip joint.
- Poor congruence between femoral head and acetabulum; creates abnormal forces across joint; interferes with normal development (leading to irregularly shaped acetabula and femoral heads); overloads articular cartilage (causing microfractures and OA).

SYSTEMS AFFECTED

Musculoskeletal

GENETICS

- Complicated, polygenic transmission. Genetic markers for diagnosis and prevention are under development but are not standardized or routinely used.
- Expression is determined by interaction of genetic and environmental factors, the latter including overall excess caloric consumption and excess calcium during growth.
- Heritability index—depends on breed, but generally estimated at 0.3.

INCIDENCE/PREVALENCE

- One of most common skeletal diseases encountered clinically in dogs.
- Actual incidence unknown; depends on breed.
- Incidence in cats significantly lower than dogs.

SIGNALMENT

Species

Dog, rarely cat.

Breed Predilections

- Large-breed dogs—Saint Bernard, German shepherd, Labrador retriever, golden retriever, Rottweiler.
- Smaller-breed dogs—may be affected; in fact, incidence of disease in pugs is highest of all breeds, approaching 70%; small-breed dogs less likely to exhibit clinical signs.
- Cats—more commonly affects purebred cats; reportedly affects ~18% of Maine coon cats.

Mean Age and Range

- Onset of clinical signs varies with severity of hip laxity in immature dog and with worsening secondary OA in mature dog.
- Clinical signs—may develop after 4 months of age in dogs with severe laxity; may also develop at any age after onset of secondary OA.
- Clinical signs are biphasic in dogs; young dogs often exhibit most severe clinical signs

between 6 and 12 months of age; clinical signs often diminish in animals 12–18 months of age, worsening again in older dogs in 4–8-year age period.

Predominant Sex

- Dogs—none.
- Cats—more common in female cats.

SIGNS

General Comments

- Severity of signs depends on degree of joint laxity, degree of OA, and chronicity of disease.
- Early—related to joint laxity.
- Later—related to severity of OA.

Historical Findings

- Decreased activity.
- Difficulty or slow rising.
- Reluctance to run, jump, or climb stairs.
- Intermittent or persistent hind limb lameness—often worse after exercise.
- Pelvic limb lameness may be unilateral or bilateral.
- Bunny-hopping or swaying gait.
- Narrow stance in hind limbs.

Physical Examination Findings

- Pain on palpation or manipulation of hip joint(s); particularly extension.
- Increased joint laxity (positive Ortolani sign)—characteristic of early disease; may not be finding in chronic cases owing to periarthritis fibrosis.
- Crepitus during hip motion.
- Decreased range of motion in hip joints.
- Atrophy of thigh muscles.

CAUSES

- Genetic predisposition for hip laxity.
- Rapid weight gain may be associated with onset of clinical signs due to increased demands on joint.
- Nutritional influences, particularly excess caloric intake in young dog and calcium >1.6% in diet on dry-matter basis, increase phenotypic expression, development of hip dysplasia (HD), and progression of disease.
- Decreased gluteal and caudal thigh muscle mass—increase expression and progression.

RISK FACTORS

- Overweight puppies fed in excess of caloric requirements for normal growth at risk for increased incidence of HD.
- Additional calcium supplementation in diet of young large-breed dogs contraindicated and may predispose to development of HD.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cranial cruciate ligament rupture—up to ½ of dogs referred for treatment of HD actually suffer from concurrent cranial cruciate rupture; cranial cruciate ligament rupture must remain alternative diagnosis

for lameness in large-breed dogs until definitively eliminated from consideration.

- Degenerative myelopathy.
- Lumbosacral instability.
- Unilateral or bilateral stifle disease.
- Panosteitis.
- Polyarthropathies.

IMAGING

- Ventrodorsal hip-extended radiographs—commonly used for diagnosis; may need sedation or general anesthesia for accurate positioning.
- Early radiographic signs—subluxation of hip joint with poor congruence between femoral head and acetabulum; initially normally shaped acetabulum and femoral head; with disease progression, shallow acetabulum and flattened femoral head.
- Radiographic evidence of OA—flattening of femoral head; shallow acetabulum; periaricular osteophyte production; thickening of femoral neck; sclerosis of subchondral bone; periarthritis soft tissue fibrosis. Remodeling of femoral neck is uncommon in cats.
- Distraction radiographs—quantify joint laxity; may accentuate laxity for more accurate diagnosis. Distraction radiographic procedures such as PennHip® have been standardized and allow better prediction of dogs likely to develop secondary hip OA and better selection of dogs for breeding potential.
- Dorsal acetabular rim view radiographs—evaluate acetabular rim; assess dorsal coverage of femoral head. Clinical efficacy of such views in diagnosis and treatment of HD has not been definitively established.

DIAGNOSTIC PROCEDURES

- Commercial genetic markers are under development but not in widespread use at this time.
- Arthroscopy of hip joint has been described in diagnosis of HD, but does not add useful clinical information regarding treatment.

PATHOLOGIC FINDINGS

- Early—normal conformation of femoral head and acetabulum; may note joint laxity and excess synovial fluid.
- With progression—malformed acetabulum and femoral head; synovitis; articular cartilage degeneration. Formation of periarthritis osteophytes leads to radiographic formation of “Morgan’s line,” linear formation of enthesiophytes at origin of joint capsule on femoral neck.
- Chronic—may note full-thickness cartilage erosion.



TREATMENT

APPROPRIATE HEALTH CARE

- May treat with conservative medical therapy or surgery.

HIP DYSPLASIA

(CONTINUED)

- Depends on patient's size, age, and intended function; severity of joint laxity; degree of OA; clinician's preference; financial considerations of owner.

NURSING CARE

- Physical therapy (passive joint motion)—decreases joint stiffness; helps maintain muscle integrity.
- Swimming (hydrotherapy)—excellent nonconcussive form of physical therapy; encourages joint and muscle activity without exacerbating joint injury.

ACTIVITY

- As tolerated.
- Swimming—recommended to maintain joint mobility while minimizing weight-bearing activities.

DIET

- Weight control—important and first goal of therapy; decrease load applied to painful joint; minimize weight gain associated with reduced exercise.
- Supplementation with omega-3 fatty acids (in commercial diets or as food additive) beneficial to decrease pain and inflammation and improve function. While optimum dosage/feeding of omega-3 fatty acids yet to be determined, clinical efficacy of commercial diets containing 1.7–3.4% of omega-3 fatty acids and precursors has been established.

CLIENT EDUCATION

- Discuss heritability of the disease, recommend neutering of affected animals and elimination as breeding sources.
- Explain that medical therapy is palliative.
- Warn client that joint degeneration often progresses unless corrective osteotomy procedure is performed early in disease.
- Explain that surgical procedures can salvage joint function once severe joint degeneration occurs.

SURGICAL CONSIDERATIONS

Triple, Double, or 2.5 Pelvic Osteotomy

- Corrective procedure; designed to reestablish congruity between femoral head and acetabulum.
- Immature patient (6–10 months of age) without signs of OA.
- Rotate acetabulum—improve dorsal coverage of femoral head; correct forces acting on joint; minimizes progression of OA, but OA frequently progresses on radiographs even though progression not clinically apparent.
- Surgical procedure necessitates implantation of surgical implants, commonly bone plate and screws specially designed for procedure; large dogs may necessitate use of two bone plates; outcomes improved and complication rates decreased with use of locking implants.

Juvenile Pubic Symphysiodesis

- Pubic symphysis is fused at early age (8–16 weeks) using electrocautery.

- Requires extremely early diagnosis of condition, or use as preventative in nonbreeding animals to decrease need for more aggressive surgical procedure in dogs likely to develop secondary OA or more severe clinical signs.
- Causes ventroversion of acetabulum during growth to better cover femoral head.
- Improves joint congruence and stability—similar effects to triple pelvic osteotomy without osteotomy and surgical implants.
- Minimal morbidity; easy to perform—must be performed very early (ideally 3–4 months of age) to achieve effect; minimal effect achieved if performed after 5 months of age.

Total Hip Replacement

- Indicated to salvage function in mature dogs with severe degenerative disease unresponsive to medical therapy.
- Multiple systems exist to replace both acetabular and femoral head surfaces and comprising both cemented and noncemented (ingrowth) implants; noncemented implants have best prognosis for long-term use and implant stability.
- Pain-free joint function—reported in >90% of cases.
- Unilateral joint replacement—provides acceptable function in ~80% of cases.
- Staged bilateral joint replacement now chosen by 50% of owners.
- Complications—luxation; femoral fracture, sciatic neuropraxia; infection; incidence of infection decreased with use of noncemented implant systems compared to cemented systems.

Excision Arthroplasty

- Removal of femoral head and neck to eliminate joint pain.
- Extremely important to achieve smooth osteotomy close to femoral shaft.
- Primarily a salvage procedure—for significant OA; when pain cannot be controlled medically; when total hip replacement is cost-prohibitive.
- Best results—small, light dogs (<20 kg); patients with good hip musculature.
- Can provide good results in larger dogs.
- Slightly abnormal gait often persists and consistently seen on objective gait analysis of patients, despite lack of lameness detection by owners or veterinarians on casual observation.
- Postoperative muscle atrophy—common, particularly in large dogs.

Denervation Procedure

- Surgical procedure described in anecdotal and research literature to reduce pain associated with HD.
- Does not improve joint conformation or OA.
- Little objective scientific evidence exists for this procedure's effectiveness despite numerous clinical reports.
- Recent blinded studies suggest the treatment does not improve the treated hip, but may slow development of further clinical signs.



MEDICATIONS

DRUG(S) OF CHOICE

- Analgesics and anti-inflammatory drugs—minimize joint pain (and thus stiffness and muscle atrophy caused by limited usage); decrease synovitis.
- Medical therapy—does not correct biomechanical abnormality; degenerative process likely to progress; often provides only temporary relief of signs.
- Agents—carprofen (2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h); etodolac (10–15 mg/kg PO q24h); deracoxib (3–4 mg/kg PO q12h for 1 week, then 2 mg/kg PO q12h); firocoxib (4 mg/kg PO q24h).
- Diet supplementation with omega-3 fatty acids (fish oils) decreases joint inflammation and provides pain relief; commercial diets containing 1.7–3.4% omega-3 fatty acids and precursors are most consistent and easiest method of administration.

CONTRAINDICATIONS

Avoid corticosteroids—potential side effects; articular cartilage damage associated with long-term use.

PRECAUTIONS

- Nonsteroidal anti-inflammatory drugs—gastrointestinal upset may preclude use in some patients.
- Carprofen—reported to cause acute hepatotoxicity in some dogs.

ALTERNATIVE DRUG(S)

- Polysulfated glycosaminoglycan injections, or oral glucosamine, and chondroitin sulfate—may have chondroprotective effect in OA, but recent evidence suggests are not or are only minimally efficacious.
- There are single reports of agents such as elk antler velvet suggesting their efficacy for OA, but no confirmation or widespread acceptance for efficacy.
- Prophylactic laser therapy, extracorporeal pulse therapy, and acupuncture have been suggested for treatment, but no documented evidence demonstrating efficacy of these modalities for OA despite numerous research studies.
- Stem cell therapy, primarily mesenchymal stromal cell extractions, have been investigated in research studies and individual clinical patients, but show no clinical benefit at present.



FOLLOW-UP

PATIENT MONITORING

- Clinical and radiographic monitoring—assess progression.
- Medical treatment—clinical deterioration suggests alternative dosage or medication or

(CONTINUED)

HIP DYSPLASIA**H**

surgical intervention; weight management is important continuing consideration in management of HD.

- Triple pelvic osteotomy—monitored radiographically; assess healing, implant stability, joint congruence, and progression of OA; over 50% of dogs may develop radiographic signs of OA after pelvic osteotomy, but clinical signs or their lack remain stable in spite of OA.
- Hip replacement—monitored radiographically on annual basis; assess implant stability.

PREVENTION/AVOIDANCE

- Best prevented by not breeding affected dogs.
- Pelvic radiographs—may help identify phenotypically abnormal dogs; may not identify all dogs carrying the disease.
- Do not repeat dam–sire breedings that result in affected offspring.
- Special diets designed for rapidly growing large-breed dogs—may decrease severity.

EXPECTED COURSE AND PROGNOSIS

Joint degeneration usually progresses—most patients lead normal lives with proper medical or surgical management.

**MISCELLANEOUS****PREGNANCY/FERTILITY/BREEDING**

Do not breed affected dogs; added weight owing to pregnancy may exacerbate clinical signs.

ABBREVIATIONS

- HD = hip dysplasia.
- OA = osteoarthritis.

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Author James K. Roush

Consulting Editor Mathieu M. Glassman



**Client Education Handout
available online**

HOOKWORMS (ANCYLOSTOMIASIS)



BASICS

OVERVIEW

- Nematode parasites of small intestine—dogs: *Ancylostoma caninum*, *A. braziliense*, *Uncinaria stenocephala*; cats: *A. tubaeforme*, *A. braziliense*, *U. stenocephala*. • Eggs larvae, hatch, develop into third-stage larvae (L3) in environment; transmitted by ingestion of infective larvae in food, water, or transport hosts and by larval skin penetration; *A. caninum* is transmitted via colostrum/milk to pups. • Some L3 migrate through lungs, enter somatic tissue, and become dormant; pregnancy and removal of adults from intestine can reactivate these larvae; many ingested larvae remain in gastrointestinal (GI) tract and mature. • Blood-sucking adults and fourth-stage larvae of *A. caninum* and *A. tubaeforme* cause blood-loss anemia and enteritis; leave bite sites with ongoing hemorrhage.
- Disease severity:
 - Peracute—neonates; results from transmammary infection.
 - Acute disease—older pups.
 - Acute, chronic compensatory—adults.
 - Chronic noncompensatory—immunosuppressed or debilitated dog.
 - *Uncinaria*—of little clinical concern.
- A. braziliense*—major cause of cutaneous larval migrans (CLM) in humans.
- Respiratory disease may result from larval migration in lungs.

SIGNALMENT

- Peracute to acute disease (young animals); asymptomatic or chronic (mature animals). • More severe clinical disease in dogs than cats.

SIGNS

Historical Findings

- Pallor, melena, diarrhea, constipation, loss of condition, poor appetite, and/or dry cough. • Sudden death.

Physical Examination Findings

- Poor body condition, ill-thrift, poor hair coat. • Pallor. • Erythematous, pruritic lesions, papules on feet (especially between toes). • Shock—tachycardia, weak pulse, prolonged/absent capillary refill time.

CAUSES & RISK FACTORS

- Neonatal animals at highest risk. • Infected bitch or queen. • Environmental contamination.
- Concurrent enteric infections.
- Immunocompromise.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Causes of anemia and hypovolemic/hemorrhagic shock; trichuriasis. • Ascariasis,

coccidiosis, strongyloidosis—similar signs without significant anemia. • Physalopteriosis—melena, mild anemia.

CBC/BIOCHEMISTRY/URINALYSIS

- Eosinophilia. • Anemia—normochromic, normocytic, regenerative; chronically microcytic, hypochromic (iron deficiency).

DIAGNOSTIC PROCEDURES

- Disease/death may occur prior to egg shedding. • Fecal flotation with centrifugation—morulated strongylid eggs; minor size differences among species. • Fecal ELISA—detects antigen from adult and immature worms, can detect prepatent infection. • Necropsy of littermates with similar clinical signs.

PATHOLOGIC FINDINGS

- Gross—hookworms attached to small intestinal mucosa, multifocal hemorrhagic ulcerations (bite sites) on mucosa, blood in intestinal lumen. • Microscopic—eosinophilic enteritis.



TREATMENT

- Peracute and severe acute cases treated as inpatients—anthelmintic, fluid therapy, blood transfusion, supplemental oxygen, symptomatic/supportive care as indicated.
- Chronic compensatory cases—anthelmintic, iron supplement.



MEDICATIONS

DRUG(S) OF CHOICE

Adulticide/Larvicide Anthelmintics

- Fenbendazole 50 mg/kg PO q24h for 3 consecutive days (dogs). • Milbemycin oxime 0.5 mg/kg (dogs) or 2 mg/kg (cats) PO q30 days. • Emodepside 3 mg/kg/praziquantel 12 mg/kg topically once (cats). • Moxidectin 0.17 mg/kg SC q6 months (dogs). • Moxidectin 2.5 mg/kg (dogs) or 1.0 mg/kg (cats)/imidoclopramide 10 mg/kg, topically q30 days. • Ivermectin 24 µg/kg PO q30 days (cats).

Adulticide Activity (Label Dose unless Stated)

- Pyrantel pamoate (dogs) 10–20 mg/kg PO (cats: extra-label). • Praziquantel/pyrantel pamoate/febantel (dogs).
- Praziquantel/pyrantel pamoate (cats).
- Ivermectin/pyrantel pamoate or ivermectin/pyrantel pamoate/praziquantel (dogs). • Selamectin 6 mg/kg topically q30 days (cats).



FOLLOW-UP

Monitor fecal egg counts and hematocrit after treatment.

PREVENTION/AVOIDANCE

- Routine deworming does not eliminate dormant L3; eliminate intestinal stages and reactivated larvae in breeding bitch using fenbendazole (50 mg/kg/day PO from day 40 of gestation to day 14 of lactation) or ivermectin (0.5 mg/kg PO 4–9 days prior to whelping, again 10 days later). • Begin biweekly anthelmintic treatment of pups at 2 weeks; continue until weaned, especially high-risk pups; treat monthly after weaning. • Treat queen with adulticide/larvicide anthelmintic prior to breeding, after queening. • Begin anthelmintic treatment of kittens at 3–4 weeks of age; treat monthly thereafter. • Promptly remove, dispose of feces to prevent environmental contamination. • Prevent hunting and ingestion of potential transport hosts.

H

EXPECTED COURSE AND PROGNOSIS

- Puppies (and rarely adults) with peracute/acute *A. caninum* infection may die despite treatment.
- Early recognition, anthelmintic treatment, prompt treatment of anemia, nutritional support necessary for successful outcome. • Anthelmintic treatment of adults can result in larval reactivation, repopulation of small intestine.



MISCELLANEOUS

AGE-RELATED FACTORS

- Disease more acute in young, usually chronic in adults. • Transmission of *A. caninum* from bitch to offspring results in high rate of infection in pups.

ZOONOTIC POTENTIAL

- All hookworms, especially *A. braziliense*, cause human CLM. • *A. caninum* larvae can cause visceral larva migrans or migrate to GI tract, causing abdominal pain and eosinophilia without becoming patent.

ABBREVIATIONS

- CLM = cutaneous larva migrans.
- GI = gastrointestinal.
- L3 = third-stage larvae.

INTERNET RESOURCES

- <https://capcvet.org> • <https://www.cdc.gov/parasites/zoonotichookworm>

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Author Matt Brewer and Katy A. Martin
Consulting Editor Amie Koenig

HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—CATS



BASICS

OVERVIEW

Feline Cushing's syndrome (FCS) or hyperadrenocorticism is a consequence of abnormally increased functional activity of the adrenal cortex.

Pathophysiology

- Caused by increased glucocorticoid secretion by the adrenal gland(s).
- Approximately 85% of cases due to bilateral adrenocortical hyperplasia from pituitary hyperplasia or tumor—pituitary-dependent hyperadrenocorticism (PDH).
- Remaining 15% caused by adrenal tumor (AT), half of which are benign.
- Regardless of etiology, concurrent unregulated diabetes mellitus (DM) is frequent (90%) and other concurrent diseases (e.g., pancreatitis, chronic kidney, or cardiac disease) are reported.

SIGNALMENT

- Middle-aged to old cat.
- No known breed or sex predisposition.

SIGNS

- Dermatologic abnormalities (alopecia; unkempt hair coat; thin, fragile skin that is easily bruised or torn), polyuria, polydipsia, polyphagia, weight loss, muscle wasting, and pot-bellied appearance.
- Weight gain (unless concurrent DM causes weight loss), hepatomegaly, and curled pinnae also seen.
- Lethargy (dullness) secondary to muscle weakness or effects of pituitary mass.
- Excess sex hormones can cause signs such as penile barbs and behavioral changes (sexual).

CAUSES & RISK FACTORS

- Pituitary adenoma with subsequent corticotropin hyperplasia and excess glucocorticoid secretion.
- Autonomously functioning benign adrenal adenoma (50%) or malignant adeno-carcinoma (50%).
- Iatrogenic from glucocorticoid administration (rare).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Insulin-resistant DM.
- Acromegaly.
- Hepatopathy.
- Renal disease.
- Sex hormone-secreting adrenal tumor.
- Hyperprogesteronism.
- Dermatologic disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Lymphopenia, anemia.
- Hyperglycemia, hypercholesterolemia, hypertriglyceridemia, hypochloremia.
- Elevated urine cortisol : creatinine (UC : Cr) ratio, proteinuria.
- Azotemia, hyperglobulinemia (less common).
- Elevated serum alkaline phosphatase uncommon.

OTHER LABORATORY TESTS

Screening Tests

- UC : Cr—sensitive (good negative predictive value).
- Low-dose dexamethasone-suppression test—good sensitivity. Dose: 0.1 mg/kg IV. Failure to suppress consistent with FCS.
- Adrenocorticotrophic hormone (ACTH) stimulation test—specific but poorly sensitive, not recommended as initial diagnostic test.
- Assays for plasma sex hormone and progesterone concentrations may rule out differentials.

Differentiating Tests

- Plasma endogenous ACTH concentration high normal or greater with PDH compared to low plasma ACTH levels with AT (<10 pg/mL). Reference ranges vary with laboratories.
- Imaging.

IMAGING

- Abdominal ultrasound—accurate to differentiate PDH from AT in most cases; operator dependent. Symmetric adrenal glands of normal or enlarged size are suggestive of PDH; unilateral enlargement or asymmetric adrenal glands support AT.
- CT and MRI—visualization and measurement of pituitary tumors or characterization of adrenal tumors.



TREATMENT

- FCS is a debilitating disease. Prognosis is guarded due to severity of complications and concurrent diseases.
- Presurgical medical treatment is beneficial to prevent complications from fragile skin and infections.
- Radiation therapy of macroadenomas allows better control of the disease and insulin resistance.
- Unilateral adrenalectomy for AT and medical therapy for PDH are the most readily available effective treatment options.
- Hypophysectomy (microsurgical transsphenoidal) is effective and available at some institutions.



MEDICATIONS

DRUG(S) OF CHOICE

- Trilostane reversibly blocks steroid synthesis. In most patients with FCS from PDH, trilostane reduces clinical signs and improves endocrine test results. A starting dose of 5–10 mg/cat PO q12h is recommended.
- Mitotane (Lysodren®; o,p'-DDD) is not recommended for treatment of FCS.
- Other medications have limited efficacy (ketoconazole, metyrapone, and amino-glutethimide).

FOLLOW-UP

- Clinical improvement and improved diabetic control are indicative of successful drug therapy.
- ACTH stimulation tests are recommended for dose adjustments of trilostane.

H



MISCELLANEOUS

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- AT = adrenal tumor.
- DM = diabetes mellitus.
- FCS = feline Cushing's syndrome.
- PDH = pituitary-dependent hyperadrenocorticism.
- UC : Cr = urine cortisol : creatinine.

Suggested Reading

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Acknowledgment The author and book editors acknowledge the prior contribution of Deirdre Chiaramonte.

HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS



BASICS

DEFINITION

- Spontaneous hyperadrenocorticism (HAC)—disorder due to excessive production of cortisol by adrenal cortex.
- Iatrogenic HAC—from excessive exogenous administration of glucocorticoids by any route.
- Clinical signs due to effects of elevated circulating glucocorticoid concentrations.

PATHOPHYSIOLOGY

- ~80–85% of cases of naturally occurring HAC due to bilateral adrenocortical hyperplasia resulting from pituitary corticotroph adenoma or hyperplasia with oversecretion of adrenocortotropic hormone (ACTH).
- In remaining 15–20%, cortisol-secreting adrenocortical neoplasia (AN) present; ~50% malignant.
- Rarely caused by ectopic ACTH secretion from nonpituitary tumor.
- One case of food-dependent hypercortisolemia reported, with increased cortisol concentration after meal; likely due to aberrant gastric inhibitory peptide receptors stimulating adrenal steroidogenesis.
- Iatrogenic HAC from excessive administration of exogenous glucocorticoids.

SYSTEMS AFFECTED

- Variable.
- Signs referable to urinary tract or skin common.
- Skin—bilaterally symmetric alopecia, comedones, hyperpigmentation, recurrent pyoderma.
- Renal/urologic—polyuria/polydipsia (PU/PD; 85–90% of cases), proteinuria, urinary tract infections (UTIs).
- Endocrine/metabolic—hyperglycemia; diabetes mellitus (DM) in 10%.
- Cardiovascular—hypertension (usually mild).
- Gastrointestinal—polyphagia.
- Hemic/lymphatic/immune—stress leukogram, immunosuppression, mild erythrocytosis and thrombocytosis, occasional nucleated red blood cells.
- Hepatobiliary—hepatopathy due to glycogen deposition, increased serum alkaline phosphatase (ALP) activity due to corticosteroid-induced isoenzyme; alanine aminotransferase (ALT) activity also increased, but by less.
- Neuromuscular—muscle weakness; CNS signs from macroadenoma may include anorexia, abnormal mentation, blindness, rarely seizures.
- Reproductive—testicular atrophy, anestrus.
- Respiratory—panting, pulmonary thromboembolism possible.

INCIDENCE/PREVALENCE

One of most common endocrine disorders in dogs.

SIGNALMENT

Species

Dog

Breed Predilections

Poodle, dachshund, Boston terrier, German shepherd dog, beagle.

Mean Age and Range

Generally, middle-aged to older animals; pituitary-dependent HAC (PDH) rarely seen in dogs as young as 1 year.

SIGNS

General Comments

- Severity varies greatly, depending on duration and extent of cortisol excess.
- In some cases physical presence of neoplastic process (pituitary or adrenal) contributes to illness.

Historical and Physical Examination Findings

PU/PD, polyphagia, pendulous abdomen, increased panting, hepatomegaly, hair loss, cutaneous hyperpigmentation, thin skin, muscle weakness, obesity, lethargy, muscle atrophy, comedones, bruising, testicular atrophy, anestrus, calcinosis cutis, facial nerve palsy.

CAUSES

- PDH—adenoma most common; adenocarcinomas rare; anterior pituitary involved in ~80% of cases, intermediate lobe in remainder; exact incidence of pituitary macroadenomas (tumors >1 cm diameter) unknown, may be 10–25%.
- AN—adenoma or carcinoma (50%).
- Ectopic ACTH secretion and food-dependent hypercortisolism—rare.
- Iatrogenic—due to glucocorticoid administration.

RISK FACTORS

- None known for spontaneous disease.
- Administration of exogenous glucocorticoids (risk for iatrogenic HAC).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Depends on clinical and laboratory abnormalities.
- Hypothyroidism, sex hormone dermatoses, alopecia X, sex hormone–secreting tumors, acromegaly, DM, hepatopathies, renal disease, other causes of PU/PD.
- Cortisol can decrease concentration of total T₄; important to check for HAC in dogs with weight gain or dermatologic disease that could be misdiagnosed as hypothyroidism.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram may show eosinopenia, lymphopenia, leukocytosis, neutrophilia, erythrocytosis, thrombocytosis.

- Serum chemistry may show elevated cholesterol concentration; ALP activity high in ~85–90% and elevations proportionately greater than for ALT.

- Mild hyperglycemia common but only ~10% of dogs with HAC have concurrent DM.
- Urinalysis may reveal low specific gravity, proteinuria, hematuria, pyuria, and/or bacteriuria.

OTHER LABORATORY TESTS

- Endocrine testing required in dogs with history, clinical signs, and laboratory abnormalities suggestive of HAC; see Appendix II.
- Do not perform HAC testing in sick dogs unless clinical signs consistent with HAC.
- Screening tests determine if HAC present or not.
- Once diagnosis of HAC made, perform differentiation test to determine if PDH or AN present; differentiation crucial for therapeutic decisions and prognosis.
- To convert cortisol concentration in nmol/L to µg/dL, divide by 27.6.
- All cortisol concentrations below for illustration; normal ranges and cut-off values vary with lab.

Screening Tests

Urine Cortisol : Creatinine Ratio (UC : Cr)

- Urine cortisol excretion increases with augmented adrenal secretion of cortisol, whether due to PDH or AN.
- Should be measured in urine sample collected at home when pet not stressed.
- Elevated UC : Cr is sensitive marker of HAC, present in 90–100% of affected dogs; normal ratio makes diagnosis of HAC very unlikely.
- False-positive results common; only ~20% of dogs with elevated UC : Cr have HAC.
- Due to chance of false-positive, always do ACTH stimulation test or low-dose dexamethasone suppression test to confirm presence of HAC.

Low-Dose Dexamethasone Suppression Test (LDDST)

- Lack of suppression 8h after injection of low dose of dexamethasone consistent with diagnosis of HAC.
- Sensitivity ~95% in dogs.
- In dogs with nonadrenal illness, relatively high chance of false-positive.
- Lack of suppression at 4h but full suppression at 8h technically not consistent with HAC, but suspicious for its presence; further testing warranted.
- LDDST may also serve as differentiation test; if 8h sample >1.4 µg/dL, result consistent with HAC; if also suppression to <1.4 µg/dL at 4h post dexamethasone (i.e., “escape” at 8h post dexamethasone) or 4h and/or 8h post-dexamethasone samples <50% of baseline, results consistent with

(CONTINUED)

HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS

PDH; if criteria for PDH not met, chances still ~½ for PDH vs. AN.

- If baseline values close to 1.4 µg/dL or suppression just at 50%, confirm presence of PDH by other means.
- Protocol exists in Utrecht, Netherlands, where min 2 morning urine samples collected and then dexamethasone administered (3 doses over 24h) for differentiating purposes and another urine sample collected; protocol reportedly has high sensitivity and specificity, but urinary cortisol assay proprietary and not commercially available; accuracy of protocol using cortisol assays commercially available in United States not established, so method not recommended in North America.

ACTH Stimulation Test

- Response > normal consistent with diagnosis of spontaneous HAC, but cannot differentiate between PDH and AN.
- Overall sensitivity of test ~80%; for PDH, sensitivity ~87%; for HAC due to AN sensitivity ~61%.
- More specific in dogs than LDDST (only 15% chance of false-positive with nonadrenal illness).
- Only test that can diagnose iatrogenic HAC; diagnosis made with history of glucocorticoid exposure by any route, consistent clinical signs, and post-ACTH cortisol concentration < reference range.
- Cosyntropin (or tetracosactrin) recommended form; if using compounded ACTH, collect samples before and at 1h and 2h post ACTH administration so peak response not missed.

Differentiating Tests***High-Dose Dexamethasone Suppression Test (HDDST)***

- Two responses consistent with PDH—suppression to <1.4 µg/dL at 4h and/or 8h post dexamethasone; or 4h and/or 8h post-dexamethasone samples <50% of baseline.
- If baseline values close to 1.4 µg/dL or suppression just at 50%, confirm presence of PDH by other means.
- Can never confirm presence of AN; if criteria for diagnosis of PDH not met, 50/50 chance patient has PDH or AN; since HDDST does not significantly increase ability to differentiate PDH from AN, endogenous ACTH (eACTH) and/or abdominal US used instead.

eACTH Concentration

- Requires only single blood sample, but inappropriate handling can lead to decreased eACTH concentrations due to degradation.
- In patients with PDH, eACTH concentration usually normal to increased; with AN, eACTH concentration < normal.
- If concentration increased, consistent with PDH, but due to episodic secretion of ACTH

even in patients with PDH, low value does not always confirm AN.

- If eACTH concentration falls in gray zone, results not diagnostic.

IMAGING

- Abdominal radiographs—~40–50% of canine ANs seen; adrenal mineralization suspicious for AN.
- Thoracic radiographs indicated in patients with AN to check for metastases.
- US—useful for staging AN, but poor screening test (adrenal enlargement occurs with chronic nonadrenal illness, AN may be difficult to see with US); adrenal atrophy can be difficult to determine with US, but bilaterally enlarged adrenal glands consistent with PDH; vena caval invasion and metastasis may be present with AN.
- CT and MRI—can show pituitary macroadenomas and assess AN invasion into adjacent structures; follow-up and treatment recommendations (e.g., radiation therapy) may vary with tumor size.

DIAGNOSTIC PROCEDURES

Adrenal histopathology following adrenalectomy for AN often needed to differentiate benign vs. malignant tumor; biopsy prior to removal may result in complications.

PATHOLOGIC FINDINGS

- PDH—normal to enlarged pituitary and bilateral adrenocortical enlargement.
- Microscopically, pituitary adenoma, adeno-carcinoma, or corticotroph hyperplasia of pars distalis or pars intermedia and adrenocortical hyperplasia.
- AN—variable-sized adrenal mass, atrophy of contralateral gland (rarely bilateral tumors), metastasis and invasion into vena cava with thrombosis possible.
- Microscopically, adrenocortical adenoma or carcinoma.

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

Dictated by severity of clinical signs, patient's overall condition, any complicating factors (e.g., DM, pulmonary thromboembolism).

CLIENT EDUCATION

- For medical therapy, lifelong therapy required.
- If adverse reaction to mitotane or trilostane occurs—discontinue drug, give dexamethasone, have veterinarian reevaluate next day; if no response noted in few hours, veterinarian should evaluate immediately.

SURGICAL CONSIDERATIONS

- Hypophysectomy—described, but limited availability.
- Bilateral adrenalectomy not used for treatment of PDH.

• Surgery treatment of choice in dogs with adrenocortical adenomas and carcinomas unless patient poor surgical candidate.

- Appropriate personnel and facilities required as adrenalectomy (especially with vena caval thrombi) is technically demanding and intensive postoperative management required.
- Surgery not curative, but long-term survival possible
- Medical control of HAC may be desirable prior to surgery.

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

- Trilostane (Vetoryl®) inhibits adrenocortical enzyme 3-β-hydroxysteroid dehydrogenase and maybe others, thereby suppressing production of progesterone and its end-products, including cortisol and aldosterone (less than cortisol); efficacy and survival time for treatment of PDH excellent.

- Initial dose 2–3 mg/kg PO q24h (in morning) or divided q12h with food; twice-daily dosing more expensive, but quicker resolution of clinical signs, fewer dose changes and monitoring tests; if q24h dosing elected and patient controlled during day but has more clinical signs at night, splitting daily dose ½ morning and ½ evening may improve clinical signs.

- Side effects include lethargy, decreased appetite, vomiting, diarrhea; sometimes occur within first few days of therapy and associated with gastrointestinal upset due to administration of oral medication; hypocortisolism can also occur due to oversuppression of cortisol production and cause same clinical signs; rarely, idiosyncratic adrenal necrosis with hypocortisolism and hypoadosteronism, but less common with lower doses (as recommended above).

- Monitoring—primary goals to control clinical signs and avoid complications (especially hypocortisolism); should include assessment of clinical signs (PU/PD, polyphagia, panting) and cortisol testing (see below) to ensure cortisol not suppressed excessively; obtaining detailed history and evidence of potential oversuppression of cortisol imperative.

- Historically, ACTH stimulation test used to monitor trilostane therapy, 4–6h post trilostane administration; 1 µg/kg cosyntropin IV effective for monitoring, but not for diagnosis (must use 5 µg/kg); ideal post-ACTH cortisol concentration 2–6 µg/dL, but must consider clinical signs; e.g., if patient clinically controlled with post-ACTH cortisol of 7.2 µg/dL, no need to increase dose; if clinical signs persist, dose increase recommended.

HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS (CONTINUED)

H

- Studies show post-ACTH stimulation cortisol values do not always correlate well with clinical signs; measuring cortisol concentration before morning dose of trilostane may correlate better; assessing clinical signs imperative when using pre-pill cortisol concentration for monitoring; if patient showing signs of hypocortisolism (vomiting, diarrhea, decreased appetite), must use ACTH stimulation test; data lacking on decision-making using pre-pill cortisol, but some guidelines: cortisol concentration used to confirm patient not cortisol deficient ($<1.4\text{--}2 \mu\text{g/dL}$), clinical signs used to determine whether dose adequate; if patient clinically controlled and cortisol $2\text{--}6 \mu\text{g/dL}$, appropriate to continue current dose; if $<2 \mu\text{g/dL}$, perform ACTH stimulation test or decrease dose; if patient still clinical (PU/PD, polyphagia, panting) and pre-pill cortisol $>6 \mu\text{g/dL}$, safe to increase dose; in clinically uncontrolled patient, cortisol concentration $2\text{--}6 \mu\text{g/dL}$ is gray zone: probably safe to increase dose if pre-pill cortisol $5 \mu\text{g/dL}$, but probably not at $2.5 \mu\text{g/dL}$; perform ACTH stimulation test in this situation.
- Perform either ACTH stimulation test or pre-pill cortisol at 10–14 days, 30 days, and 90 days after each dose change; if at 10–14-day recheck any improvement seen, do not increase dose even if cortisol concentration above ideal; wait until 30-day recheck and change dose then if necessary, as effect of trilostane often increases between 2 and 4 weeks; assess renal profile, including electrolytes, at 14- or 30-day exam; once clinical condition and dose stabilized, perform pre-pill cortisol or ACTH stimulation test, and electrolyte panel, q3–6 months.
- If lethargy, decreased appetite, vomiting, or diarrhea occurs, ACTH stimulation test to confirm dog not hypocortisolemic (post-ACTH stimulation cortisol $<2 \mu\text{g/dL}$); if hypocortisolism confirmed, assess electrolyte panel to ensure hyponatremia and hyperkalemia not present; discontinue trilostane until clinical signs of HAC recur and baseline and/or post-ACTH cortisol concentrations $>5\text{--}6 \mu\text{g/dL}$.
- If signs of hypocortisolism more severe than mild lethargy, vomiting, decreased appetite, give dexamethasone $0.1 \text{ mg/kg/day PO/IV}$, then taper to lowest effective dose to control signs; if signs of HAC recur, taper dexamethasone and discontinue, then perform baseline cortisol and/or ACTH stimulation test interpreted as above; if dexamethasone unavailable and prednisone used instead, delay cortisol testing until at least 24h after last prednisone dose, as prednisone can cross-react with cortisol assay.
- If more severe signs occur, hospitalization with IV fluids, dexamethasone, and other supportive therapy necessary.
- Hypocortisolism secondary to trilostane administration usually resolves within 48–72h

of drug discontinuation, but temporary cortisol suppression of weeks to months and even permanent suppression can occur.

- Trilostane can be used to treat hypercortisolism from AN and usually controls clinical signs; although mitotane theoretically preferred due to chemotherapeutic properties, no difference shown between survival of patients with AN treated with mitotane or trilostane.

Mitotane

- Mitotane (o,p'-DDD, Lysodren[®]) selectively destroys glucocorticoid-secreting cells of adrenal cortex; in patients with AN may destroy tumor cells as well as controlling cortisol secretion, but no difference in survival between dogs with AN receiving mitotane vs. trilostane.
- PDH—initial loading dose $40\text{--}50 \text{ mg/kg PO}$ divided twice daily; evaluate efficacy with ACTH stimulation test after 8 days, or sooner if decreased appetite, vomiting, diarrhea, listlessness, decreased water intake ($<60 \text{ mL/kg/day}$); target for both basal and post-ACTH cortisol concentration $1\text{--}5 \mu\text{g/dL}$; continue induction with repeat testing as necessary until adequate response, then initiate maintenance therapy at 50 mg/kg/week PO divided in 2–3 doses; adjust dosage based on ACTH stimulation testing (to maintain basal and post-ACTH cortisol levels in ideal range); if serum cortisol concentration pre- or post-ACTH $<1 \mu\text{g/dL}$, measure electrolyte concentrations, stop administering mitotane, and give physiologic doses of prednisone ($0.1 \text{ mg/kg PO q12h}$; do not give within 24h before ACTH stimulation test); cortisol secretion usually recovers in weeks to months but can take longer; once cortisol concentration in ideal range, discontinue prednisone and begin maintenance therapy; if dog was on maintenance therapy when became cortisol deficient, restart maintenance at 25% lower dose; if relapse occurs at any time on maintenance therapy (as indicated by cortisol levels above ideal range), dose adjustment required; if post-ACTH serum cortisol concentration $5\text{--}10 \mu\text{g/dL}$, increase maintenance mitotane dose by 25% and reevaluate in 4 weeks; if post-ACTH serum cortisol concentration $>10 \mu\text{g/dL}$, repeat loading sequence for 5–7 days and repeat ACTH stimulation test; continue loading until cortisol concentration in ideal range, then reinitiate weekly maintenance dose at $\sim 50\%$ higher dose.
- AN—goal of mitotane to achieve low to nondetectable ($<1 \mu\text{g/dL}$) basal and post-ACTH cortisol concentrations; starting dose $50\text{--}75 \text{ mg/kg PO divided daily}$; perform ACTH stimulation test after 10–14 days of therapy to evaluate efficacy, sooner if decreased appetite, vomiting, diarrhea,

lethargy, decreased water intake ($<60 \text{ mL/kg/day}$); induction typically requires higher doses and longer duration than for treatment of PDH and dose should be increased by $50 \text{ mg/kg/day q10\text{--}14 days}$ if control not achieved (based on ACTH stimulation test); if adverse effects develop, continue administration at highest tolerable dose; once control achieved, begin maintenance therapy at $75\text{--}100 \text{ mg/kg/week PO}$ divided into 2–3 doses; if cortisol levels pre- and post-ACTH rise into normal resting range ($1\text{--}5 \mu\text{g/dL}$), increase maintenance dose by 50%; if cortisol levels rise above normal resting range pre- and post-ACTH, reload until control achieved and increase weekly maintenance dose $\sim 50\%$; because goal of induction and maintenance is to create glucocorticoid insufficiency, prednisone should be administered at 0.2 mg/kg/day PO .

- Aldosterone deficiency possible from mitotane therapy; if it occurs, patient will likely have permanent complete adrenocortical insufficiency and treatment for hypoadrenocorticism should be initiated.

I-Deprenyl

- I-Deprenyl (selegiline hydrochloride); FDA approved for treatment of PDH; decreases pituitary ACTH secretion, thus decreasing serum cortisol concentration.
- Questionable efficacy; not currently recommended.

Ketoconazole

Ketoconazole (10 mg/kg PO q12h initially; up to 20 mg/kg PO q12h in some dogs) inhibits cortisol synthesis; no longer recommended (trilostane causes fewer side effects).

CONTRAINdications

- Do not use ketoconazole with trilostane therapy (increased potential for hypocortisolism).
- Monitor for hyperkalemia if concurrent angiotensin-converting enzyme inhibitor therapy.

PRECAUTIONS

- Side effects of trilostane include anorexia, lethargy, vomiting, diarrhea; usually mild and resolve with discontinuation and dose adjustment; Addisonian crisis and adrenocortical necrosis reported.
- Use trilostane and mitotane with caution in patients with renal insufficiency and hepatic disease; trilostane contraindicated in pregnancy.
- Side effects of mitotane mild in most dogs; include lethargy, anorexia, vomiting, diarrhea, ataxia, iatrogenic hypoadrenocorticism.
- Side effects more common in dogs with AN given high dose mitotane.
- In diabetic patients, insulin requirement can decrease with control of HAC.

(CONTINUED) **HYPERADRENOCORTICISM (CUSHING'S SYNDROME)—DOGS****ALTERNATIVE DRUG(S)**

Radiation therapy possible to treat pituitary macroadenomas. Treatment with trilostane or mitotane still usually required afterwards. ACTH levels may take several months to decrease and HAC controlled with drugs in interim.

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

- Response to therapy—use periodic ACTH stimulation and/or cortisol testing to assess trilostane and mitotane efficacy (see above); once on maintenance mitotane therapy, test at 1, 3, and 6 months and q3–6 months thereafter or if clinical signs of HAC recur.
- Adequacy of any mitotane reloading period checked with ACTH stimulation test before higher maintenance dose initiated.
- Adequacy of trilostane dose alterations checked with ACTH stimulation test performed 4–6h after dosing.

PREVENTION/AVOIDANCE

For prevention of recurrence and hypocortisolism, regular administration of medications with appropriate follow-up required.

POSSIBLE COMPLICATIONS

- Hypertension.
- Proteinuria.
- Recurrent infections.
- Urinary calculi (calcium oxalate).
- DM.
- Pulmonary thromboembolism.
- Neurologic signs secondary to pituitary macroadenoma.
- Hypoadrenocorticism secondary to treatment.

EXPECTED COURSE AND PROGNOSIS

- Untreated HAC—progressive disorder with survival of 6–18 months.

- Treated PDH—usually good prognosis; median survival time with mitotane or trilostane treatment ~2 years; at least 10% survive 4 years; dogs living >6 months tend to die of causes unrelated to HAC.

- Macroadenomas in animals with no or mild neurologic abnormalities have fair to good prognosis with radiation and medical therapy; in patients with significant neurologic abnormalities, prognosis poor to grave.
- Adrenal adenomas—usually good to excellent prognosis; small carcinomas (not metastasized) fair to good prognosis overall, good to excellent with surgical resection.
- Large carcinomas and AN with widespread metastasis—generally poor to fair prognosis, but impressive responses to high doses of mitotane occasionally seen.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Neurologic signs in dogs with pituitary tumors; glucose intolerance or concurrent DM; pulmonary thromboembolism; increased incidence of infections, especially UTI and skin; hypertension; proteinuria/glomerulopathy.

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone.
- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- AN = adrenal neoplasia.
- DM = diabetes mellitus.
- eACTH = endogenous ACTH.
- HAC = hyperadrenocorticism.
- HDDST = high-dose dexamethasone-suppression test.
- LDDST = low-dose dexamethasone-suppression test.
- PDH = pituitary-dependent HAC.

- PU/PD = polyuria/polydipsia.
- UC : Cr = urine cortisol : creatinine.
- UTI = urinary tract infection.

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Author Patty A. Lathan

Consulting Editor Patty A. Lathan

Acknowledgment The author and book editors acknowledge the prior contribution of Deborah S. Greco



Client Education Handout available online

(CONTINUED)

HYPERCALCEMIA

- Serum Vitamin D assays are available at specific laboratories.
- Fecal PCR testing for schistosomiasis.

IMAGING

- Radiography is useful for assessing renal size and shape, urolithiasis, bone lysis, pulmonary infiltration, lymphadenomegaly, and occult neoplasia.
- Ultrasonography is valuable for assessing renal architecture, abdominal lymphadenomegaly, parathyroid tumors, and urolithiasis.

DIAGNOSTIC PROCEDURES

- Cytologic examination of fine-needle aspirate of lymph nodes, liver, spleen, anal glands, or other tumors or masses to diagnose neoplasia.
- Bone marrow aspirate or biopsy—to identify occult hematopoietic neoplasia.
- Adrenocorticotrophic hormone (ACTH) stimulation testing to confirm hypoadrenocorticism.

**TREATMENT**

- Definitive treatment of hypercalcemia is achieved by identification and correction of the primary cause.
- Inpatient care may be necessary because of the deleterious effects of hypercalcemia and the need for fluid therapy (diuresis).
- Consider severe hypercalcemia (ionized calcium >2.2 mmol/L) a medical emergency.

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

- Normal saline—fluid of choice (sodium promotes calcium excretion).
- Diuretics (furosemide) and corticosteroids promote calcuressis.
- Pamidronate or other bisphosphonate drugs (e.g., alendronate) have been used successfully for treatment of hypercalcemia of various causes in dogs and cats.

CONTRAINDICATIONS

- Do not use glucocorticoids until the diagnosis of lymphoma or other round cell neoplasia is excluded; they can obfuscate the diagnosis; if hypoadrenocorticism is suspected, do not give glucocorticoids until after ACTH stimulation testing, or use

dexamethasone, which will not interfere with the serum cortisol assay.

- Thiazide diuretics can cause calcium retention.
- Oral bisphosphonates can cause esophageal erosions and should be used with caution.

PRECAUTIONS

Do not give diuretics to a dehydrated patient.

POSSIBLE INTERACTIONS

Avoid the use of calcium or phosphorus-containing compounds; they can cause soft tissue mineralization in severely hypercalcemic and hyperphosphatemic patients.

ALTERNATIVE DRUG(S)

- Sodium bicarbonate (1–4 mEq/kg) may be useful in combination with other treatments when metabolic acidosis is present.
- Calcitonin may be useful in the treatment of hypervitaminosis D.
- Hemodialysis and peritoneal dialysis are alternative treatments for some causes of hypercalcemia, but cost and availability limit their use.
- Novel therapies like calcimimetic drugs may hold potential for certain causes of hypercalcemia such as idiopathic hypercalcemia or primary hyperparathyroidism; cost is currently a deterrent, as is lack of routine efficacy.
- Mithramycin has been used in severe hypercalcemic crises; avoid its use because of associated nephrotoxicity and hepatotoxicity.

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

- Serum calcium every 12 hours (ionized calcium if possible).
- Renal function assessment—the first sign of tubular damage may be casts in the urine sediment.
- Must closely monitor urine output, particularly if oligo-anuric renal failure is present.
- Hydration status must be monitored; indicators of overhydration include increased bodyweight, chemosis, and edema (pulmonary or subcutaneous).

POSSIBLE COMPLICATIONS

- Irreversible renal failure.
- Soft tissue mineralization.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Calcium-containing urolithiasis.

AGE-RELATED FACTORS

- Mild elevations in calcium and phosphorus may be normal in growing animals.
- Middle-aged and older dogs and cats are at increased risk for cancer.

PREGNANCY/FERTILITY/BREEDING

A fetus is at the same risk as the dam; do not alter treatment because of pregnancy.

SEE ALSO

- Acute Kidney Injury.
- Chronic Kidney Disease.
- Hyperparathyroidism.
- Lymphoma—Dogs.
- Paraneoplastic Syndromes.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- PTH = parathyroid hormone.
- PTH-rp = parathyroid hormone-related peptide.
- PU/PD = polyuria/polydipsia.

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Acknowledgment The author and book editors acknowledge the prior contribution of Thomas K. Graves



**Client Education Handout
available online**

H HYPERGLYCEMIA

OTHER LABORATORY TESTS

- Fructosamine concentration identifies degree of glycemia over the previous 2–3 weeks; results are assay dependent and may be affected by hemolysis or lipemia; provides no information on variability of BG concentrations.
- Glycosylated hemoglobin concentration identifies degree of glycemia over the previous 10 weeks (cats) or 16 weeks (dogs); provides no information on variability of BG concentrations.
- Adrenocorticotropic hormone (ACTH) stimulation test or low-dose dexamethasone-suppression test to diagnose hyperadrenocorticism in dogs; false-positive results might be obtained if there is poor diabetic control.
- Serum insulin-like growth factor 1 (IGF-1) assay to diagnose hypersomatotropism in cats; false-negative results are more likely when there is severe insulin deficiency; cats should be treated with insulin for 4–6 weeks prior to testing.



TREATMENT

APPROPRIATE HEALTH CARE

- Stress hyperglycemia is self-limiting.
- Diabetic cats and dogs that are eating well—outpatient management.
- Those that are unwell, inappetent, or have other signs such as vomiting require inpatient management with insulin and IV fluids.
- Concurrent disease can compromise DM management and should be promptly diagnosed and treated.

NURSING CARE

Glucose monitoring is recommended for all hospitalized hyperglycemic patients. Venous or capillary blood testing using a veterinary glucometer is appropriate. Real-time continuous glucose monitoring systems (CGMS) or flash glucose monitoring systems (FGMS) can simplify glucose monitoring of hospitalized patients.

ACTIVITY

Activity does not need to be limited in dogs and cats with DM and may decrease insulin requirement in working diabetic dogs.

DIET

- See relevant chapters on DM.
- Nutritional requirements for concurrent diseases take precedence over nutritional requirements for DM; good diabetic control can be achieved with insulin treatment regardless of diet.

CLIENT EDUCATION

- Client education is critical, because most treatment and monitoring of a diabetic patient will be done by the owner at home, and clinical signs will guide treatment decisions.
- Owner concerns relating to the impact that treating their pet will have on their lifestyle should be addressed.

SURGICAL CONSIDERATIONS

- Approximately 8% chance of diabetic remission following neutering and insulin therapy in female dogs; those that do not achieve remission generally have improved diabetic control.
- Improved diabetic control and possibly remission will occur following hypophysectomy in cats with hypersomatotropism; however, this treatment is expensive with limited availability.



MEDICATIONS

DRUG(S) OF CHOICE

- Exogenous insulin is the mainstay of treatment of DM.
- See chapters on DM.

PRECAUTIONS

- See chapters on DM.
- Drugs that cause insulin resistance (e.g., systemic or topical corticosteroids) should be used with caution in hyperglycemic animals; an increased insulin dose may be necessary.

POSSIBLE INTERACTIONS

Concurrent use of insulin and oral hypoglycemic agents might lead to hypoglycemia.

ALTERNATIVE DRUG(S)

- Glipizide and acarbose.
- See chapters on DM.



FOLLOW-UP

PATIENT MONITORING

- See chapters on DM.
- Animals in diabetic remission require ongoing monitoring for recurrence of hyperglycemia.

PREVENTION/AVOIDANCE

- Minimize use of diabetogenic drugs, particularly in susceptible individuals.
- Prevent obesity in cats and intact female dogs.
- Neuter female dogs at risk of developing DM.

POSSIBLE COMPLICATIONS

- Severe hyperglycemia may be associated with CNS depression and coma because of hyperosmolality.
- Diabetic cataracts (dogs).
- Diabetic neuropathy in cats with poor diabetic control.
- Insulin-induced hypoglycemia.

EXPECTED COURSE AND PROGNOSIS

- Transient stress hyperglycemia is self-limiting.
- Treatment of DM often is associated with an excellent prognosis, and typically results in a very good quality of life and similar life expectancy to animals without diabetes.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hyperosmolality.
- Diabetic ketoacidosis.
- Hyperadrenocorticism.
- Hypersomatotropism.
- Pancreatitis.

PREGNANCY/FERTILITY/BREEDING

- In intact bitches, a form of diabetes analogous to human gestational diabetes can occur during diestrus or pregnancy; if insulin therapy is initiated promptly, diabetic remission can sometimes be achieved following spay or whelping.
- Increased incidence of dystocia (large fetal size) and hypoglycemia in neonates when hyperglycemia has been present during pregnancy.

SYNONYMS

High blood sugar.

SEE ALSO

- Diabetes Mellitus with Ketoacidosis.
- Diabetes Mellitus Without Complication—Cats.
- Diabetes Mellitus Without Complication—Dogs.
- Hyperosmolality.

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone.
- BG = blood glucose.
- CGMS = continuous glucose monitoring system.
- DM = diabetes mellitus.
- FGMS = flash glucose monitoring system.
- IGF-1 = insulin-like growth factor 1.
- PU = polyuria.

INTERNET RESOURCES

<https://esve.org/alive/search.aspx>

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(CONTINUED)

HYPERLIPIDEMIA



BASICS

DEFINITION

- Increased concentration of lipid in the blood of a fasted (>12 hours) patient; includes hypercholesterolemia, hypertriglyceridemia, or both.
- Lipemia—serum or plasma separated from blood that contains an excess concentration of triglycerides (>200 mg/dL).
- Lactescence—opaque, milk-like appearance of serum or plasma that contains an even higher concentration of triglycerides (>1,000 mg/dL) than lipemic serum.

PATOPHYSIOLOGY

Primary Hyperlipidemia

- Primary (idiopathic) hyperlipidemia—defect in lipid metabolism causing hypertriglyceridemia with or without hyperchylomicronemia; likely hereditary in miniature schnauzer, but the genetic defect has yet to be determined.
- Idiopathic hyperchylomicronemia in cats—familial, autosomal recessive defect in lipoprotein lipase activity.
- Primary hypercholesterolemia—occurs in some families of briard, rough collie, Shetland sheepdog, Doberman pinscher, and Rottweiler; low-density lipoprotein (LDL) cholesterol is high.

Secondary Hyperlipidemia

- Postprandial—absorption of chylomicrons from the gastrointestinal tract occurs 30–60 minutes after ingestion of a meal containing fat; may increase serum triglycerides for up to 12 hours.
- Diabetes mellitus—low lipoprotein lipase (LPL) activity; high synthesis of very-low-density lipoprotein (VLDL) by the liver.
- Hypothyroidism—low LPL activity and lipolytic activity by other hormones (e.g., catecholamines); reduced hepatic degradation of cholesterol to bile acids.
- Hyperadrenocorticism—increased synthesis of VLDL by the liver and low LPL activity causes both hypercholesterolemia and hypertriglyceridemia.
- Cholestatic liver disease—hypercholesterolemia caused by reduced excretion of cholesterol in the bile.
- Nephrotic syndrome—upregulation of common synthetic pathway for albumin and cholesterol and possibly low oncotic pressure lead to increased cholesterol synthesis.
- Pancreatitis—associated with hypertriglyceridemia in dogs, especially miniature schnauzers.
- Obesity—excessive hepatic synthesis of VLDL.

Drug-Induced Hyperlipidemia

- Glucocorticoids.

- Megestrol acetate (cat).

SYSTEMS AFFECTED

- Endocrine/metabolic.
- Gastrointestinal.
- Hepatobiliary.
- Nervous.
- Ophthalmic.

SIGNALMENT

- Dog and cat.
- Variable, depending on the cause.
- Hereditary hyperlipidemias—age of onset is >8 months in cats and >4 years in predisposed breeds of dog such as the miniature schnauzer.

SIGNS

Historical Findings

- Asymptomatic.
- Recent ingestion of a meal.
- Seizures, neurologic signs.
- Abdominal pain and distress.
- Neuropathies.

Physical Examination Findings

- Lipemia retinalis.
- Lipemic aqueous.
- Neuropathy.
- Cutaneous xanthomata.
- Lipid granulomas in abdominal organs.

CAUSES

Increased Absorption of Triglycerides or Cholesterol

Postprandial

Increased Production of Triglycerides or Cholesterol

- Idiopathic.
- Nephrotic syndrome.
- Pregnancy.
- Defects in lipid clearance enzymes or lipid carrier proteins.
- Idiopathic hyperchylomicronemia.
- Hyperchylomicronemia in cats.

Decreased Clearance of Triglycerides or Cholesterol

- Hypothyroidism.
- Hyperadrenocorticism.
- Diabetes mellitus.
- Pancreatitis.
- Cholestasis.

RISK FACTORS

- Obesity.
- High dietary intake of fats.
- Genetic predisposition in miniature schnauzer and Himalayan cat.
- Idiopathic hypercholesterolemia observed in families of briard, rough collie, Shetland sheepdog, Doberman pinscher, and Rottweiler.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Fasting Hyperlipidemia

Rule out postprandial lipemia with a 12-hour fast.

Primary Hyperlipoproteinemia

- Idiopathic hyperlipidemia is observed most commonly in the miniature schnauzer breed.
- Hyperchylomicronemia in cats often manifests as polyneuropathies and lipogranulomas.
- Idiopathic hypercholesterolemia is observed in a variety of breeds; animals are often asymptomatic.

H

Secondary Hyperlipidemia

- Diabetes mellitus.
- Hypothyroidism.
- Pancreatitis.
- Hyperadrenocorticism.
- Hepatic disease and cholestatic disorders.
- Nephrotic syndrome.

LABORATORY FINDINGS

Sample Handling

- Submit serum.
- Lipemia causes hemolysis if serum remains with red blood cells for a long time; inquire about the laboratory method of clearing lipemic samples before submission.
- Two samples may be submitted—one for biochemical analysis, which may be cleared, and one for triglycerides and cholesterol concentrations.

Drugs That May Alter Laboratory Results

- Corticosteroids.
- Phenytoin.
- Prochlorperazine.
- Thiazides.
- Phenothiazines.

Disorders That May Alter Laboratory Results

- Falsely high cholesterol.
- Nonfasted samples (<12 hours).
- Icterus—spectrophotometric techniques.
- Fluoride and oxalate anticoagulants—enzymatic techniques.
- Lipemia.

Valid If Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Results of hemogram usually normal.
- High serum triglyceride concentration—dogs: >150 mg/dL; cats: >100 mg/dL.
- High serum cholesterol concentration—dogs: >300 mg/dL; cats: >200 mg/dL.
- Serum biochemistry may reveal abnormalities consistent with causes of secondary hyperlipidemia.

HYPERLIPIDEMIA

(CONTINUED)

- Results of urinalysis often normal; proteinuria if nephrotic syndrome present.

OTHER LABORATORY TESTS

- High-density lipoprotein (HDL) and LDL determinations—used in human medicine; values reported for HDL and LDL in dogs and cats cannot be assumed to be reliable.
- Chylomicron test—obtain serum sample after a 12-hour fast and refrigerate for 12–14 hours; do not freeze; chylomicrons rise to the surface and form a creamy layer.
- Lipoprotein electrophoresis—separates LDL, VLDL, and HDL1 and HDL2 subfractions.
- LPL activity—collect serum for triglycerides and cholesterol concentrations and lipoprotein electrophoresis before and 15 minutes after administration of heparin (90 IU/kg, IV); if there is no change in values before and after heparin administration, a defective LPL enzyme system should be suspected.
- Definitive diagnostics for hypothyroidism or hyperadrenocorticism, if suspected.



TREATMENT

Diet should contain <10% fat (e.g., Royal Canin® Low Fat; Hill's Prescription Diet r/d®, w/d®, and i/d® Low Fat; Purina® OM).



MEDICATIONS

DRUG(S) OF CHOICE

Initial management is dietary; omega-3 fatty acids, fibrates, and then niacin are added to refractory cases.

ALTERNATIVE DRUG(S)

- Gemfibrozil 10 mg/kg PO q12h; cats and dogs.
- Bezafibrate 4–10 mg/kg PO q12h; dogs only.

- Fish oils—omega-3 polyunsaturated fat 50–300 mg/kg PO q24h; dogs only.
- Niacin 50–200 mg/dog/day PO (slow release); dogs only.



FOLLOW-UP

PATIENT MONITORING

- Keep serum triglyceride concentrations <500 mg/dL to avoid possibly fatal episodes of acute pancreatitis.
- Monitoring serum cholesterol concentrations often is not necessary because hypercholesterolemia is not associated with clinical signs.
- Monitor alanine aminotransferase (ALT) and alkaline phosphatase (ALP) enzyme activities when using a fibrate and/or niacin, as toxicity may occur.

POSSIBLE COMPLICATIONS

- Pancreatitis and seizures are common complications of hyperlipidemia in the miniature schnauzer.
- In cats with hereditary chylomicronemia, xanthoma formation, lipemia retinalis, and neuropathies have been reported; peripheral neuropathies usually resolve 2–3 months after institution of a low-fat diet.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Pancreatitis.
- Seizures.
- Neuropathies.

AGE-RELATED FACTORS

None

PREGNANCY/FERTILITY/BREEDING

Potential cause of high cholesterol.

SYNOMYS

- Lipemia—turbid serum or plasma secondary to significant hypertriglyceridemia.

- Hyperlipoproteinemia—increased blood concentration of lipoproteins.

SEE ALSO

- Diabetes Mellitus Without Complication—Cats.
- Diabetes Mellitus Without Complication—Dogs.
- Hyperadrenocorticism (Cushing's Syndrome)—Cats.
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs.
- Hypothyroidism.
- Nephrotic Syndrome.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- HDL = high-density lipoprotein.
- LDL = low-density lipoprotein.
- LPL = lipoprotein lipase.
- VLDL = very-low-density lipoprotein.

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Acknowledgment The author and book editors acknowledge the prior contribution of Melinda Fleming.



**Client Education Handout
available online**

HYPERPARATHYROIDISM



BASICS

DEFINITION

A pathologic, sustained, high, circulating concentration of parathyroid hormone (PTH).

PATHOPHYSIOLOGY

- PTH is secreted by the parathyroid glands in response to changes in the concentration of ionized calcium in the serum, and causes an increase in serum calcium concentration through direct effects on bone and renal tubular calcium resorption and indirectly by vitamin D-dependent intestinal calcium absorption.
- Hyperparathyroidism can develop as a primary condition or be secondary to a disorder of calcium homeostasis; primary hyperparathyroidism is usually associated with benign adenoma of the parathyroid gland(s), although adenocarcinoma and hyperplasia are possible; secondary hyperparathyroidism can be caused by a deficiency of calcium and vitamin D associated with malnutrition or chronic renal disease.

SYSTEMS AFFECTED

- Cardiovascular.
- Gastrointestinal.
- Neuromuscular.
- Renal/urologic.

GENETICS

- Autosomal dominant with possible age-dependent penetrance in the keeshond; genetic test available from Cornell.
- Secondary hyperparathyroidism can develop in association with hereditary nephropathy.

INCIDENCE/PREVALENCE

- Prevalence of primary form is unknown.
- More common in dogs than in cats.
- Common among causes of hypercalcemia, but less common than hypercalcemia of malignancy in dogs; more common in middle-aged to geriatric dogs.
- Chronic renal failure with secondary hyperparathyroidism is extremely common, more so in cats than in dogs.
- Nutritional secondary hyperparathyroidism is decreasing in prevalence as the public becomes more educated in pet nutrition.

SIGNALMENT

Species

Cat and dog.

Breed Predilections

- Keeshond, but seen in almost any breed.
- Siamese and domestic shorthair cats.

Mean Age and Range

- Cats—mean age 13 years; range: 8–20 years.
- Dogs—mean age 10 years; range: 4–17 years.

Predominant Sex

None

SIGNS

General Comments

- Most dogs and cats with primary hyperparathyroidism do not appear ill.
- Signs are usually mild and due to the effects of hypercalcemia, or lower urinary tract signs if urolithiasis is present.
- Signs become apparent when hypercalcemia is severe and chronic.

Historical Findings

- Polyuria.
- Polydipsia.
- Anorexia.
- Lethargy.
- Vomiting.
- Weakness.
- Urolithiasis.
- Stupor and coma.

Physical Examination Findings

- Often unremarkable.
- Parathyroid adenoma is not palpable in dogs but often is in cats.
- Nutritional secondary disease is sometimes associated with pathologic bone fractures and general poor body condition.

CAUSES

- Primary hyperparathyroidism—PTH-secreting adenoma of the parathyroid gland; in most cases only one gland is adenomatous; malignant tumors of the parathyroid glands are uncommon and usually noninvasive.
- Renal secondary hyperparathyroidism—renal calcium loss and reduced gut absorption of calcium due to deficiency in calcitriol production by the renal tubular cells.
- Nutritional secondary hyperparathyroidism—a nutritional deficiency of calcium and vitamin D.

RISK FACTORS

- Primary hyperparathyroidism—unknown.
- Secondary hyperparathyroidism—renal tubular disease or calcium/vitamin D malnutrition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- The differential list includes causes of hypercalcemia.
- Lymphoma—common to cause hypercalcemia in dogs, rare to do so in cats.
- Anal sac apocrine gland adenocarcinoma—dogs.
- Other miscellaneous carcinomas—dogs and cats.
- Myeloproliferative disease—cats.
- Fibrosarcoma—cats.
- Chronic kidney disease.
- Hypoadrenocorticism.
- Vitamin D intoxication—cholecalciferol-containing rodenticides, plant sources,

human anti-psoriasis topical creams, and vitamin supplements.

- Granulomatous diseases.
- Idiopathic hypercalcemia in cats.

CBC/BIOCHEMISTRY/URINALYSIS

- High serum total and ionized calcium concentrations.
- Low or low-normal serum phosphorus concentration in primary hyperparathyroidism.
- Hyperphosphatemia in renal secondary hyperparathyroidism or hypervitaminosis D.
- Serum blood urea nitrogen (BUN) and creatinine concentrations are usually normal in patients with primary hyperparathyroidism, except those with hypercalcemia-induced renal failure.

OTHER LABORATORY TESTS

- Serum ionized calcium determination is often normal (or low) in patients with chronic renal failure and high in patients with primary hyperparathyroidism or hypercalcemia associated with malignancy.
- High serum intact PTH concentration is diagnostic for primary hyperparathyroidism in the absence of azotemia; a serum PTH concentration within the normal reference range in an animal with ionized hypercalcemia should be considered *abnormal* and can signal parathyroid-dependent hypercalcemia.
- Measurement of PTH-related peptide (PTH-rp) may detect hyperparathyroidism related to neoplasia.

IMAGING

- Radiography can be useful to identify urolithiasis and occult neoplasia, as well as to assess renal morphology and bone density.
- Ultrasonography of the ventral cervical area sometimes reveals a parathyroid gland adenoma.
- Ultrasound of the abdomen can reveal lymphadenomegaly, urolithiasis, or renal morphologic abnormalities.

DIAGNOSTIC PROCEDURES

Surgical exploration of the ventral cervical area.

PATHOLOGIC FINDINGS

- Parathyroid adenoma is usually a solitary, small ($=1$ cm), round, light brown or reddish mass located in the proximity of the thyroid gland.
- Occasionally multiple adenomas are found.
- The histologic distinctions between adenomas, hyperplasia, and carcinomas of the parathyroid gland are often unclear.



TREATMENT

APPROPRIATE HEALTH CARE

- Primary hyperparathyroidism generally requires inpatient care and surgery.
- Nutritional or renal secondary hyperparathyroidism in noncritical patients can be managed on an outpatient basis.

(CONTINUED)

HYPERPARATHYROIDISM**H****ACTIVITY**

No alterations recommended.

DIET

Calcium supplementation for secondary forms.

CLIENT EDUCATION

Explain signs referable to changes in calcium status, because hypocalcemia is a potential complication of parathyroidectomy.

SURGICAL CONSIDERATIONS

- Surgery is the treatment of choice for primary hyperparathyroidism and is often important in establishing the diagnosis.
- Percutaneous ultrasound-guided heat ablation has been used successfully for treatment of parathyroid adenomas, and may be recommended if available.
- Percutaneous ultrasound-guided ethanol ablation has been reported to be less successful than surgery or heat ablation.

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

- Normal saline is the fluid of choice for treatment of hypercalcemia.
- Diuretics (furosemide) and corticosteroids can be useful in treating hypercalcemia.
- No medical treatment exists for primary hyperparathyroidism per se.
- Renal secondary hyperparathyroidism is sometimes treated with calcitriol, but its use has not gained uniform acceptance.
- A new class of calcimimetic drugs is being used to treat renal secondary hyperparathyroidism in human patients, but studies of these drugs in dogs and cats have not been reported and expense limits their use.

CONTRAINDICATIONS

Do not use glucocorticoids until the diagnosis of lymphoma has been excluded; they can obfuscate the diagnosis.

PRECAUTIONS

Use furosemide only in patients with adequate hydration.

ALTERNATIVE DRUG(S)

Pamidronate and other bisphosphonate drugs have been used to treat hypercalcemia of various causes in dogs and cats.

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

- Postoperative hypocalcemia is relatively common after treatment of primary hyperparathyroidism; recent studies have shown that preoperative ionized calcium and PTH concentrations are poor predictors of postsurgical hypocalcemia, so monitoring is essential in all cases.
- Postoperative hypocalcemia requires treatment with vitamin D (calcitriol is recommended) and calcium supplements (see treatment of hypoparathyroidism), and ionized calcium should be monitored to guide dosage adjustments; contradictory evidence exists with respect to preoperative administration of calcitriol.
- In patients with renal impairment, check serum concentrations of BUN and creatinine.

PREVENTION/AVOIDANCE

- Avoid breeding affected keeshonden.
- Nutritional secondary hyperparathyroidism is prevented by proper nutrition.

POSSIBLE COMPLICATIONS

- Irreversible renal failure secondary to hypercalcemia.
- Fractures due to decreased bone density with chronic hyperparathyroidism.

EXPECTED COURSE AND PROGNOSIS

- Untreated primary hyperparathyroidism may progress to end-stage kidney or neuromuscular disease depending on severity; many dogs clinically seem to do well even with no treatment, provided urolithiasis does not develop.
- Prognosis for surgical treatment of parathyroid adenoma is excellent.
- Recurrence is seen in a small percentage of cases.
- In animals that develop postoperative hypoparathyroidism, the return of normal parathyroid function is unpredictable and can take weeks to months.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Calcium-containing urolithiasis.

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Chronic Kidney Disease.
- Hypercalcemia.
- Hyperparathyroidism, Renal Secondary.

ABBREVIATIONS

- BUN = blood urea nitrogen.
- PTH = parathyroid hormone.
- PTH-rp = PTH-related peptide.

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Acknowledgment The author and book editors acknowledge the prior contribution of Thomas K. Graves.



**Client Education Handout
available online**

HYPERPARATHYROIDISM, RENAL SECONDARY



BASICS

OVERVIEW

- Syndrome characterized by a high parathyroid hormone (PTH) concentration secondary to chronic kidney disease (CKD); results from impaired renal excretion of phosphorus leading to hyperphosphatemia and ionized hypocalcemia, elevation of FGF-23, and suppression of renal calcitriol synthesis.
- In advanced CKD the diminished renal tubular mass produces less calcitriol. Calcitriol exerts negative feedback on PTH synthesis within the parathyroid gland. Low calcitriol, ionized hypocalcemia, and hyperphosphatemia result in increased PTH production and parathyroid gland hyperplasia.
- PTH may act as a uremic toxin, promoting nephrocalcinosis and progression of CKD.

SIGNALMENT

Dog and cat; see Chronic Kidney Disease for age and breed predilections.

SIGNS

- Uremia due to underlying CKD.
- Renal osteodystrophy or “rubber jaw” most commonly occurs in young dogs with severe renal secondary hyperparathyroidism (RSHPT).
- Pain around the head or long bones.

CAUSES & RISK FACTORS

- Any disease that causes CKD.
- Excess consumption of phosphorus.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypercalcemic nephropathy—kidney disease caused by ionized hypercalcemia; can be difficult to differentiate from longstanding RSHPT, in which hyperplasia of the parathyroid glands disrupts the normal feedback arc between PTH release and ionized calcium (tertiary hyperparathyroidism).
- Ionized serum calcium concentration is usually low or normal with RSHPT, but high with hypercalcemic nephropathy.
- Low serum PTH and PTH-related protein (PTHrP) high in animals with hypercalcemia of malignancy.
- Primary hyperparathyroidism—characterized by hypercalcemia, normal or low serum phosphorus, and inappropriate PTH concentration; kidney function is initially normal but may become compromised later.

CBC/BIOCHEMISTRY/URINALYSIS

- Azotemia.

- Hyperphosphatemia.
- Dilute urine.
- Total serum calcium does not reliably predict ionized calcium.

OTHER LABORATORY TESTS

Definitive diagnosis and therapeutic monitoring of RSHPT require measurement of serum PTH concentration using validated assay.

IMAGING

Radiographs may reveal low bone density, loss of the lamina dura around the teeth, and soft tissue mineralization of the gastric mucosa or other tissues.



TREATMENT

- See Chronic Kidney Disease for general treatment principles.
- Minimize hyperphosphatemia by feeding a low phosphorus diet formulated for kidney disease and intestinal phosphate binders in order to achieve IRIS phosphorus goals.



MEDICATIONS

DRUG(S) OF CHOICE

Intestinal Phosphate Binders

- If dietary management alone does not achieve the IRIS target serum phosphorus concentration, phosphorus binders can be used to further reduce serum phosphorus. Serum phosphorus targets based on the IRIS stages are stages 1 and 2: >2.7 to <4.6 mg/dL; Stage 3: >2.7 to <5.1 mg/dL; and Stage 4: >2.7 to <6.0 mg/dL.
- Aluminum hydroxide (60–90 mg/kg/day), calcium carbonate (90–150 mg/kg/day), calcium acetate (60–90 mg/kg/day), or lanthanum carbonate (60–90 mg/kg/day)—dose to achieve target serum phosphorus concentration, but do not exceed max dosage. All must be given with meals.
- Calcium-containing phosphate binders should be avoided with calcitriol therapy as hypercalcemia may occur. Combine different phosphate binders to reduce the dosage of each and minimize the risk of hypercalcemia or aluminum toxicity.

Calcitriol

- Low-dose calcitriol (2.0–3.5 ng/kg PO q24h)—may use after serum phosphorus is controlled, should be administered on an empty stomach and before bedtime (no food for 6–8 hours after administration).

- Maintain serum phosphorus concentration within the recommended IRIS target ranges before and during calcitriol therapy.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Calcitriol therapy may result in hypercalcemia, especially if combined with a calcium-containing phosphate binder. Increased total calcium concentration may develop in patients with long-standing CKD, but is unrelated to calcitriol treatment. Ionized calcium concentration is normal or low in these patients.
- Do not use calcium-containing intestinal phosphate binders in patients with a calcium × phosphorus product >70. Use aluminum- or lanthanum-containing intestinal phosphate binders initially to correct hyperphosphatemia. Calcium-containing phosphate binders can be used once the serum phosphorus concentration is within the target range.



FOLLOW-UP

PATIENT MONITORING

- Initially and in unstable patients, serum concentrations of calcium, phosphorus, creatinine, and urea nitrogen—monitor weekly to monthly depending on therapy and the severity of CKD.
- Patients receiving calcitriol should be monitored for hypercalcemia and hyperphosphatemia weekly for 4 weeks, then every 3–4 months.
- Serial evaluations of PTH concentration—most treated with low-dose calcitriol achieve near-normal levels of PTH within 3 months; it may be necessary to increase the dose in those with severe parathyroid gland hyperplasia.
- If hypercalcemia develops discontinue calcitriol; calcium should normalize within 5 days of discontinuation. Measurement of ionized calcium is recommended—animals with CKD may develop nonionized hypercalcemia that is unrelated to calcitriol treatment.

PREVENTION/AVOIDANCE

Dietary phosphorus restriction may delay the onset of RSHPT.

POSSIBLE COMPLICATIONS

Renal osteodystrophy and pathologic fractures (rare).

EXPECTED COURSE AND PROGNOSIS

- Progression of the underlying CKD may be slowed by minimizing phosphorus retention and RSHPT.
- Long-term prognosis is guarded to poor for patients with CKD and RSHPT.

(CONTINUED)

HYPERPARATHYROIDISM, RENAL SECONDARY**MISCELLANEOUS****AGE-RELATED FACTORS**

Young animals can develop severe renal osteodystrophy; calcitriol may be beneficial.

ABBREVIATIONS

- CKD = chronic kidney disease.
- PTH = parathyroid hormone.

- PTHrP = PTH-related protein.
- RSHPT = renal secondary hyperparathyroidism.

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H

HYPERPHOSPHATEMIA



BASICS

DEFINITION

- Serum total phosphorus >5.5 mg/dL (dogs).
- Serum total phosphorus >6 mg/dL (cats).

PATHOPHYSIOLOGY

- Control of phosphorus is complex and is influenced by the actions of parathyroid hormone (PTH) and vitamin D and the interaction of these hormones with the gastrointestinal tract, bone, kidneys, and parathyroid glands. The phosphatonin fibroblast growth factor-23 (FGF-23) also regulates phosphorus levels.
- High serum phosphorus results from excessive gastrointestinal absorption of phosphorus, excessive bone resorption of phosphorus, and/or reduced renal excretion of phosphorus.

SYSTEMS AFFECTED

- Endocrine.
- Metabolic.
- Renal.

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

- Dogs and cats.
- Any age, but commonly young, growing animals or older animals with renal insufficiency.

SIGNS

Historical Findings

- Depends on the underlying cause of hyperphosphatemia.
- No specific signs directly attributable to hyperphosphatemia.
- Acute hyperphosphatemia causes hypocalcemic tetany, seizures, or vascular collapse.

Physical Examination Findings

Chronic hyperphosphatemia causes calcification of soft tissues, resulting in chronic renal failure and tumoral calcinosis.

CAUSES

- Reduced glomerular filtration rate.
- Renal hypoperfusion (e.g., hypovolemia, systolic cardiac disease).
- Renal disease.
- Postrenal urinary tract disease (e.g., obstruction, ruptured urinary bladder).
- Metabolic acidosis.
- Excessive bone resorption.
- Rhabdomyolysis or massive tissue trauma.
- Young growing dogs.

- Hypoparathyroidism.
- Hypersomatotropism.
- Excessive gastrointestinal absorption of phosphorus.
- Osteolysis.
- Disuse osteoporosis.
- Osseous neoplasia.
- Hyperthyroidism.
- Phosphorus-containing enemas.
- Vitamin D toxicosis.
- Dietary supplementation.
- Nutritional secondary hyperparathyroidism.

RISK FACTORS

- Renal disease.
- Use of phosphorus-containing enemas, especially in smaller animals.
- Massive tissue injury.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Hypoparathyroidism—also characterized by clinical signs of hypocalcemia such as seizures and tetany.
- Prerenal azotemia as a cause of hyperphosphatemia—associated with disease states that result in low cardiac output such as congestive heart failure, hypovolemia, hypoadrenocorticism, and shock.
- Renal insufficiency, either acute or chronic renal failure—attended by azotemia and abnormal findings on urinalysis (low urinary specific gravity).
- Postrenal azotemia—associated with urinary obstruction or uroabdomen.
- Young, growing animals—can have serum phosphorus concentrations twice those of adults.
- Vitamin D intoxication—history of vitamin D supplementation or ingestion of rodenticides (e.g., Rampage® and D-CON®) or calcipotriene.
- Nutritional secondary hyperparathyroidism—history of dietary calcium–phosphorus imbalance.
- Hyperthyroidism in cats—clinical signs of weight loss, polyphagia, and polydipsia and polyuria.
- Hypersomatotropism—attended by a history of progesterone administration in dogs and insulin-resistant diabetes mellitus in cats.
- Nonazotemia tumoral calcinosis—observed in human beings as an autosomal dominant disorder; rare cause of hyperphosphatemia associated with large bone lesions.
- Jasmine toxicity—history of plant ingestion.
- Massive tissue injury.
- Rhabdomyolysis.
- Tumor lysis syndrome.
- Spurious.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

Intravenous potassium phosphate.

Disorders That May Alter Laboratory Results

- Hemolysis, hyperbilirubinemia, and lipemia can falsely raise phosphorus concentrations.
- Collection in citrate, oxalate, or EDTA.

Valid If Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Serum phosphorus >6 mg/dL.
- Low serum calcium in patients with primary hypoparathyroidism.
- High serum calcium in patients with vitamin D intoxication.
- Degree of azotemia and urine specific gravity help define level renal impairment.
- Hyperkalemia and hyponatremia suggest hypoadrenocorticism.

OTHER LABORATORY TESTS

- Serum PTH measurement—intact molecule and two-site assay methods have the greatest specificity; high-normal or high concentrations with concurrent hyperphosphatemia suggest primary hyperparathyroidism; low concentrations with concurrent hypocalcemia and hyperphosphatemia suggest neoplasia.
- Thyroxine concentrations—indicated in cats with hyperphosphatemia and clinical signs consistent with hyperthyroidism.
- Insulin-like growth factor 1 (IGF-1) concentrations—indicated in dogs or cats with unexplained hyperphosphatemia and clinical signs consistent with acromegaly; IGF-1 concentrations are elevated in animals with hypersomatotropism.
- Vitamin D assays are not readily available.
- Adrenocorticotropic hormone (ACTH) stimulation testing to confirm hypoadrenocorticism.

IMAGING

- Abdominal radiography to assess renal size and symmetry.
- Renal ultrasonography to detect soft tissue mineralization.
- Nuclear scintigraphy to rule out hyperthyroidism.
- Radiography of long bones to detect osteoporosis or neoplasia.

DIAGNOSTIC PROCEDURES

Renal biopsy.

PATHOLOGIC FINDINGS

Mineralization of soft tissues may be noted radiographically or histopathologically.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient, because of the deleterious effects of hyperphosphatemia and the need for fluid therapy; consider severe hyperphosphatemia a

(CONTINUED)

HYPERPHOSPHATEMIA**H**

medical emergency. Long-term monitoring and management may be necessary.

NURSING CARE

Isotonic crystalloid fluids to increase glomerular filtration rate and promote phosphorus excretion.

ACTIVITY

N/A

DIET

Restrict dietary phosphorus.

CLIENT EDUCATION

Long-term monitoring and management may be necessary with phosphorus-restricted diets and/or oral phosphate binders.

SURGICAL CONSIDERATIONS

N/A

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

- Dextrose (0.5–1 g/kg IV) and regular insulin (0.25–0.5 U/kg IV), to shift phosphorus intracellularly.
- Avoid phosphorus-containing fluids.

Chronic Hyperphosphatemia

Oral administration of phosphorus binders (e.g., aluminum hydroxide or aluminum carbonate, 30–100 mg/kg/day PO, or calcium carbonate at 90–150 mg/kg/day PO, both with meals).

CONTRAINDICATIONS

N/A

PRECAUTIONS

Calcium carbonate should be avoided with hypercalcemia.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

The oral phosphate binders sevelamer hydrochloride and lanthanum carbonate may

be used as oral phosphate binders, but relatively little information is available in the veterinary literature.

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

- Serum calcium every 12 hours.
- Renal function tests—urine output must be monitored, particularly if oliguric renal failure is suspected, in which case urine output should be measured carefully; oliguria cannot be determined unless the patient is fully hydrated.
- Hydration status—indicators of overhydration include increased bodyweight, chemosis, increased central venous pressure, and edema (pulmonary or subcutaneous).
- Long-term serial monitoring of phosphorus is used to make dose adjustments in oral phosphate binders.

PREVENTION/AVOIDANCE

- Avoid ingestion of cholecalciferol rodenticides, calcipotriene, or Vitamin D supplementation.
- Avoid phosphate-containing enemas.
- Well-balanced veterinary diets prevent nutritional secondary hyperparathyroidism.

POSSIBLE COMPLICATIONS

- Hypophosphatemia resulting in hemolysis.
- Soft tissue mineralization.

EXPECTED COURSE AND PROGNOSIS

Depends on the underlying cause. Chronic kidney disease often causes chronic hyperphosphatemia and has a poor to guarded prognosis in dogs.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Hypocalcemia

AGE-RELATED FACTORS

Mild elevations in phosphorus may be normal in growing animals.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

N/A

SEE ALSO

- Acute Kidney Injury.
- Chronic Kidney Disease.
- Hypoparathyroidism.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- FGF-23 = fibroblast growth factor-23.
- IGF-1 = insulin-like growth factor I.
- PTH = parathyroid hormone.

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Acknowledgment The author and book editors acknowledge the prior contribution of Deborah S. Greco.

HYPERTHYROIDISM



BASICS

DEFINITION

A state of increased metabolism caused by increased circulating concentrations of thyroid hormone.

PATHOPHYSIOLOGY

- Feline hyperthyroidism most often caused by benign adenomatous hyperplasia or follicular cell adenoma, causing increased secretion of thyroxine (T_4) and triiodothyronine (T_3).
- Naturally occurring hyperthyroidism rare in dogs; most often malignant carcinoma (<2% of cats have malignant thyroid carcinoma).
- Oversupplementation with exogenous thyroid hormone may cause hyperthyroidism in dogs.

SYSTEMS AFFECTED

- Cardiovascular—systemic hypertension, thyrotoxic cardiomyopathy.
- Gastrointestinal (GI)—malabsorption, hypermotility.
- Nervous/behavioral—restlessness, irritability, aggression, vocalization, pacing.
- Urologic—increased glomerular filtration rate (GFR).
- Musculoskeletal—catabolism, cachexia.

GENETICS

None known.

INCIDENCE/PREVALENCE

- Most common feline endocrinopathy; affects 3–8% of cats >10 years old.
- Rare in dogs.

SIGNALMENT

- Cats 4–22 years old; mean age of onset is 13 years.
- <5% of affected cats <8 years old.
- Most common in dogs >10 years old.

SIGNS

General Comments

- Signs related to increased metabolism.
- Small number of cats show atypical signs; the human term “apathetic hyperthyroidism” is characterized by lethargy, decreased appetite, and muscle weakness; signs may be more common with advanced hyperthyroidism.

Historical Findings

- Weight loss.
- Polyphagia.
- Hyperactivity/irritability/restlessness.
- Polyuria/polydipsia.
- Vomiting.
- Diarrhea.
- Increased vocalization.
- Tachypnea.
- Muscle weakness.

Physical Examination Findings

- Cachexia/muscle loss.
- Palpable thyroid gland (unilateral or bilateral).
- Tachycardia/heart murmur/gallop rhythm.
- Systemic hypertension/retinopathy.
- Unkempt hair/hair loss.
- Thickened nails.
- Ventroflexion of neck (advanced disease).

CAUSES

- In cats, benign adenomatous hyperplasia and follicular cell adenoma lead to oversecretion of T_4 and T_3 ; thyroid carcinoma is rare.

- In dogs, thyroid carcinoma is more likely; hyperthyroidism in dogs may be secondary to oversupplementation of T_4 .

RISK FACTORS

- Increased risk with aging.
- Decreased risk in Burmese, Tonkinese, Persian, Siamese, Abyssinian, and British shorthair cats; possible increased risk in domestic longhair cats.
- Multifactorial environmental contributors are possible, including bisphenol A (BPA) associated with canned food diets, and polybrominated diphenyl ether (PBDE) flame retardants, but further study is needed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Any of the differentials for hyperthyroidism can reflect concurrent disease.
- Neoplasia.
- Inflammatory bowel conditions.
- Diabetes mellitus.
- Chronic kidney disease.
- Cardiomyopathy.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—mild packed cell volume (PCV) elevation or stress leukogram.
- Elevated alanine aminotransferase (ALT) activity is common.
- Elevated alkaline phosphatase (ALP), aspartate aminotransferase (AST) activities, and blood urea nitrogen, creatinine, phosphorus, bilirubin, and glucose concentrations may be seen.
- Urinalysis (UA) shows variable urine specific gravity; pre-treatment specific gravity does not predict post-treatment renal function.
- Glucosuria and evidence of urinary tract infection possible.

OTHER LABORATORY TESTS

- Elevated serum total T_4 (TT $_4$) concentration is diagnostic for hyperthyroidism in cats with clinical signs.
- T_4 concentrations naturally decrease with age; early hyperthyroid cats may have T_4 levels in high-normal range.
- T_4 concentration may be decreased by concurrent disease.
- Free T_4 concentration measured by equilibrium dialysis may be helpful in cats with concurrent disease or early hyperthyroidism, but is not a screening test.
- T_3 suppression test or thyrotropin-releasing hormone (TRH) stimulation test can help to confirm diagnosis in mild cases.
- Fructosamine concentration may be decreased by concurrent hyperthyroidism.
- Cardiac biomarker concentrations (*N*-terminal pro brain natriuretic peptide, cardiac troponin I) may be elevated; myocardial disease and biomarkers may return to normal after control of hyperthyroidism.

IMAGING

- Thoracic and abdominal radiography helpful to evaluate for neoplasia and cardiac disease.
- Abdominal ultrasound helpful in determining concurrent disease.
- Echocardiography to evaluate cardiac function.
- Thyroid scintigraphy can determine location of abnormal and ectopic thyroid tissues.

DIAGNOSTIC PROCEDURES

- BP measurement is part of baseline database.
- GFR measurement is possible but not always practical.

PATHOLOGIC FINDINGS

- Multinodular adenomatous hyperplasia can be unilateral or bilateral (98% of cats).
- Thyroid carcinoma in dogs and <2% of hyperthyroid cats.



TREATMENT

APPROPRIATE HEALTH CARE

- Advanced hyperthyroidism with concurrent congestive heart failure requires hospitalization for stabilization.
- Most cases managed on an outpatient basis.
- Radioactive iodine and surgical treatments require hospitalization.

ACTIVITY

No activity restrictions.

DIET

- Because of increased metabolism and hypermotility of intestinal tract, highly digestible diets preferred.
- Malabsorption improves with resolution of hyperthyroid state.
- Vitamin B₁₂ supplementation may be helpful.
- An iodine-deficient therapeutic diet is available and effective in appropriate situations.

CLIENT EDUCATION

- Hyperthyroidism in cats is common and treatable.
- Treatment with medication or diet restriction is lifelong.
- Medication dosing needs to be monitored regularly and adjusted accordingly.
- Comorbidities are possible.
- Hyperthyroidism in dogs is usually a malignancy and carries a poor long-term prognosis.
- Possible side effects of medication.
- Surgical thyroidectomy—anesthetic risks, risk of damage to parathyroid glands.
- In some cases, radioactive iodine (I-131) treatment may need to be repeated.
- Resolution of thyrotoxicosis may reveal other, previously masked conditions (e.g., renal disease).

SURGICAL CONSIDERATIONS

- Surgical thyroidectomy is an accepted treatment option.
- Thyroidectomy for carcinoma is not curative, but may be helpful with or without subsequent radioactive iodine treatment.

HYPERTHYROIDISM



MEDICATIONS

DRUG(S) OF CHOICE

- I-131 is treatment of choice for hyperthyroidism.
- Methimazole (2.5–5 mg/cat PO q12–24h) is most common medication.
- Methimazole should be dosed below expected therapeutic dose and titrated upward to minimize side effects.
- Transdermal methimazole is available and effective; ideally, initial management with oral methimazole will stabilize patient, then transition to transdermal; resolution may be prolonged if treatment initiated with transdermal medication.
- Methimazole may cause anorexia, vomiting, skin excoriations, thrombocytopenia, hepatopathy, and hypothyroidism; side effects occur within first weeks to months of treatment.
- Anorexia, vomiting, and skin excoriations can be mitigated by starting at very low doses of methimazole and increasing to therapeutic levels; cessation of drug can resolve these issues, and restarting with transdermal methimazole may avoid recurrence of GI side effects.
- Bleeding disorders, bone marrow dyscrasias, and hepatic issues require discontinuation of methimazole and choosing an alternative therapy.
- Severe blood dyscrasias may require hospitalization and supportive care, but should resolve with appropriate treatment.
- Atenolol may be used for severe tachycardia.

POSSIBLE INTERACTIONS

Concurrent use of phenobarbital may reduce effectiveness of methimazole.

ALTERNATIVE DRUG(S)

- Carbimazole—converted to methimazole after absorption; effective, may have fewer side effects than methimazole; not available in United States.
- Propylthiouracil—not recommended.
- Iopodate—for short-term treatment only, not effective for most hyperthyroid cats; not recommended in most cases.



FOLLOW-UP

PATIENT MONITORING

- Regardless of treatment option, GFR and renal function may decline after treatment, but will stabilize within 1 month of thyroid control.
- I-131—physical exam (PE), BP, T_4 serum chemistry, and UA at 1, 3, 6, and 12 months post treatment.
- Methimazole—PE, CBC, serum chemistry, T_4 , and UA every 2–4 weeks after starting

treatment and after every dose change until T_4 is stabilized between 1 and 2.5 $\mu\text{g/L}$.

- In cats with renal insufficiency, serum T_4 should be maintained in upper half of reference interval.
- Thyroidectomy—hypocalcemia can occur within several days post surgery; monitor for postoperative laryngeal paralysis; PE, T_4 , serum chemistry, and UA 2–4 weeks post surgery, then every 3–6 months; supplementation should not be started postsurgically unless T_4 levels remain low after 3 months; hypothyroidism may be transient with subtotal thyroidectomy.
- Therapeutic diet—PE, BP, serum chemistry, CBC, T_4 , and UA every 4–6 months; may take as long as 6 months for cats with severe T_4 elevations to become euthyroid, if at all.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Fatal, if untreated.
- Complications of thyroidectomy include hypothyroidism, hypoparathyroidism, laryngeal paralysis.
- I-131, antithyroid drugs, and thyroidectomy can all lead to hypothyroidism; proper dosing of I-131 and methimazole is imperative.
- Iatrogenic hypothyroidism associated with worsening renal function and decreased survival.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is excellent in cats without concurrent disease.
- Cats on methimazole are likely to relapse if medication is not administered correctly.
- Cats eating a therapeutic diet who do not strictly follow diet will not be successful.
- Post I-131 treatment—mean survival time is 4 years.
- Treatment with methimazole—mean survival time is 2 years.
- Overall mean survival time can be up to 5.3 years.
- Cats with preexisting renal disease have a poorer prognosis.
- Cats and dogs with carcinoma have a poor prognosis—best option for treatment may be surgical debulking of tumor followed by high dose I-131; recurrence is common.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Because hyperthyroidism is life-threatening, treatment of all hyperthyroid cats is recommended, with concurrent management of any comorbidities.
- Less aggressive treatment options should be considered for cats with advanced (IRIS stage 3–4) renal disease.

AGE-RELATED FACTORS

Mature to geriatric cats and dogs.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Thyrotoxicosis.
- Plummer's disease.

SEE ALSO

- Cardiomyopathy, Hypertrophic—Cats.
- Chronic Kidney Disease.
- Congestive Heart Failure, Right-Sided.
- Hypertension, Systemic Arterial.
- Hypoparathyroidism.

ABBREVIATIONS

- ALT = alanine aminotransferase.
- ALP = alkaline phosphatase.
- AST = aspartate aminotransferase.
- BPA = bisphenol A.
- GFR = glomerular filtration rate.
- GI = gastrointestinal.
- I-121 = radioactive iodine.
- PBDE = polybrominated diphenyl ether.
- PCV = packed cell volume.
- PE = Physical exam.
- T_3 = triiodothyronine.
- T_4 = thyroxine.
- TRH = thyrotropin-releasing hormone.
- TSH = thyroid-stimulating hormone.
- TT₄ = total thyroxine.
- UA = urinalysis.

INTERNET RESOURCES

https://www.catvets.com/public/PDFs/Client_Brochures/Hyperthyroidism-WebView.pdf

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Client Education Handout
available online

HYPOADRENOCORTICISM (ADDISON'S DISEASE)



BASICS

DEFINITION

- Endocrine disorder resulting from deficient production of glucocorticoids and, usually, mineralocorticoids.
- Primary hypoadrenocorticism (Addison's disease) is due to destruction of the adrenal cortices resulting in glucocorticoid and mineralocorticoid deficiency.
- The term atypical hypoadrenocorticism has been applied to the subset of dogs with primary hypoadrenocorticism and normal electrolyte concentrations.
- Secondary hypoadrenocorticism results from pituitary adrenocorticotrophic hormone (ACTH) insufficiency, resulting in inadequate glucocorticoid production by the adrenal cortices.

PATOPHYSIOLOGY

- Mineralocorticoid (aldosterone) deficiency results in a diminished ability to excrete potassium and retain sodium, disrupting sodium and potassium balance in the body.
- Sodium loss leads to diminished effective circulating volume; this contributes to pathophysiologic changes and clinical abnormalities, including prerenal azotemia, hypotension, dehydration, weakness, and depression.
- Hyperkalemia can result in weakness, lethargy, and anorexia; it may result in bradycardia.
- Glucocorticoid (cortisol) deficiency contributes to anorexia, vomiting, diarrhea, melena, lethargy, and weight loss; due to its role in glucose homeostasis, hypocortisolemia predisposes to hypoglycemia.

SYSTEMS AFFECTED

- Gastrointestinal.
- Musculoskeletal.
- Cardiovascular.
- Renal/urologic.

GENETICS

A genetic basis has been determined in standard poodles, bearded collies, Nova Scotia duck tolling retrievers, and Leonbergers.

INCIDENCE/PREVALENCE

Unknown; considered uncommon in dogs and very rare in cats.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Great Danes, Rottweilers, Portuguese water dogs, standard poodles, bearded collies, Leonbergers, West Highland white terriers, Nova Scotia duck tolling retrievers and soft coated wheaten terriers have increased relative risk; golden retrievers and Chihuahuas have decreased relative risk.

• No predilection in cats.

MEAN AGE AND RANGE

- Dogs—range: <1 to >12 years; median: 4 years; young to middle-aged.
- Cats—range: 1–9 years; middle-aged.

PREDOMINANT SEX

Female dogs at increased relative risk; no predilection in cats.

SIGNS

General Comments

- Signs vary from mild in patients with chronic hypoadrenocorticism to severe and life-threatening in an acute Addisonian crisis.
- Multiple organ systems may be involved; type and extent of involvement vary with case.

Historical Findings

- Dogs—lethargy, anorexia, vomiting, weakness, weight loss, diarrhea, waxing/waning course, previous response to therapy, polyuria/polydipsia (PU/PD), melena.
- Cats—lethargy, anorexia, weight loss, vomiting, waxing/waning course, previous response to therapy, PU/PD.

Physical Examination Findings

- Dogs—depression, weakness, hypovolemia, dehydration, collapse, hypothermia, melena, hypotension, bradycardia, painful abdomen, hair loss.
- Cats—dehydration, hypovolemia, weakness, hypothermia, depression, hypotension, bradycardia, collapse.

CAUSES

- Primary hypoadrenocorticism—idiopathic (immune-mediated), mitotane or trilostane overdose, granulomatous disease, metastatic tumors, fungal disease, coagulopathy, adrenal hemorrhage or necrosis.
- Secondary hypoadrenocorticism—iatrogenic following withdrawal of long-term glucocorticoid administration, ACTH deficiency, panhypopituitarism, pituitary or hypothalamic lesions.

RISK FACTORS

N/A



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signs are nonspecific and often mimic gastrointestinal and renal diseases; differential diagnoses for gastrointestinal distress include intestinal obstruction (e.g., foreign body, intussusception, neoplasia), gastrointestinal perforation, pancreatitis, infectious disease, and others (see Acute Vomiting).
- Differential diagnoses for hyperkalemia include acute kidney injury, urinary tract obstruction, third-space fluid loss (e.g.,

peritoneal or pleural effusion, uroabdomen), and Trichuriasis.

- Although no signs are pathognomonic, a waxing and waning course and previous response to nonspecific medical intervention should alert the clinician.

CBC/BIOCHEMISTRY/URINALYSIS

- Hematologic abnormalities may include anemia, eosinophilia, and lymphocytosis.
- The absence of a stress leukogram in a sick patient should prompt consideration of hypoadrenocorticism.
- Serum biochemical findings may include hyperkalemia, azotemia, hyponatremia, hypochloremia, hyperphosphatemia, hypercalcemia, hypoalbuminemia, increased alanine aminotransferase (ALT) activity, and hypoglycemia.
- Urinalysis often reveals impaired urine-concentrating ability and in some cases isothenuria; some patients with isothenuria are also azotemic, potentially causing confusion with primary renal disease.
- Some patients with hypoadrenocorticism exhibit normal electrolyte levels (so-called atypical hypoadrenocorticism).

OTHER LABORATORY TESTS

- Definitive diagnosis is by demonstration of undetectable to low (<2 µg/dL) baseline serum cortisol concentrations that fail to increase above 2 µg/dL following ACTH administration.
- Cortisol concentrations should be measured before and 1 hour after administration of synthetic ACTH (1 µg/kg, IV in dogs and 5 µg/kg, IV in cats).
- The ACTH stimulation test can be performed during initial stabilization and treatment if dexamethasone is used (does not cross-react with the cortisol assay).
- If prednisone, prednisolone, or hydrocortisone has been administered, the treatment must be discontinued, and the ACTH stimulation test performed at least 24 hours after changing the glucocorticoid to dexamethasone (do not withhold corticosteroids from a patient in acute crisis).
- A low resting cortisol does not confirm hypoadrenocorticism; an ACTH stimulation test is required.
- Plasma ACTH concentration can be measured in patients with normal electrolyte concentrations to differentiate primary from secondary hypoadrenocorticism; must collect sample before initiating therapy, especially glucocorticoids; carefully follow sample handling instructions from the laboratory; plasma ACTH concentrations are high with primary hypoadrenocorticism and undetectable to low with secondary hypoadrenocorticism.

IMAGING

- Radiographs may reveal microcardia, narrowed vena cava or descending aorta, hypoperfused lung fields, less commonly microhepatica, and very rarely megaesophagus.

HYPOADRENOCORTICISM (ADDISON'S DISEASE)

(CONTINUED)

- Abdominal ultrasound may reveal small adrenal glands.
- Imaging is not usually necessary for diagnosis, but is often performed during the diagnostic workup in patients with gastrointestinal signs.

PATHOLOGIC FINDINGS

- Gross examination—atrophy of the adrenal glands.
- Microscopically—lymphocytic-plasmacytic adrenalitis and/or adrenocortical atrophy; other abnormalities may be present depending on etiology (neoplasia, fungal disease, etc.).



TREATMENT

APPROPRIATE HEALTH CARE

- An acute Addisonian crisis is a medical emergency requiring intensive therapy and 24-hour observation and care; the diagnostic workup is performed while initial treatment and stabilization are ongoing; cats often respond more slowly than dogs.
- The intensity of treatment for patients with chronic hypoadrenocorticism depends on the severity of clinical signs; usually initial stabilization and therapy are conducted on an inpatient basis.

NURSING CARE

- Treat acute Addisonian crisis with rapid correction of hypovolemia and restoration of volume status using isotonic fluids, preferably Plasma-Lyte® or lactated Ringer's solution; although normal saline (0.9% NaCl) was historically recommended, it can exacerbate existing acidosis, but can be used in the absence of other isotonic crystalloid fluids.
- Do not increase sodium concentration by more than 12 mEq/L every 24 hours to prevent CNS myelinolysis; this is more likely to occur when the initial sodium concentration is <120 mEq/L; lactated Ringer's solution has a sodium content of 130 mEq/L and will increase the sodium concentration more slowly than Plasma-Lyte (140 mEq/L) and 0.9% saline (154 mEq/L).
- Although most cases respond to fluid resuscitation alone, severe hyperkalemia (>8.5–9.0 mEq/L and/or bradycardia or other ECG abnormalities) may require additional therapy; see Hyperkalemia.
- If necessary, a colloid fluid also can be given to treat hypotension and hypovolemia.
- Treat hypoglycemia, if present, with IV dextrose; due to hyperosmolarity, 50% dextrose should be diluted a minimum of 1 : 3 prior to IV administration.
- Monitor hydration status, blood pressure, urine output, rectal temperature, and heart rate and rhythm.

ACTIVITY

Avoid unnecessary stress and exertion during an Addisonian crisis.

DIET

No need to alter.

CLIENT EDUCATION

- Lifelong glucocorticoid and/or mineralocorticoid replacement therapy is required.
- Increased dosages of glucocorticoid (above maintenance requirements) are required during periods of stress such as travel, boarding, hospitalization, and surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- In an Addisonian crisis, parenteral administration of a rapidly acting glucocorticoid such as dexamethasone sodium phosphate is indicated; dexamethasone sodium phosphate is given at a dose of 0.25 mg/kg IV on the first day, and 0.15 mg/kg on the second day; glucocorticoid is gradually tapered and changed to oral prednisone or prednisolone as the condition improves.
- Alternatively, hydrocortisone (0.5–0.625 mg/kg/h) has both mineralocorticoid and glucocorticoid properties, and prednisolone sodium succinate (2 mg/kg IV initially, and then 0.5 mg/kg IV q12h) is also an option; since both of these cross-react with cortisol assays (dexamethasone does not), they should be administered after the ACTH stimulation test is complete, or ACTH stimulation testing should be delayed at least 24 hours after administration.
- During an Addisonian crisis, supportive therapy, including gastroprotectants and anti-emetics, is often necessary.
- Chronic primary hypoadrenocorticism—most patients will need daily glucocorticoid replacement (prednisone 0.1–0.2 mg/kg/day PO), as well as mineralocorticoid replacement (desoxycorticosterone [DOCP], 2.2 mg/kg IM/SC, typically given monthly and adjusted as needed on the basis of serial electrolyte determinations); the initial monthly DOCP dose for an average-sized cat is 12.5 mg IM/SC; though not preferred, an alternative means of administering glucocorticoid replacement to cats is Depo-Medrol® (10 mg IM monthly).
- Prednisone dose is adjusted based on clinical signs and side effects; the dose is decreased if PU/PD, polyphagia, and muscle wasting are present, but increased if vomiting, diarrhea, or lethargy occurs; some dogs, particularly large breeds, require less than 0.1 mg/kg/day, but all dogs with hypoadrenocorticism require some prednisone, but all dogs with hypoadrenocorticism require some glucocorticoid.
- The label dose of DOCP is 2.2 mg/kg, but this author routinely begins at 1.5 mg/kg

with owner consent to use an off-label dose.

- Alternatively, an oral mineralocorticoid replacement can be used (fludrocortisone acetate 5–10 µg/kg PO q12h, adjusted by 0.05–0.1 mg increments on the basis of serial electrolyte determinations); fludrocortisone has some glucocorticoid activity and the maintenance dose of prednisone for patients receiving fludrocortisone may be lower than for dogs receiving DOCP; a few dogs develop PU/PD and/or polyphagia from fludrocortisone.
- Patients with confirmed atypical and secondary hypoadrenocorticism require only glucocorticoid supplementation (prednisone 0.1–0.2 mg/kg/day PO), adjusted as described above.

PRECAUTIONS

N/A

ALTERNATIVE DRUG(S)

See Hyperkalemia; Hyponatremia.



FOLLOW-UP

PATIENT MONITORING

- Depending on clinical presentation, patients hospitalized for treatment of hypoadrenocorticism may require intensive monitoring and frequent laboratory evaluations; monitor clinical status, urine output, CBC, blood chemistry, and ECG as needed; blood glucose and electrolytes may need to be evaluated several times daily during initial therapy; arterial or venous blood gas analysis may be of benefit.
- Monitor for melena, as some dogs experience severe gastrointestinal blood loss during and following a crisis, sometimes requiring blood transfusion.
- Measure electrolyte concentrations 2 and 4 weeks following the first injection of DOCP, to determine whether the dose (2 weeks) and the dosing interval (4 weeks, prior to next injection) are appropriate; recheck electrolytes prior to next injection and each time the dose or dosing interval is adjusted; then check electrolyte concentrations every 6 months, or when the patient is sick.
- DOCP is usually required at monthly intervals; rare patients need injections as often as every 3 weeks; some dogs may require DOCP less than every 28–30 days; however, the author prefers to adjust the dose instead of extending the dosing interval, and does not decrease the dose (as directed below) and extend the dosing interval in the same dog.
- The majority of dogs with hypoadrenocorticism will be well controlled on a maintenance DOCP dose of 1.5 mg/kg/injection every month; if necessary based on expense, the DOCP dosage can be sequentially decreased by 10% each month

(CONTINUED)

HYPOADRENOCORTICISM (ADDISON'S DISEASE)

based on electrolyte determinations, as some dogs can be controlled on a monthly dosage that is less than 1.5 mg/kg; make sure that the owner is aware that this is off-label use.

- Adjust the daily dose of fludrocortisone by 0.05–0.1 mg increments as needed, based on serial electrolyte determinations; following initiation of therapy, check electrolyte levels weekly until they stabilize in the normal range; thereafter, check electrolyte concentrations monthly for the first 3–6 months and then every 3–12 months.
- In many dogs given fludrocortisone, the daily dose required to control the disorder increases incrementally, usually during the first 6–24 months of therapy; in most dogs, the final fludrocortisone dosage needed is 20–30 µg/kg/day PO; very few can be controlled on 10 µg/kg/day or less.
- In patients that were initially azotemic, monitor creatinine concentrations as needed following discharge from the hospital.

PREVENTION/AVOIDANCE

- Continue hormone replacement therapy for the lifetime of the patient.
- Increase the dosage of replacement glucocorticoid during periods of stress such as travel, boarding, hospitalization, and surgery.

POSSIBLE COMPLICATIONS

- PU/PD may occur from prednisone administration, but this usually resolves with a decrease in dosage; rarely, it is necessary to try an alternative glucocorticoid, such as methylprednisolone, when the dog's clinical signs are not controlled on a dose of prednisone that is low enough to eliminate side effects.

- PU/PD may occur from fludrocortisone administration.

- Side effects from DOCP are uncommon; rarely weight gain and PU/PD are seen.

EXPECTED COURSE AND PROGNOSIS

- Except for patients with primary hypoadrenocorticism caused by granulomatous or metastatic disease and secondary hypoadrenocorticism caused by a pituitary mass, the vast majority of patients have a good to excellent prognosis following proper stabilization, treatment, and monitoring.
- Owners must be reminded that they should not skip DOCP injections, as this could precipitate a potentially fatal, and inevitably costly, Addisonian crisis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Concurrent endocrine gland failure occurs in up to 5% of dogs—hypothyroidism, diabetes mellitus, and/or hypoparathyroidism.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

None

SYNONYMS

Addison's disease.

SEE ALSO

- Hyperkalemia.
- Hyponatremia.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- ALT = alanine aminotransferase.
- DOCP = desoxycorticosterone.
- PU/PD = polyuria/polydipsia.

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Acknowledgment The author and book editors acknowledge the prior contribution of Deborah S. Greco.



**Client Education Handout
available online**

HYPOALBUMINEMIA



BASICS

DEFINITION

Hypoalbuminemia defined as measured serum albumin value less than reference range.

PATHOPHYSIOLOGY

- Albumin—constitutive protein exclusively synthesized in liver.
- Provides 75–80% of plasma colloid oncotic pressure.
- Low oncotic pressure due to serum albumin <1.5 g/dL permits fluid extravasation into interstitial and third-space compartments, causing edema and body cavity effusion.

SYSTEMS AFFECTED

Cardiovascular and respiratory—transudative effusions (pleural effusion, ascites); peripheral edema; pulmonary edema.

INCIDENCE/PREVALENCE

Accompanies many primary diseases that cause hepatic insufficiency, protein-losing enteropathy (PLE), protein-losing nephropathy (PLN), hemorrhage, negative acute-phase response in chronic disease.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Underlying disease may have breed predilection.

Mean Age and Range

Varies with syndrome association.

Predominant Sex

N/A

SIGNS

General Comments

- Reflect primary disease leading to hypoalbuminemia.
- Hypoalbuminemia influences metabolite and xenobiotic protein binding, plasma oncotic pressure, third-space fluid distribution, acid-base balance, and ability to maintain intravascular perfusion pressure.

Historical Findings

- Vary with underlying disease.
- Increased drug-related effects due to reduced protein binding.

Physical Examination Findings

- Vary with underlying primary disease.
- Serum albumin ≤1.5 g/dL often associated with pitting edema, decreased heart/lung sounds, and/or abdominal fluid wave.

CAUSES

Decreased Albumin Production

- Chronic hepatic insufficiency—chronic hepatitis; cirrhosis; idiopathic hepatic fibrosis; granulomatous hepatitis; congenital portosystemic shunt (PSS; dogs).

- Inadequate nutritional intake/absorption (modest effect).

Extracorporeal Albumin Loss

- PLN—amyloidosis; glomerulonephritis.
- PLE—lymphangiectasia; lymphoma; severe inflammatory bowel disease (IBD); histoplasmosis; pythiosis; chronic intussusception; Addison's disease.
- Severely exudative cutaneous lesions.
- Chronic severe blood loss—usually enteric.
- Repeated large-volume paracentesis of abdominal or pleural effusion.

Sequestration: Body Cavities/Tissues

- Inflammatory effusions—pancreatitis; septic or aseptic peritoneal or pleural effusions; chylous effusions (modest effect).
- Vasculopathies—immune-mediated (systemic lupus erythematosus [SLE]); infectious (Ehrlichia, Rocky Mountain spotted fever); sepsis syndrome; other (modest effect).

Miscellaneous

Downregulated albumin synthesis—hyperglobulinemia, negative acute-phase response, negative nitrogen intake, catabolism (modest effect).

RISK FACTORS

- Diseases of the liver, kidney, intestines, and blood vessels.
- Negative nitrogen balance; poor nutrition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Severe hepatic disease—may see jaundice; hepatic encephalopathy (HE); ascites.
- PLE—diarrhea common but inconsistent.
- Cutaneous lesions—must be severe and exudative (burns, toxic epidermal necrolysis [TEN], vasculitis, tumors, trauma).
- External blood loss—hemorrhage (enteric, urinary, other).
- Malnutrition—mild hypoalbuminemia.
- Aggressive fluid therapy—exacerbates low albumin.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Depends on underlying disease.
- Severe hepatic disease—red blood cell (RBC) microcytosis suggests PSS.
- Severe blood loss—regenerative anemia or microcytic/hypochromic anemia.

Biochemistry

- Chronic hepatic disease—low albumin; normal to high globulin.
- PLE—low albumin; variable globulin.
- PLN—low albumin; globulin usually normal but may be low with severe PLN.
- Exudative losses—low albumin; variable globulin.
- Malnutrition—low albumin; normal globulin.
- Severe blood loss—low albumin; low to normal globulin.

- Cholesterol—low with chronic hepatic disease, severe PLE, Addison's disease, and severe malnutrition; high with PLN and pancreatitis.
- Hepatic enzymes—alanine aminotransferase (ALT) may be high with chronic hepatitis, IBD causing PLE; high alkaline phosphatase (ALP) often seen with systemic inflammation as well as hepatic disease.
- Bilirubin—sometimes high with hepatic disease.
- Blood urea nitrogen (BUN)—often low with hepatic insufficiency or patients undergoing diuresis; high with reduced renal function or dehydration.
- Hyperkalemia and hyponatremia—suggest hypoadrenocorticism, third-space effusions, or pseudohypoadrenocorticism (endoparasitism).
- Spurious hypocalcemia—due to low protein.

Urinalysis

- Rules out PLN and urologic blood loss.
- Obtain urine by cystocentesis to avoid lower-tract contamination; *caution:* beware cystocentesis-induced microhematuria.
- Proteinuria—confirm dipstick detection with chemical determination.
- Urine protein : creatinine (UP : UCr) ratio—important; >3.0 compatible with nephrotic range proteinuria; must evaluate urine sediment: spurious positive values with active sediment (i.e., substantial pyuria, macroscopic hematuria, bacteriuria); many dogs with glomerulonephritis have hyaline, waxy, or granular casts; bacterial culture of urine necessary to rule out bacteriuria as cause of increased urine protein.
- Microalbuminuria—not helpful.
- Ammonium biurate crystalluria—hepatic insufficiency, PSS, or acquired portosystemic shunt (APSS).

OTHER LABORATORY TESTS

- Total serum bile acids (TSBA)—usually high with severe hepatic disease; sometimes spurious low values with PLE (fat malabsorption).
- Physicochemical evaluation of effusion—transudate (usually pure) if hypoalbuminemia is the major causal factor.
- Antithrombin (AT)—may be low with PLE, PLN, and hepatic synthetic failure.
- Protein C (PC)—may be low with severe hepatic disease/failure, PSS, sepsis.

IMAGING

- Thoracic radiography—pleural effusion; pulmonary edema; lymphadenopathy, metastatic disease, cardiac or pulmonary disorders.
- Abdominal radiographs—effusion; altered hepatic size; mass lesions; pancreatic disease.
- Abdominal ultrasonography—small liver, lymphangiectasia in intestinal wall/mucosa, mass lesions, fluid pockets, altered portal blood flow, mesenteric lymphadenopathy, biliary tree abnormalities, renal abnormalities.

DIAGNOSTIC PROCEDURES

- Hepatic biopsy—after evaluating coagulation (mucosal bleeding time, platelet count) status.
- Renal biopsy—differentiates

(CONTINUED)

amyloidosis from glomerulonephritis; submit samples for special renal panel staining and electron microscopy. • Intestinal biopsy—endoscopic or surgical.

PATHOLOGIC FINDINGS

Depend on underlying causal disease.



TREATMENT

APPROPRIATE HEALTH CARE

- Diverse, depends on cause. • Pleural/peritoneal effusion restricting ventilation—perform centesis.

NURSING CARE

Provide physical therapy and walk patient to improve mobilization of peripheral edema.

DIET

- Achieve positive energy and nitrogen balance. • HE—control protein intake (see Hepatic Encephalopathy). • PLE with IBD component—novel/hydrolyzed protein (see Inflammatory Bowel Disease). • PLE due to lymphangiectasia—feed ultra-low-fat diet. • PLN—feed high-quality/reduced-protein diet.

SURGICAL CONSIDERATIONS

Severe hypoalbuminemia delays healing, anesthetic drug metabolism, body cavity effusions may complicate drug dosing and dispersal, surgical approach, patient ventilation.



MEDICATIONS

DRUG(S) OF CHOICE

- Depend on underlying disease.
- Glucocorticoids—for some types of chronic hepatitis and some PLEs; prednisolone is preferred if it is effective; dexamethasone lacks mineralocorticoid effects that lessens sodium and water retention, but has greater potential for ulceration/erosion. • Diuretics—furosemide (1–4 mg/kg IV/IM/PO q4–12h) in combination with spironolactone (1–4 mg/kg q12h) in patients with hepatic or cardiac disease, combine with low-salt diet, use judiciously to avoid intravascular volume contraction; for body cavity effusion mobilization, taper diuretic dose after initial positive response; diuretics may be used intermittently to mobilize recurring ascites.
- Antithrombotic treatment (low AT, PC, evidence of thrombi)—clopidogrel (0.5–1.0 mg/kg PO q24h), especially in PLN.

- Enalapril (0.5 mg/kg PO q12–24h)—for dogs with PLN; alternatives are benazepril or the angiotensin receptor blocker telmisartan (1 mg/kg PO q24h).

CONTRAINdications

Synthetic colloids—avoid with anuria, renal failure, congestive heart failure, severe coagulopathy, or von Willebrand disease.

PRECAUTIONS

- Fluid therapy—avoid overdosing crystalloid fluids, especially when administered with synthetic colloids as these are rapidly distributed into interstitial spaces (70% volume within 1 hour), aggravating antecedent pulmonary or limb edema, and body cavity effusions; restrict maintenance fluid volume of crystalloids to one-third normal (depending on contemporary losses) when used with colloids.
- Transfusion of canine plasma or human albumin—may be complicated by transfusion or allergic reactions; plasma and albumin transfusions of dubious value if severe ongoing protein loss due to PLN, PLE, vasculitis.
- Diuretic therapy—high doses may cause severe intravascular volume contraction leading to azotemia, hypotension, and electrolyte and acid-base derangements. • Unanticipated drug side effects—due to reduced albumin drug binding. • Use of 1 desamino-8-darginine vasopressin (DDAVP) for bleeding—may aggravate fluid retention and associated complications. • Glucocorticoids—mineralocorticoid effects of some drugs may worsen fluid accumulation; prefer synthetic glucocorticoids without mineralocorticoid effects.

POSSIBLE INTERACTIONS

Inadvertent overdosing of drugs with high-protein binding.



FOLLOW-UP

PATIENT MONITORING

- Bodyweight—especially during fluid therapy; monitors fluid retention. • Vital signs, thoracic auscultation for crackles—monitor for pulmonary edema. • Sequential serum albumin concentrations. • Blood pressure—monitors vascular expansion. • Abdominal girth—monitors ascites. • Central venous pressure—unreliable; potentially dangerous in patients with bleeding or thrombotic tendencies.

PREVENTION/AVOIDANCE

Limit glucocorticoid exposure as much as possible; use alternative medications to control primary illness if possible.

Hypoalbuminemia

POSSIBLE COMPLICATIONS

- PLN/PLE—may be complicated by thromboembolism; minimize IV catheterization and trauma. • Hypovolemia—from dehydration, Addisonian crisis, blood loss, or diuretic overdose predisposes to acute renal failure, disseminated intravascular coagulation (DIC), or HE.

EXPECTED COURSE AND PROGNOSIS

Depend on underlying cause.

H



MISCELLANEOUS

ASSOCIATED CONDITIONS

Numerous diverse diseases or syndromes.

PREGNANCY/FERTILITY/BREEDING

Condition complicates pregnancy.

SEE ALSO

- Amyloidosis.
- Cirrhosis and Fibrosis of the Liver.
- Ductal Plate Malformation (Congenital Hepatic Fibrosis).
- Glomerulonephritis.
- Lymphangiectasia.
- Portosystemic Shunting, Acquired.
- Portosystemic Vascular Anomaly, Congenital.
- Protein-Losing Enteropathy.

ABBREVIATIONS

- ALP = alkaline phosphatase.
- ALT = alanine aminotransferase.
- APSS = acquired portosystemic shunt.
- AT = antithrombin.
- BUN = blood urea nitrogen.
- DDAVP = 1 desamino-8-darginine vasopressin.
- DIC = disseminated intravascular coagulation.
- HE = hepatic encephalopathy.
- IBD = inflammatory bowel disease.
- PC = protein C.
- PLE = protein-losing enteropathy.
- PLN = protein-losing nephropathy.
- PSS = portosystemic shunt.
- RBC = red blood cell.
- SLE = systemic lupus erythematosus.
- TEN = toxic epidermal necrolysis.
- TSBA = total serum bile acids.
- UP : UCr = urine protein : urine creatinine ratio.

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HYPOGLYCEMIA



BASICS

DEFINITION

Blood glucose concentration below the lower reference interval (generally <60 mg/dL).

PATHOPHYSIOLOGY

Mechanisms responsible for hypoglycemia:

- Excess insulin or insulin-like factors (e.g., insulinoma, extrapancreatic paraneoplasia [insulin-like growth factor-2 (IGF-2)], xylitol toxicosis, iatrogenic insulin overdose).
- Reduced hepatic gluconeogenesis and glycogenolysis (e.g., hepatic disease, glycogen storage diseases, hypoadrenocorticism, sepsis).
- Excessive metabolic use of glucose (e.g., in hunting dogs, pregnancy, neoplasia, polycythemia, and sepsis).
- Reduced intake or underproduction of glucose (e.g., in puppies and kittens, toy breeds, glycogen storage disease, and severe malnutrition or starvation).

SYSTEMS AFFECTED

- Musculoskeletal.
- Nervous.

SIGNALMENT

- Dog and cat.
- Variable, depending on the underlying cause.

SIGNS

- Seizures.
- Posterior paresis.
- Weakness.
- Collapse.
- Muscle fasciculations.
- Abnormal behavior.
- Lethargy and depression.
- Ataxia.
- Polyphagia.
- Weight gain.
- Exercise intolerance.
- Some animals appear normal aside from findings associated with underlying disease.
- Many animals have episodic signs.
- Polyneuropathy.

CAUSES

Endocrine

- Insulinoma.
- Extrapancreatic neoplasia associated with IGF-2 overproduction (e.g., hepatocellular carcinoma, hepatocellular adenoma, intestinal leiomyoma or leiomyosarcoma).
- Iatrogenic insulin overdose.
- Hypoadrenocorticism.
- Islet cell hyperplasia (nesidioblastosis).

Hepatic Disease

- Portosystemic shunt.
- Cirrhosis.
- Severe hepatitis (e.g., toxic and inflammatory).
- Glycogen storage diseases.

Overuse

- Hunting dog (exertional) hypoglycemia.
- Pregnancy.
- Polycythemia.
- Neoplasia.
- Sepsis—increased glucose utilization induced by cytokine production in macrophage-rich tissues.

Reduced Intake/Underproduction

- Young puppies and kittens.
- Toy-breed dogs.
- Severe malnutrition or starvation.
- In sepsis there is also cytokine-induced inhibition of gluconeogenesis in the setting of nutritional glycogen depletion.

Toxicosis

- Iatrogenic insulin overdose.
- Xylitol toxicosis.
- Antihyperglycemic agent toxicosis (e.g., sulfonylureas).

RISK FACTORS

- Low energy intake predisposes to hypoglycemia in patients with conditions causing overuse and underproduction.
- Fasting, excitement, exercise, and eating may or may not increase the risk of hypoglycemic episodes in patients with insulinoma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Patients with hyperinsulinism—signs of hypoglycemia or a normal physical examination.
- Patients with hypoadrenocorticism—waxing, waning, nonspecific signs (e.g., vomiting, diarrhea, melena, weakness); Addisonian patients that present in a crisis usually display hypovolemia and hyperkalemia rather than hypoglycemia (e.g., shock, bradycardia, dehydration).
- Patients with portosystemic shunts—usually young to middle-aged; often thin or appear to have stunted growth; rarely, they have ascites or edema.
- Patients with cirrhosis and severe hepatitis usually have other signs of their disease (e.g., gastrointestinal abnormalities, icterus, and ascites or edema).
- Patients with sepsis—critical; usually in shock; pyrexia or hypothermia revealed by examination; may have gastrointestinal abnormalities.
- Glycogen storage diseases—rare; usually younger animals.
- Extrapancreatic neoplasia and large neoplastic processes (hepatoma) that cause hypoglycemia may be detected by physical examination.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

None

Procedures That May Alter Laboratory Results

Delayed separation of serum causes falsely low serum glucose values; if serum cannot be separated within 30 minutes of collection, it should be collected in a sodium fluoride (gray-stoppered) tube. Polycythemia may result in false hypoglycemia if measured on a point-of-care glucometer.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Patients with hyperinsulinism may have normal results.
- Patients with hypoadrenocorticism may have hypocholesterolemia, hypoalbuminemia, lymphocytosis, eosinophilia, hyperkalemia, hyponatremia, azotemia, or hypercalcemia.
- Patients with congenital portosystemic shunts may have microcytosis, hypoalbuminemia, low blood urea nitrogen, slightly elevated liver enzyme activities, ammonium biurate crystalluria, and hyposthenuria. Serum bilirubin concentration sometimes increased.
- Patients with cirrhosis, severe hepatitis, and hepatic neoplasia may have anemia associated with chronic disease, high liver enzyme activities, hyperbilirubinemia, hypoalbuminemia, bilirubinuria, and hyposthenuria.
- Patients with xylitol toxicosis may have hypokalemia and later signs of hepatic failure.

OTHER LABORATORY TESTS

- Simultaneous fasting glucose/insulin determination—indicated when insulinoma is suspected; plasma insulin concentration within the upper end or above reference range in the face of hypoglycemia (glucose <60 mg/dL) suggests insulinoma.
- Baseline cortisol ± adrenocorticotropic hormone stimulation test—to diagnose hypoadrenocorticism.
- Fasting and postprandial serum bile acids—diagnose portosystemic shunt or functional hepatic disease.
- Free abdominal fluid should be collected and analyzed.
- Fructosamine—chronic hypoglycemia will result in low fructosamine concentrations.

IMAGING

- Abdominal radiography and ultrasonography—useful in patients with extrapancreatic neoplasia and large neoplastic processes (may see organomegaly or masses), as well as portosystemic shunt (microhepatica), cirrhosis (microhepatica, hyperechogenicity), and severe hepatopathy. Not very sensitive nor specific for detecting insulinoma. Abdominal CT more accurately detects pancreatic endocrine tumors.

HYPOGLYCEMIA

(CONTINUED)

- Ultrasound-guided, laparoscopic, or surgical hepatic biopsy—useful to evaluate hepatic parenchymal disease.
- Technetium-99m quantitative hepatic scintigraphy—to detect portosystemic shunt.
- Mesenteric portography—to detect portosystemic shunt (requires surgery).

DIAGNOSTIC PROCEDURES

H

Ultrasound-guided or surgical tissue biopsy—useful to evaluate hepatic parenchymal disorders and extrapancreatic neoplasia.



TREATMENT

- Animals with clinical hypoglycemia should be treated as inpatients.
- If able to eat (i.e., responsive, no vomiting), feeding should be part or all of initial treatment.
- If unable to eat, start continuous IV fluid therapy with 2.5–5% dextrose solution.
- Surgery is indicated if a portosystemic shunt or neoplasia is the cause of hypoglycemia.



MEDICATIONS

DRUG(S) OF CHOICE

Emergency/Acute Treatment

- In hospital—administer 50% dextrose 0.5 g/kg IV, diluted 1 : 3 as slow bolus. Glucagon as IV CRI at 5–10 ng/kg/min is transiently effective in cases of insulin-secreting tumors.
- At home—client should not administer medication orally during a seizure; hypoglycemic seizures usually abate within 1–2 min; if a seizure is prolonged, recommend transport to hospital; if a short seizure has ended or other signs of a hypoglycemic crisis exist, recommend rubbing corn syrup or 50% dextrose on the buccal mucosa, followed by 2 mL/kg of the same solution orally once the patient can swallow; then seek immediate attention.
- Owners of diabetic animals can be taught to inject prescribed glucagon 0.03 mg/kg IM.
- Initiate frequent feeding of a diet low in simple sugars or, if patient is unable to eat, continuous fluid therapy with 2.5 or 5% dextrose solution.

Long-Term Treatment

- See Insulinoma for treatment considerations.
- Hunting dog hypoglycemia—feed moderate meal of fat, protein, and complex carbohydrates a few hours before hunting;

can feed snacks (e.g., dog biscuits) every 3–5 hours during the hunt.

- Toy-breed hypoglycemia—increase frequency of feeding.
- Puppy and kitten hypoglycemia—increase frequency of feeding.
- Other causes of hypoglycemia require treating the underlying disease and do not usually need long-term treatment (exception: glycogen storage disease type 1).

CONTRAINdications

- Insulin.
- Barbiturates and diazepam do not treat cause in patients with hypoglycemic seizures; may potentially worsen hepatoencephalopathy in patients with hepatic disease.

PRECAUTIONS

- 50% dextrose causes tissue necrosis and sloughing if given extravascularly; may cause phlebitis at concentrations above 5%.
- Administration of a dextrose bolus without subsequent frequent feedings or IV fluids with dextrose can predispose to hypoglycemic episodes.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Based on underlying disease.
- At home—for return or progression of clinical signs of hypoglycemia; assess serum glucose if signs recur.
- Single, intermittent serum glucose determinations may not reflect true glycemic status of patient because of counter-regulatory hormones.
- If due to insulin overdose in the diabetic (or postinsulinoma resection diabetes), reassess response to insulin with a blood glucose curve and adjust the insulin dose accordingly. Check for metastatic insulinoma.

POSSIBLE COMPLICATIONS

Recurrent, progressive episodes of hypoglycemia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Prolonged hypoglycemia can cause transient (hours to days) to permanent dementia and blindness.

AGE-RELATED FACTORS

Neonatal animals have poor glycogen storage capacity and reduced capacity for gluconeogenesis; thus, short periods of fasting (6–12 hours) can cause hypoglycemia.

Important to remember when fasting prior to and following anesthesia.

PREGNANCY/FERTILITY/BREEDING

Hypoglycemia can lead to weakness and dystocia.

SEE ALSO

- Cirrhosis and Fibrosis of the Liver.
- Glycogen Storage Disease.
- Hepatocellular Adenoma.
- Hepatocellular Carcinoma.
- Hypoadrenocorticism.
- Insulinoma.
- Leiomyoma, Stomach, Small and Large Intestine.
- Leiomyosarcoma, Stomach, Small and Large Intestine.
- Paraneoplastic Syndromes.
- Portosystemic Shunting, Acquired.
- Portosystemic Vascular Anomaly, Congenital.
- Sepsis and Bacteremia.
- Xylitol Toxicosis.

ABBREVIATIONS

- IGF = insulin-like growth factor.

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Client Education Handout
available online

HYPOKALEMIA



BASICS

DEFINITION

Serum potassium concentration <3.5 mEq/L (normal range: 3.5–5.5 mEq/L).

PATHOPHYSIOLOGY

- Potassium is primarily an intracellular electrolyte (98% of total body potassium is intracellular); serum levels, however, may not accurately reflect total body stores.
- It is predominantly responsible for the maintenance of intracellular fluid volume and required for normal function of many enzymes.
- Resting cellular membrane potential is determined by the ratio of intracellular to extracellular potassium concentration and maintained by the Na^+/K^+ -adenosine triphosphate (ATPase) pump. Conduction disturbances in susceptible tissues (cardiac, nerve, muscle) are caused by rapid shifts in this ratio causing myoneural membrane hyperpolarization.
- Hypokalemia can be caused by decreased intake, loss (via the gastrointestinal tract or kidneys), or translocation of potassium from the extracellular to the intracellular fluid space.

SYSTEMS AFFECTED

- Neuromuscular—muscle weakness, including skeletal and muscles of respiration.
- Cardiac—electrocardiac changes and arrhythmias.
- Renal—hyposthenuria, nephropathy, and renal failure.
- Metabolic—acid-base balance (metabolic alkalosis); glucose homeostasis.

SIGNALMENT

- Dogs and cats with predispositions to increased potassium loss, translocation of potassium, or decreased intake of potassium.
- Young Burmese cats with recurrent hypokalemic periodic paralysis episodes.

SIGNS

- Generalized muscle weakness or paralysis.
- Muscle cramps.
- Lethargy and confusion.
- Vomiting.
- Anorexia.
- Carbohydrate intolerance and weight loss.
- Polyuria (PU).
- Polydipsia (PD).
- Decreased bowel motility (humans; maybe dogs and cats).
- Hyposthenuria.
- Ventroflexion of the neck.
- Respiratory muscle failure.

CAUSES

Decreased Intake

- Anorexia or starvation.
- Potassium deficient diet.
- Administration of potassium-deficient or potassium-free intravenous fluids.

- Bentonite clay ingestion (e.g., clumping cat litter).

Gastrointestinal Loss

- Vomiting.
- Diarrhea.
- Both upper and lower gastrointestinal obstruction, especially pyloric outflow obstruction.

Urinary Loss

- Chronic kidney disease (CKD).
- Renal tubular acidosis.
- Hypokalemic nephropathy.
- Postobstructive diuresis.
- Dialysis (hemodialysis or peritoneal).
- Intravenous fluid diuresis.
- Hyperaldosteronism.
- Hypochloremia.
- Drugs (loop diuretics, amphotericin B, penicillins, fludrocortisone, desoxycorticosterone pivalate).

Translocation (Extracellular to Intracellular Fluid)

- Glucose administration.
- Insulin administration or release.
- Sodium bicarbonate administration.
- Catecholamines.
- Alkalemia.
- Beta2-adrenergic agonist overdose (e.g., albuterol, terbutaline).
- Hypokalemic periodic paralysis (Burmese cats).
- Rattlesnake envenomation (presumably from catecholamine release).

RISK FACTORS

- Acidifying diets with negligible potassium.
- Diuresis or dialysis with potassium-deficient fluids.
- Chronic illness (sustained anorexia and muscle wasting).
- Hypomagnesemia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- PU/PD, hyperglycemia, and glucosuria—rule out diabetes mellitus.
- PU/PD, azotemia, and isosthenuria—rule out CKD and nephropathy, especially in cats.
- Vomiting, metabolic alkalosis, and hypochloremia—rule out upper gastrointestinal obstruction.
- Metabolic acidosis with urine pH >6.5—rule out renal tubular acidosis.
- Urethral obstruction—rule out postobstructive diuresis.
- Hypertension with or without azotemia—rule out hyperaldosteronism.
- Young Burmese cat with episodic muscle weakness—rule out hypokalemic periodic paralysis.

LABORATORY FINDINGS

Chemicals That May Alter Laboratory Results

Falsely elevated potassium measurement can be caused by excessive K_3EDTA relative to the blood sample, as found in “purple-top” blood tube for hematology; not a problem with additive-free “red-top” tubes for serum.

Valid if Run in Human Laboratory?

Yes

H

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperglycemia, glucosuria, ± ketonuria, ± ketoacidosis in patients with diabetes mellitus.
- Normocytic, normochromic, nonregenerative anemia in patients with CKD.
- Elevated blood urea nitrogen (BUN) and creatinine concentrations, with isosthenuria in patients with CKD or hypokalemic nephropathy.
- Low total CO_2 or HCO_3^- —in patients with renal tubular acidosis (RTA) or renal failure.
- Normal anion gap metabolic acidosis in RTA.
- Urine pH >6.5 in patients with distal tubular acidosis.
- High total CO_2 or HCO_3^- —in patients with metabolic alkalosis.
- High PCO_2 with hypoventilation.

OTHER LABORATORY TESTS

- Increased aldosterone and decreased renin in patients with primary hyperaldosteronism.
- Elevated urinary fractional excretion of potassium in patients with CKD, hypokalemic nephropathy, and primary hyperaldosteronism.
- Adrenocorticotrophic hormone (ACTH) stimulation tests are used to diagnose adrenal gland disorders.

IMAGING

- Radiography, ultrasonography are helpful to diagnose gastrointestinal tract obstructions (mass or foreign bodies), pancreatitis, CKD workup, adrenal gland diseases (adrenocortical hyperplasia, adrenocortical neoplasia).
- Upper gastrointestinal barium study to additionally diagnose gastrointestinal obstructions (anatomic or functional).
- CT to further diagnose adrenal gland, renal, and gastroenteric disorders.

DIAGNOSTIC PROCEDURES

Upper gastrointestinal endoscopy to diagnose upper gastrointestinal disorders.



TREATMENT

- Mild hypokalemia (3.0–3.5 mEq/L) can be treated by oral supplementation.
- Moderate hypokalemia (2.5–3.0 mEq/L) is best treated by inpatient administration of oral ± intravenous supplementation and carefully monitored.
- Patients with severe hypokalemia (<2.5 mEq/L) should be hospitalized for intensive intravenous potassium supplementation.

HYPOKALEMIA

(CONTINUED)

Table 1

| Patient's K ⁺ Concentration | KCl/L (mEq) | Dosage (mEq K ⁺ /kg/h, IV) |
|----------------------------------------|-------------|---------------------------------------|
| 3.5–4.5 | 20 | 0.05–0.1 |
| 3.0–3.5 | 30 | 0.1–0.2 |
| 2.5–3.0 | 40 | 0.2–0.3 |
| 2.0–2.5 | 60 | 0.3–0.4 |
| <2.0 | 80 | 0.5–1.5 |

Note: do not exceed an intravenous supplementation rate of 0.5 mEq/kg/h unless continually monitoring and on the verge of ventilator muscle failure. With severe life-threatening hypokalemia (serum potassium <2.0 mEq/L), potassium chloride can be administered at a rate of 1.0–1.5 mEq/kg/h with ECG monitoring.

Patients, especially cats, should be carefully monitored for cardiac arrhythmias, rhabdomyolysis and impaired ventilation.

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

- Oral supplementation with potassium gluconate (e.g., Tumil-K[®]) is effective in mildly affected patients. The initial dosage is 2 mEq/4.5 kg bodyweight in food twice daily.
- Parenteral supplementation is required in anorectic or vomiting patients or in patients with moderate to severe hypokalemia (<3.0 mEq/L). Potassium chloride is added to intravenous fluids and delivered according to Table 1, best administered via infusion pump or with a pediatric fluid administration set (60 drops/mL). Monitor and taper accordingly.
- Provide magnesium sulfate, if hypomagnesemic; 1.0 mEq/kg/24h by CRI, or a 0.25 mEq/kg slow IV bolus.

CONTRAINDICATIONS

- Glucose supplementation.
- Insulin administration.
- Sodium bicarbonate administration.
- Untreated hypoadrenocorticism.
- Hyperkalemia.
- Oliguric or anuric renal failure or severe renal impairment.
- Rapid rehydration to correct severe dehydration (i.e., potassium-supplemented fluids should not be bolused IV).

PRECAUTIONS

Administer with caution, avoid over-supplementation, do not bolus, monitor frequently.

POSSIBLE INTERACTIONS

Concurrent potassium supplementation with angiotensin-converting enzyme (ACE) inhibitors (e.g., enalapril), potassium-sparing diuretics (e.g., spironolactone), prostaglandin inhibitors (e.g., nonsteroidal anti-inflammatory drugs), beta blockers (e.g., atenolol), or cardiac glycosides (e.g., digoxin) can cause adverse effects.

ALTERNATIVE DRUG(S)

Potassium phosphate can be used in patients with concurrent hypophosphatemia where one-half of the potassium dose (in mEq) is administered in the form of potassium phosphate solution.

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

Check serum potassium every 6–24 hours based on severity of hypokalemia.

POSSIBLE COMPLICATIONS

Electrolyte disturbances and severe bradycardia. It is essential to close the IV fluid outflow valve and thoroughly mix the fluid contents when adding potassium chloride solution to the parenteral fluid bag.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Hypokalemic nephropathy.
- Hypophosphatemia.
- Hypomagnesemia.
- Metabolic alkalosis.

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING
N/A**SEE ALSO**

- Alkalosis, Metabolic.
- Chronic Kidney Disease.
- Diarrhea, Chronic—Cats.
- Diarrhea, Chronic—Dogs.
- Hypochloremia.
- Renal Tubular Acidosis.
- Vomiting, Chronic.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- ACTH = adrenocorticotrophic hormone.
- ATPase = adenosine triphosphate.
- BUN = blood urea nitrogen.
- CKD = chronic kidney disease.
- PD = polydipsia.
- PU = polyuria.
- RTA = renal tubular acidosis.

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HYPOPARATHYROIDISM



BASICS

DEFINITION

Absolute or relative deficiency of parathyroid hormone (PTH) secretion leading to hypocalcemia.

PATHOPHYSIOLOGY

- Dogs—most commonly idiopathic immune-mediated parathyroiditis, rarely following bilateral thyroidectomy or following severe cervical trauma.
- Cats—most commonly iatrogenic secondary to damaged or removed parathyroid glands during thyroidectomy; idiopathic atrophy and immune-mediated parathyroiditis uncommon.

SYSTEMS AFFECTED

- Cardiovascular—ECG changes and bradycardia.
- Gastrointestinal—anorexia and vomiting, possibly (altered gastrointestinal muscular activity).
- Nervous/neuromuscular—seizures, tetany, ataxia, weakness (diminished neuronal membrane stability).
- Ophthalmic—posterior lenticular cataracts.
- Respiratory—panting (neuromuscular weakness, anxiety).

INCIDENCE/PREVALENCE

- Dog—uncommon.
- Cat—common (10–82%) following bilateral thyroidectomy; spontaneous occurrence rare.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Toy poodle, miniature schnauzer, German shepherd dog, Labrador retriever, terrier breeds; mixed-breed cats.

Mean Age and Range

- Dogs—mean 4.8 years; range: 6 weeks–13 years.
- Cats—secondary to thyroidectomy, mean 12–13 years; range: 4–22 years.
- Cats—spontaneous, mean 2.25 years; range: 6 months–7 years.

Predominant Sex

Dogs—female (60%); cats—male (64%).

SIGNS

Historical Findings

Dogs

- Seizures (49–86%).
- Ataxia/stiff gait (43–62%).
- Facial rubbing (62%).
- Muscle trembling, twitching, and fasciculations (57%).
- Growling (57%).
- Panting (35%).
- Weakness.
- Vomiting.
- Anorexia.

Cats

- Lethargy, anorexia, and depression (100%).
- Seizures (50%).
- Muscle trembling, twitching, and fasciculations (83%).
- Panting (33%).
- Bradycardia (17%).

Physical Examination Findings

Dogs

- Tense, splinted abdomen (50–65%).
- Ataxia/stiff gait (43–62%).
- Fever (30–70%).
- Muscle trembling, twitching, and fasciculations (57%).
- Panting (35%).
- Posterior lenticular cataracts (15–32%).
- Weakness.
- Normal physical examination (20%).

Cats

- Muscle trembling, twitching, and fasciculations (83%).
- Panting (33%).
- Posterior lenticular cataracts (33%).
- Bradycardia (17%).
- Fever (17%).
- Hypothermia (17%).

CAUSES

See Pathophysiology.

RISK FACTORS

Dogs, cats—bilateral thyroidectomy.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Seizures

- Cardiovascular—syncope.
- Metabolic—hepatoencephalopathy, hypoglycemia, other causes of hypocalcemia.
- Neurologic—epilepsy, neoplasia, toxin, inflammatory disease.

Weakness

- Cardiovascular—congenital defects, arrhythmias, heart failure, pericardial effusion.
- Metabolic—hypoadrenocorticism, hypoglycemia, anemia, hypokalemia (especially cats), hypothyroidism.
- Neurologic/neuromuscular—myasthenia gravis, polymyositis, polyradiculoneuropathy, spinal cord disease.
- Toxic—tick paralysis, botulism, chronic organophosphate exposure, snake envenomation (Eastern coral snake and other elapids, Mojave and certain other pit vipers), lead poisoning.

Muscle Trembling, Twitching, and Fasciculations

- Metabolic—puerperal tetany (i.e., eclampsia), other causes of hypocalcemia.
- Toxic—tetanus, strychnine, permethrin, snake envenomation.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram and urinalysis usually normal; perform to rule out other differential diagnoses.
- Hypocalcemia (usually <6.5 mg/dL) and normal or mild to moderate hyperphosphatemia.
- Evaluate serum albumin carefully in all patients with hypocalcemia; hypoalbuminemia is most common asymptomatic cause of hypocalcemia (assuming ionized fraction is adequate).
- The only other intrinsic disease process besides hypoparathyroidism that reduces serum calcium and raises serum phosphorus is renal failure, which is easily distinguished from hypoparathyroidism by presence of azotemia; highly concentrated

phosphate enema solutions can also cause hyperphosphatemia and hypocalcemia, as can excessive potassium phosphate parenteral fluid supplementation.

OTHER LABORATORY TESTS

Serum PTH—undetectable or very low PTH concentration; patients with other processes causing hypocalcemia (e.g., renal failure) have normal to high serum PTH concentration.

IMAGING

Atrophic parathyroid glands will not be visible with ultrasonography (normally 2–3 mm).

DIAGNOSTIC PROCEDURES

- ECG changes from hypocalcemia include prolongation of ST and QT segments; sinus bradycardia and wide T waves; occasionally T wave alternans.
- Cervical surgical exploration reveals absence or atrophy of parathyroid glands.

PATHOLOGIC FINDINGS

- Dogs—normal or diminished tissue with mature lymphocytes, plasma cells, and fibrous connective tissue along with chief cell degeneration.
- Cats—parathyroid gland atrophy more common, although histopathologic findings similar to dogs also found.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalize for medical management of hypocalcemia until clinical signs of hypocalcemia are controlled and serum total calcium concentration is >7 mg/dL.
- See Hypocalcemia for emergency inpatient management and appropriate fluid therapy.

NURSING CARE

No specific care other than seizure watch.

DIET

Avoid calcium-poor diets; for dogs, puppy diets generally higher in calcium than adult dog food.

CLIENT EDUCATION

- Naturally occurring primary hypoparathyroidism requires lifelong therapy and monitoring.
- Most cases of iatrogenic hypoparathyroidism (e.g., bilateral thyroidectomy) will recover over days to months and only require transient management and monitoring.



MEDICATIONS

DRUG(S) OF CHOICE

Emergency/Acute Therapy
See Hypocalcemia.

Short-Term Post-tetany Therapy
See Hypocalcemia.

(CONTINUED)

HYPOPARATHYROIDISM**H****Table 1**

| Vitamin D preparations. | | | |
|----------------------------------------------------------------------------|-------------------------------------------------------------------|----------------|--------------------------------------------------------------------------------------------------------------------|
| Preparation | Dose | Maximal Effect | Size |
| 1,25 Dihydroxycholecalciferol (active vitamin D ₃ , calcitriol) | 0.03–0.06 µg/kg/day | 1–4 days | 0.25 and 0.5 µg capsules, 1.0 µg/mL oral solution, and 1 and 2 µg/mL injectable |
| Dihydrotachysterol | Initial—0.02–0.03 mg/kg/day Maintenance—0.01–0.02 mg/kg/24–48h | 1–7 days | Currently unavailable in United States; formerly available as 0.125 mg, 0.2 mg, 0.4 mg tablets and 0.2 mg/mL syrup |
| Ergocalciferol (vitamin D ₂) | Initial—4000–6000 U/kg/day Maintenance—1000–2000 U/kg/day–week | 5–21 days | 25,000 and 50,000 U capsules and 8000 U/mL syrup |

Table 2

| Calcium preparations. | | | |
|-----------------------|----------------------------------------|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| Preparation | Dose of Elemental Calcium | Available Calcium | Size Available (Needs to Be Converted to Elemental Calcium) |
| Calcium carbonate | Canine—1–4 g/day Feline—0.5–1 g/day | 40% | Tablets—500, 600, 650, 1250, 1500 mg Chewable tablets—400, 420, 500, 750, 50, 1000, 1250 mg Capsules—1250 mg Oral suspension—250 mg/mL |
| Calcium gluconate | Canine—1–4 g/day Feline—0.5–1 g/day | 10% | Tablets—500, 650, 975 mg Chewable tablets—500 mg Capsules—500, 700 mg Powder for suspension—70 mg/mL |
| Calcium lactate | Canine—1–4 g/day Feline—0.5–1 g/day | 13% | Tablets—650, 770 mg Capsules—500 mg |
| Calcium acetate | Canine—1–4 g/day Feline—0.5–1 g/day | 25% | Tablets, gelcaps, and capsules—667 mg |
| Calcium citrate | Canine—1–4 g/day Feline—0.5–1 g/day | 21% | Tablets—950, 1150 mg Effervescent tablets—2,380 mg Capsules—850, 1070 mg Powder for oral suspension—725 mg/mL |
| Calcium glubionate | Canine—1–4 g/day Feline—0.5–1 g/day | 30% | Syrup—360 mg/mL |

Long-Term Therapy

- Vitamin D administration is needed indefinitely for primary hypoparathyroidism and total parathyroidectomy; dosage should be adjusted based on serum calcium concentration.
- Shorter-acting preparations of vitamin D are preferred so that overdosage (causing hypercalcemia) can be quickly corrected (see Table 1).
- A more economical approach to treatment is to maximize oral administration of calcium and reduce oral administration of vitamin D (see Table 2); calcium is usually less expensive than vitamin D; dosage is influenced by each product's available elemental calcium content.

CONTRAINDICATIONS**Hypercalcemia****PRECAUTIONS**

All calcium preparations given orally can cause nausea and constipation; calcium carbonate may be less irritating because of its high calcium availability and lower dosage requirement.

POSSIBLE INTERACTIONS

- Injectable and sometimes oral calcium solutions and tablets are incompatible with tetracycline drugs, cephalothin, methylprednisolone sodium succinate, dobutamine, metoclopramide, and amphotericin B.
- Thiazide diuretics used in conjunction with

large doses of calcium may cause hypercalcemia.

- Patients on digitalis are more likely to develop arrhythmias if calcium is administered intravenously.
- Calcium administration may antagonize effects of calcium channel blocking agents.

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

- Hypocalcemia and hypercalcemia are both concerns with long-term management.
- Once serum calcium is stable and normal, assess

HYPOPARTHYROIDISM

(CONTINUED)

serum calcium concentration monthly for the first 6 months, then every 2–4 months; goal is to maintain serum total calcium between 8 and 10 mg/dL. • Inform clients about clinical signs of hypo- and hypercalcemia.

POSSIBLE COMPLICATIONS

- Hypocalcemia if undertreated.
- Hypercalcemia, which can lead to nephrocalcinosis and kidney injury (see Hypercalcemia) and resistance to antidiuretic hormone.

EXPECTED COURSE AND PROGNOSIS

- With close monitoring of serum calcium and client dedication, the prognosis for long-term survival is excellent.
- Adjustments in vitamin D and oral calcium administration can be expected during the course of management, especially during the initial 2–6 months.
- Cats with hypoparathyroidism secondary to thyroidectomy usually require only transient treatment because they typically regain normal parathyroid function within 4–6 months, often within 2–3 weeks.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Excess muscular activity can lead to hyperthermia, which may necessitate treatment.

PREGNANCY/FERTILITY/BREEDING

Hypocalcemia can lead to weakness and dystocia.

SEE ALSO

- Hypercalcemia.
- Hyperthyroidism.
- Hypocalcemia.

ABBREVIATIONS

- PTH = parathyroid hormone.

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**Client Education Handout
available online**

HYPOTHERMIA



BASICS

Due to limited clinical literature in veterinary science, much of the information below has been extrapolated from human medical literature and experimental animal studies.

DEFINITION

- Core body temperature drops below that required for normal metabolism. In primary hypothermia, the healthy individual's compensatory responses to heat loss are overwhelmed by exposure, whereas secondary hypothermia complicates many systemic diseases.
- Stage I—90–95 °F (32–35 °C).
- Stage II—82–90 °F (28–32 °C).
- Stage III—75–82 °F (24–28 °C).
- Stage IV—<75 °F (24 °C).

PATHOPHYSIOLOGY

Normal thermoregulation balances heat gained or lost to the environment with heat produced via central thermogenesis; it is controlled by the hypothalamus with input from thermoreceptors; heat can be gained or lost to the environment via four mechanisms: evaporation, radiation, convection, and conduction; central thermogenesis generates heat via basal metabolism, muscle activity, and uncoupling of brown fat (neonates). Heat production can be augmented via shivering and increased basal metabolic rate; activation of both sympathetic nervous and endocrine systems results in increased circulating levels of thyroid-releasing hormone, catecholamines, growth hormone, and glucocorticoids, which all contribute to increased glucose utilization and basal metabolic rate. Adaptations to minimize heat loss include cutaneous vasoconstriction, piloerection, and behavioral responses such as curling up, sharing body heat, and seeking shelter.

SYSTEMS AFFECTED

- Cardiovascular**—in mild hypothermia, sympathetic stimulation induces tachycardia and peripheral vasoconstriction with normal or elevated cardiac output (CO) and BP; as the patient becomes colder, cardiac pacemaker cell depolarization is slowed, resulting in bradycardia resistant to treatment with atropine; the resultant fall in CO is balanced by increased systemic vascular resistance; at lower temperatures, bradycardia becomes progressively extreme and systemic vascular resistance falls as catecholamine release and adrenergic receptor responsiveness are blunted.
- Endocrine**—sympathetic activation and release of counter-regulatory hormones trigger increased glycogenolysis, gluconeogenesis, and lipolysis as well as inhibit the release and uptake of insulin resulting in hyperglycemia; when hypothermia develops slowly or is longlasting, glycogen stores become depleted and hypoglycemia develops.
- Gastrointestinal**—increased gastric acid production and reduced

duodenal bicarbonate secretion may predispose to gastrointestinal ulceration; ileus is common.

- Hemic**—plasma shifts and consequent hemoconcentration may lead to hyper- and hypocoagulopathy; depressed enzymatic activity of clotting factors and platelet hyporeactivity may exacerbate hypocoagulability.
- Hepatobiliary/pancreatic**—hypoxia leads to hepatocellular damage and pancreatitis.
- Musculoskeletal**—increased joint fluid viscosity and muscle stiffness.
- Nervous**—CNS metabolism and level of consciousness decrease and nerve conduction velocity progressively slows; mild incoordination is followed by lethargy, obtundation, and coma.
- Renal**—peripheral vasoconstriction increases renal blood flow and glomerular filtration rate resulting in increased urine production; progressive tubular dysfunction and antidiuretic hormone resistance contribute further to cold diuresis; later, urine output decreases as result of falling CO; acute kidney injury may ensue.
- Respiratory**—initial tachypnea replaced by decreased respiratory rate and tidal volume and increased airway secretions; as temperature falls, protective airway reflexes are reduced; below 93.2 °F (34 °C) ventilatory drive is attenuated and increased pulmonary vascular resistance leads to ventilation-perfusion mismatch; progressive hypoventilation, apnea, and, more rarely, pulmonary edema may develop; hypothermia shifts the oxyhemoglobin dissociation curve to the left; this may be masked by concurrent lactic and respiratory acidosis that may become so profound the overall result is a right shift.
- Skin**—edema secondary to increased vascular permeability.

GENETICS

Unknown

INCIDENCE/PREVALENCE

Varies with geographic location.

GEOGRAPHIC DISTRIBUTION

Most common in cold climates.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Smaller breeds with increased surface area.

Mean Age and Range

More common in neonates and geriatrics.

Predominant Sex

None

SIGNS

General Comments

A thorough search should be made to find precipitating, comorbid conditions.

Historical Findings

- Known prolonged exposure to cold ambient temperatures.
- Possibly, disappearance from home or a history of trauma.

Physical Examination Findings

Stage I: 90–95 °F (32–35 °C)

- Lethargy and weakness.
- Vigorous shivering (variable).
- Variable heart rate, rhythm, and BP.
- Light pink to pale mucous membranes.
- Confusion, agitation, or obtundation.
- Variable respiratory rate.

Stage II: 82–90 °F (28–32 °C)

- Collapse.
- Reduced shivering (variable).
- Bradyarrhythmia with hypotension.
- Pale mucous membranes.
- Muscle and joint stiffness.
- Obtundation, stupor, or coma.
- Ataxia and hyporeflexia.
- Reduced depth and rate of respiration.

Stage III: 75–82 °F (24–28 °C)

- Moribund with cold, edematous skin.
- Loss of shivering (variable).
- Bradyarrhythmia with hypotension.
- Pale mucous membranes.
- Muscle and joint stiffness.
- Coma with fixed, dilated pupils.
- Areflexia.
- Reduced depth and rate of respiration or respiratory arrest.
- Pulmonary edema.

Stage IV: <75 °F (<24 °C)

- No vital signs.
- Cardiac arrest.

CAUSES

- Inadequate thermogenesis:
 - Normal thermogenesis is overwhelmed.
 - Serious illness.
- Extreme heat loss:
 - Excessive evaporation, conduction, convection, and radiation.
 - Inability to vasoconstrict blood vessels or piloerect hair.
 - Loss of behavioral adaptations.
 - Thermoregulatory center failure:
 - Hypothalamic injury or disease.

RISK FACTORS

- Extremes of age.
- Low body fat and glycogen stores.
- Burn injury.
- Intracranial injury or disease.
- Hypothyroidism.
- Diabetic ketoacidosis.
- Sepsis.
- Trauma.
- General anesthesia.
- Medications including but not limited to beta blockers, barbiturates, narcotics, phenothiazines.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary CNS disease, hypoglycemia, anemia, hepatic encephalopathy, myxedema, electrolyte disturbances, sepsis, intoxication, neoplasia, and death.
- Bradyarrhythmia—cardiac disease, medication side effects, and toxicities.

CBC/BIOCHEMISTRY/URINALYSIS

- Results depend on severity and presence of comorbidities.
- CBC—hemoconcentration, leukopenia, and thrombocytopenia.
- Biochemistry—azotemia, hyper- and hypoglycemia, variable electrolyte abnormalities, elevated liver enzyme activity, hyperbilirubinemia.
- Urinalysis—isosthenuria and glucosuria.

HYPOTHERMIA

OTHER LABORATORY TESTS

- Blood gas—variable; metabolic and respiratory acidosis is common.
- Hyperlactatemia—shivering, reduced tissue perfusion, and impaired hepatic clearance.
- Coagulation—hyperfibrinogenemia and disseminated intravascular coagulation; *in vivo* prolongation of clotting times may not be reflected by *in vitro* assays and should correct with rewarming.
- Thyroid hormone evaluation may confirm underlying hypothyroidism.

IMAGING

To investigate recovery complications or comorbid conditions.

DIAGNOSTIC PROCEDURES

ECG

Classic findings include presence of Osborn or J-waves, atrial and ventricular dysrhythmias, and prolongation of PR, QRS, and QT intervals with progression from sinus bradycardia through atrial fibrillation to ventricular fibrillation and ultimately asystole.

PATHOLOGIC FINDINGS

- Findings in patients who succumb to primary hypothermia are variable and nonspecific; if body cooling and death occur rapidly, necropsy findings are minimal but may include reddish discoloration of skin, hemorrhagic gastric erosions, and lipid deposits in epithelial cells of renal proximal tubules and other organs.
- Patients who die from secondary hypothermia may have similar findings; however, they will also have evidence of a separate and significant disease process.



TREATMENT

APPROPRIATE HEALTH CARE

Emergency inpatient intensive care until normothermic and stable.

NURSING CARE

- Warming:
 - Active external rewarming using warm blankets, heating pads, radiant heat, forced warm air, and administration of warm parenteral fluids (stage II) is used in patients with stage I-II hypothermia; complications include core temperature after-drop whereby return of cold blood from periphery to central circulation causes further core cooling; rewarming of the trunk should be performed before the extremities to minimize this risk.
 - Techniques to warm patients with stage III-IV hypothermia include administration of warm humidified oxygen, warmed IV fluids, and bladder or gastric lavage with warm saline; more invasive and technically demanding methods include closed thoracic and peritoneal lavage, and extracorporeal rewarming.
 - Whole-body immersion in hot water is contraindicated, as it will cause massive vasodilation and hypotension and is likely to provoke dysrhythmias and cardiovascular collapse.
 - Fluid therapy:
 - IV crystalloid fluids

warmed to 104 °F (40 °C).

- During rewarming, these patients have significant IV fluid requirements as vasoconstriction relaxes and cold diuresis is reversed.
- Patients must be closely monitored for volume overload during resuscitation.
- Consider inotropic drugs in patients unresponsive to volume resuscitation.
- Mechanically ventilate patients with respiratory failure.

ACTIVITY

Minimally affected patients should be encouraged to be active, as muscle activity will generate more endogenous body heat.

DIET

Withhold oral intake until patient is alert.

CLIENT EDUCATION

Prevention of exposure to cold temperatures is imperative in preventing primary hypothermia. Clients with very young and very old patients as well as those with serious medical conditions or taking medications that inhibit thermoregulatory ability should be counseled to keep their pets indoors and to take protective measures if they are to be exposed to cold temperatures.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Hypoglycemic patients warrant dextrose supplementation.
- Antiarrhythmic agents generally not warranted as most arrhythmias will resolve with rewarming.

CONTRAINdications

No evidence to support routine use of steroids or antibiotics.

PRECAUTIONS

Systemic clearance of metabolized drugs is slowed proportionately—consider dose reduction to minimize likelihood of unanticipated toxicity.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Continuous core body temperature.
- Continuous ECG and frequent BP during rewarming.
- Frequent assessment (q6–12h) of electrolytes, acid-base status, packed cell volume, total protein, and blood glucose.
- Daily monitoring of blood urea nitrogen, urine specific gravity, coagulation indices, and liver enzymes in severely affected patients.

PREVENTION/AVOIDANCE

- Avoid prolonged exposure to cold.
- Monitor and maintain body temperature in anesthetized animals.

POSSIBLE COMPLICATIONS

- Peripheral vasodilation during rewarming may further drop BP and body temperature.
- Iatrogenic burns.
- Return of cool peripheral blood to the heart may precipitate cardiac arrhythmias.
- Cardiac arrest.
- Gastric lavage increases the risk of aspiration pneumonia and fluid and electrolyte shifts.
- Thoracic and/or peritoneal lavage increases the risk for hemorrhage, lung or bowel trauma, and fluid and electrolyte shifts.
- Extracorporeal rewarming techniques have increased risk for local vascular complications, air embolism, hypotension, hemorrhage, thrombosis, and hemolysis.

EXPECTED COURSE AND PROGNOSIS

Variable—depend on severity, underlying cause, and patient health status.



MISCELLANEOUS

ASSOCIATED CONDITIONS

None

AGE-RELATED FACTORS

Sick or hypoglycemic neonates can become markedly hypothermic in normal environments.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

None

SEE ALSO

Shock, Cardiogenic.

ABBREVIATIONS

- CO = cardiac output.

Suggested Reading

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Client Education Handout
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(CONTINUED)



BASICS

DEFINITION

Clinical manifestations that result from inadequate production of thyroxine (T_4) and 3,5,3'-triiodothyronine (T_3) by the thyroid gland. Characterized by a generalized decrease in cellular metabolic activity.

PATHOPHYSIOLOGY

Acquired Hypothyroidism

- In dogs, acquired hypothyroidism can be primary, secondary, or tertiary.
- Primary hypothyroidism is associated with a defect localized to the thyroid gland. The thyroid tissue has been destroyed or replaced and thus becomes less responsive to thyroid-stimulating hormone (TSH). T_3 and T_4 levels gradually decline, with a compensatory increase in TSH.
 - Lymphocytic thyroiditis is an immune-mediated process characterized by chronic and progressive lymphocytic infiltration and destruction of the thyroid gland. This process is gradual and accounts for the slow onset of clinical signs associated with hypothyroidism. The immune-mediated process is associated with production of autoantibodies, predominantly against thyroglobulin; however, autoantibodies against T_3 and T_4 have been reported.
 - Idiopathic thyroid atrophy does not demonstrate an inflammatory component and is caused by the replacement of normal thyroid tissue with adipose tissue.
 - Together, these processes account for 95% of the clinical cases of hypothyroidism in dogs; each accounts for 50% of reported cases.
 - Rare causes of primary hypothyroidism include neoplastic destruction of thyroid tissue, iodine deficiency, infection, and iatrogenic destruction secondary to drugs, surgery, or radioiodine treatment.
- Secondary acquired hypothyroidism is rare. The defect is localized to the pituitary, where the ability to synthesize and secrete TSH is impaired. Secondary hypothyroidism may be caused by pituitary tumors, congenital malformation of the pituitary, infection, or TSH suppression. Drugs, hormones, or concurrent illness can cause TSH suppression.
- Tertiary hypothyroidism (not reported in the veterinary literature) is hypothalamic in origin, and production of thyrotropin-releasing hormone (TRH) is either decreased or nonexistent.
- Hypothyroidism may occur following radioactive iodine (I-131) therapy for hyperthyroidism in cats.

Congenital Hypothyroidism

- Congenital hypothyroidism is a rare disease that is categorized as goitrous or nongoitrous.

Goiter (enlargement of the thyroid gland) develops when there is increased release of TSH, along with an intact thyroid TSH receptor.

- An autosomal recessive form of congenital hypothyroidism has been reported in specific dog and cat breeds. Affected animals have a thyroid peroxidase deficiency.
- Congenital hypothyroidism is also noted as an element of panhypopituitarism.

SYSTEMS AFFECTED

- Behavioral.
- Cardiovascular.
- Endocrine/metabolic.
- Gastrointestinal (GI).
- Nervous.
- Neuromuscular.
- Ophthalmic.
- Reproductive.
- Skin/exocrine.

GENETICS

- No known genetic basis for heritability associated with adult-onset primary hypothyroidism in dogs, although some breeds appear to be predisposed to thyroiditis.
- An autosomal recessive form of congenital hypothyroidism has been reported in toy fox terriers, giant schnauzers, Tenterfield terriers, and Abyssinian cats.

INCIDENCE/PREVALENCE

- Primary hypothyroidism is the most common endocrinopathy in dogs. Prevalence appears to average about 1 : 250.
- Hypothyroidism is rare in cats.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog, rarely cat.

Breed Predilections

Larger-breed dogs are more likely to develop hypothyroidism (golden retriever, Doberman pinscher, Great Dane, Irish setter), though several smaller-breed dogs do appear to also be predisposed (miniature schnauzer, cocker spaniel, poodle, dachshund).

Mean Age and Range

Most commonly seen in middle-aged dogs, with the average age of onset being 7 years.

Predominant Sex

None

SIGNS

General Comments

Clinical signs associated with hypothyroidism are vague and involve many different systems.

Historical Findings

- Lethargy, weight gain, and hair loss are the most common signs (40–50% of all cases).
- Pyoderma (often recurrent), hyperpigmentation of the skin, and a dry, brittle hair coat (10% of cases).

HYPOTHYROIDISM

- Rarely (<5% of cases), facial paralysis, weakness, or conjunctivitis.

Physical Examination Findings

- Most changes appear to be secondary to decreased metabolism due to a lack of circulating thyroid hormones.
- The most common findings include dermatologic abnormalities (88% of hypothyroid dogs):
 - Bilateral symmetric nonpruritic truncal alopecia; hair loss is noted in areas of increased wear and usually includes the ventral thorax and neck, ventral abdomen, elbows, and tail. Loss of primary hair is most common, with retention of guard hairs, resulting in a short, fine hair coat.
 - Dry, lackluster hair coat.
 - Seborrhea is common and may be localized or have a more generalized distribution pattern.
 - Pyoderma is noted in 14% of hypothyroid dogs and may be recurrent in nature. Generalized demodicosis and *Malassezia* spp. infections are common. Though primary dermatologic conditions are nonpruritic, pruritis may accompany secondary parasitic, yeast, or bacterial infections. Chronic changes to the skin can result in thickening and hyperpigmentation.
- Otitis externa.
- Weight gain.
- Decreased activity/lethargy.

- Most neurologic signs are associated with polyneuropathy and include weakness, facial nerve paralysis, vestibular signs (usually peripheral), and hyporeflexia. No data support a direct association between megaesophagus or laryngeal paralysis and hypothyroidism.
- CNS signs, including seizures, ataxia, and coma (myxedema coma), are rare.

- In females, hypothyroidism is associated with increased periparturient mortality and lower birth rate in pups. In males, decreased fertility has been reported, but not confirmed, in hypothyroid dogs.

- Cardiovascular abnormalities are rare. Bradycardia, arrhythmias, decreased conduction, decreased contractility, and diastolic dysfunction have been reported.
- Ocular changes including corneal cholesterol deposits, keratoconjunctivitis sicca (KCS), and conjunctivitis are seen in less than 1% of hypothyroid dogs.

Congenital Hypothyroidism

- Lethargy and general inactivity.
- Dwarfism.
- Alopecia.
- Constipation (more common in cats).

CAUSES

- Lymphocytic thyroiditis.
- Idiopathic thyroid atrophy.
- Neoplasia.
- Pituitary disease.
- Congenital abnormalities.

HYPOTHYROIDISM

(CONTINUED)

- Iodine deficiency (dietary).
- Iatrogenic (secondary to surgery or radiation).

RISK FACTORS

- Surgical removal (bilateral) of the thyroid gland.
- I-131 therapy for hyperthyroidism in cats.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Primary dermatologic disease.
- Other endocrinopathies (hyperadrenocorticism, diabetes mellitus, growth hormone deficiency).
- Pancreatitis.
- Nephrotic syndrome.
- Hepatobiliary disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Useful to rule out nonthyroidal illness.
- Normochromic, normocytic, and nonregenerative anemia is a common finding (28–32% of hypothyroid dogs).
- Hyponatremia.
- Hypercholesterolemia (present in over 75% of hypothyroid dogs).
- Hypertriglyceridemia.
- Elevated levels of cholesterol and triglycerides have been associated with atherosclerosis in dogs, although this is rare.
- No specific changes are noted on urinalysis.

OTHER LABORATORY TESTS

- Diagnosing hypothyroidism is complex. The TSH stimulation test is a reliable single test used to diagnose hypothyroidism and is considered the gold standard. However, there is limited access to test reagents and the cost is often prohibitive.
- Several tests are available to assess thyroid function, thyroid hormone levels, and antithyroglobulin antibody levels. These tests include total T_4 , free T_4 , endogenous TSH, antithyroglobulin antibodies, anti- T_3 antibodies, anti- T_4 antibodies, total T_3 , reverse T_3 , and free T_3 .
- Combination testing will yield a reliable result.

Total T_4

- Initial screening (high sensitivity) test of thyroid function.
- This test measures both protein-bound and free T_4 levels.
- The test is a direct assessment of the ability of the thyroid gland to produce hormone.
- A decreased total T_4 level is a common finding in hypothyroid animals, but is not diagnostic of hypothyroidism as concurrent illness can cause an artificial decrease in total T_4 level.

Free T_4

- Measures metabolically active portion of total T_4 level.
- Hypothyroid animals would be expected to have a low free T_4 level.

- Concurrent illness has less effect on the free T_4 level compared with the total T_4 level.
- Measurement by equilibrium dialysis (fT_4 ED) has been demonstrated to be more reliable than radioimmunoassay, because it mitigates the influence of antithyroglobulin antibodies.

- Newer methods of free T_4 analysis utilize chemiluminescent technology with comparable sensitivity and specificity to fT_4 ED, but the effect of antibodies on this assay is unclear, and the fT_4 ED is still the gold standard.

Endogenous TSH Level

- Measurement of canine endogenous TSH is available.
- Cross-reactivity allows this assay to be used in cats; however, it may be accurate only 50% of the time in cats.
- This test has high specificity and low sensitivity; best used as a confirmatory test and not as a screening test.
- TSH level is expected to be elevated in primary hypothyroid animals due to loss of negative feedback; however, 20–40% of hypothyroid dogs have TSH values in the reference range.
- Interpretation of the TSH level requires knowledge of the total or free T_4 level.
- Methods of assessing TSH levels are less sensitive at low levels and evaluation of endogenous TSH cannot be used to diagnose secondary hypothyroidism.

Antithyroglobulin Antibodies

- Antithyroglobulin antibodies include antithyroglobulin, anti- T_3 , and anti- T_4 antibodies.
- A positive titer is predictive of immune-mediated thyroiditis, and suggestive of hypothyroidism, but only 20% of euthyroid dogs with antibodies develop hypothyroidism within 1 year.
- Anti- T_3 and - T_4 antibodies are similar to T_3 and T_4 and can cross-react to falsely elevate these assay levels. In animals who are slightly hypothyroid (as measured by total T_4), the presence of anti- T_4 antibodies may make it appear as if these animals are euthyroid, leading to a delay in the diagnosis and treatment of hypothyroidism.

TSH Stimulation Test

- Historically considered the gold standard for diagnosing hypothyroidism.
- Pharmaceutical-grade bovine TSH was used to conduct this test; however, this is no longer available.
- Recombinant human TSH can be used safely in both dogs and cats to effectively conduct the test, but is expensive. Therefore, this test is unlikely to become routine.

Total T_3 , Reverse T_3 , and Free T_3

- Total T_3 measurement is an unreliable indicator of thyroid function.
- The total T_3 level has been demonstrated to be normal in up to 90% of hypothyroid dogs.

- The reverse T_3 level has not been validated in companion animals.
- Evaluation of total T_3 , reverse T_3 , and free T_3 levels is not recommended to assess thyroid function.

Nonthyroid Factors That Alter Thyroid Function Tests

- In addition to sick euthyroid syndrome, other factors alter the results of thyroid function tests, which may result in a misdiagnosis.
- Most nonthyroid factors cause an artificial decrease in thyroid hormone levels.
- Some drugs can decrease thyroid hormone levels, but do not usually result in an animal developing clinical signs of hypothyroidism. Glucocorticoids, phenobarbital, and nonsteroidal anti-inflammatory drugs (NSAIDs) can decrease circulating thyroid hormone levels.
- Sulfonamides can decrease thyroid hormone levels and lead to clinical disease. This effect is noted to occur within weeks of initiation of therapy and disappears 2 weeks after therapy has been discontinued.
- Glucocorticoids inhibit the entire hypothalamic-pituitary-thyroid axis and have a direct effect against thyroid hormone.
- Phenobarbital causes a decrease in thyroid levels only in animals receiving long-term treatment. Phenobarbital should not be administered for 4 weeks prior to thyroid function testing.
- The influence of NSAIDs is variable and evaluation of thyroid function should be made with caution, and preferably after stopping NSAIDs well in advance of testing.
- Well-conditioned and athletic dogs consistently have lower total and free T_4 levels. Certain breeds have normal ranges of thyroid hormones that are different from other breeds. The greyhound, Scottish deerhound, saluki, and whippet have total T_4 concentrations that are well below the mean concentrations for other dogs. Alaskan sled dogs have serum T_4 , T_3 , and free T_4 concentrations below the normal reference range.
- Vaccination causes a transient increase in circulating autoantibody levels, which may cause a truly hypothyroid animal to appear euthyroid. Thyroid function testing should not be conducted if a patient has been vaccinated within the previous 2 weeks.

IMAGING

Radiographic Findings

Developmental bone problems (delayed epiphyseal ossification or dysgenesis) are usually noted with congenital hypothyroidism.

Ultrasonographic Findings

- Significant differences in thyroid gland volume and echogenicity exist between hypothyroid and euthyroid patients, but interpretation is highly user dependent.
- No significant difference is noted between euthyroid and sick euthyroid subjects.

(CONTINUED)

PATHOLOGIC FINDINGS

- Lymphocytic thyroiditis is characterized by chronic and progressive lymphocytic infiltration and destruction of the thyroid gland. Cytotoxic T cells initiate inflammation, leading to thyrocyte destruction and parenchymal fibrosis.
- Idiopathic thyroid atrophy is characterized by the replacement of normal thyroid parenchyma with adipose and connective tissue.
- Many cutaneous changes are nonspecific. However, certain findings, including dermal thickening, myxedema, and vacuolation of arrector pili muscles, are most characteristic.

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

Outpatient medical management.

CLIENT EDUCATION

- Lifelong therapy required.
- Easily managed with oral thyroid hormone supplementation.
- Dose adjustments are common in the early stages of treatment.
- Most clinical signs will resolve over time with appropriate thyroid hormone supplementation.

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

- Synthetic thyroid hormone supplementation easily treats hypothyroidism.
- Levothyroxine sodium is available as both human and veterinary products.
- Generic forms of the drug should be avoided, as human studies have demonstrated wide variability in the bioavailability of generic forms. If a generic form is used, always prescribe the same formulation.
- Hormone supplementation is initiated at 0.02 mg/kg PO q12h.
- Supplementation can often eventually be decreased to once daily after proper control is achieved.
- Levothyroxine doses for dogs exceed those for humans and may confuse pharmacists or human endocrinologists.
- Humans are instructed to take the medication on an empty stomach and proton pump inhibitors can impede absorption. This should be considered if a dog is difficult to regulate.

PRECAUTIONS

Patients with concurrent metabolic conditions (hepatic disease, endocrinopathies, renal disease, cardiac disease) should have supplementation started slowly (about 25% of recommended dose) and slowly increased over time (3 months) to the recommended maintenance level.

POSSIBLE INTERACTIONS

- Glucocorticoids, NSAIDs, furosemide may increase metabolism of levothyroxine.
- GI protectants can decrease absorption and administration should be separated from thyroid hormone supplementation by 2 hours.

ALTERNATIVE DRUG(S)

- If T_4 levels do not normalize after attempting monitoring and treatment, treatment can be attempted with liothyronine (4–6 mg/kg PO q8–12h).
- Monitoring is based on T_3 levels. However, there is no reliable method by which to measure T_3 .

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

- Assessment of clinical signs, weight, and thyroid function testing is recommended 6–8 weeks after therapy has begun, 2–4 weeks after each dose change, and then once to twice yearly. Patients should also be monitored if signs of thyroid toxicosis (e.g., polyuria/polydipsia [PU/PD], polyphagia) occur.
- The total T_4 level should be monitored and timed so that blood is taken 4–6 hours after pill administration.
- Once stable and well controlled, the total treatment dose may be given once daily in some dogs.
- For animals receiving supplementation once daily, blood should be taken immediately before the medication is given and then again 4–6 hours later, to measure trough and peak concentrations.
- When supplementation therapy is appropriate, the total postdose T_4 level should be in the upper half of the reference range, or slightly above it.
- If the total T_4 level is significantly increased above normal, the medication dose should be decreased or the frequency of administration reduced.
- If the total T_4 level is low, an increase in the dose may be necessary.
- Before increasing dose, assess client compliance, evaluate GI status to ensure there is no impact on absorption, and confirm there has been no change in the levothyroxine formulation.

PREVENTION/AVOIDANCE

Adequate hormone supplementation with routine monitoring should avoid recurrence of this condition.

POSSIBLE COMPLICATIONS

- If untreated hypothyroid animals are at increased risk of developing myxedema, myxedema coma, and atherosclerosis.
- Oversupplementation of thyroid hormone can result in iatrogenic hyperthyroidism.

HYPOTHYROIDISM
EXPECTED COURSE AND PROGNOSIS

- Primary hypothyroidism can be easily and successfully controlled; the prognosis for affected animals, when appropriately treated, is excellent. Resolution of clinical signs is an important predictor of adequate supplementation therapy.
- Significant improvement in attitude, activity level, and alertness should occur within 1 week of starting therapy.
- Dermatologic abnormalities improve slowly, with complete resolution taking up to 3 months.
- Polyneuropathies usually begin improving quickly; complete resolution may take several months.
- Anemia and serum cholesterol levels gradually resolve in the first weeks of therapy.
- Life expectancy usually normal.
- Congenital hypothyroidism has a guarded to poor prognosis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

May rarely be associated with other endocrinopathies.

PREGNANCY/FERTILITY/BREEDING

Increased periparturient mortality and lower birthweight pups.

SEE ALSO

Myxedema and Myxedema Coma

ABBREVIATIONS

- FT₄ED = Free T4 measured by equilibrium dialysis.
- GI = gastrointestinal.
- I-131 = radioactive iodine.
- KCS = keratoconjunctivitis sicca.
- NSAID = nonsteroidal anti-inflammatory drug.
- PU/PD = polyuria/polydipsia.
- TRH = thyrotropin-releasing hormone.
- TSH = thyroid-stimulating hormone.

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Acknowledgment The author and book editors acknowledge the prior contribution of Deborah S. Greco.



**Client Education Handout
available online**

HYPOXEMIA



BASICS

DEFINITION

- A decrease in partial pressure of arterial oxygen (PaO_2), resulting in marked desaturation of hemoglobin.
- PaO_2 at sea level ranges from 80 to 100 mmHg in normal animals.

H

PATHOPHYSIOLOGY

Six physiologic causes:

- Low partial pressure of inspired oxygen (PIO_2).
- Hypoventilation (increase in partial pressure of carbon dioxide in arterial blood [PaCO_2]).
- Mismatching of alveolar ventilation and perfusion so that areas of the lung that are not ventilated properly are still perfused adequately.
- Alveolar–capillary membrane diffusion defect.
- Right-to-left cardiac or pulmonary shunting.

SYSTEMS AFFECTED

- All organs—oxygen essential for normal cellular function; individual tissue oxygen requirements vary by organ.
- Cardiovascular—can result in focal or global ischemia; if prolonged, can develop arrhythmias and cardiac failure.
- Nervous—brain and CNS most important; hypoxemia can result in irreversible brain damage because there are no large oxygen stores in brain tissue.

SIGNALMENT

Any breed, age, and sex of dog and cat.

SIGNS

Historical Findings

- Breathing problems—especially open-mouth breathing.
- Trauma.
- Episodes of coughing.
- Gagging.
- Exercise intolerance.
- Cyanosis.
- Collapse.

Physical Examination Findings

- Tachypnea.
- Dyspnea.
- Orthopnea.
- Pale mucous membranes.
- Cyanosis.
- Coughing.
- Open-mouth breathing.
- Tachycardia.
- Poor peripheral pulse.
- Abnormal thoracic auscultation.

CAUSES

- Low PIO_2 —high altitude (the higher the elevation, the lower the barometric pressure, which results in a decrease in PIO_2 ; fraction

of oxygen in inspired air (FIO_2) is fixed at 0.21); suffocation; enclosure in small areas with improper ventilation.

- Hypoventilation—result of inadequate alveolar ventilation; muscular paralysis; upper airway obstruction; air or fluid in the pleural space; restriction of the thoracic cage, diaphragmatic hernia; CNS disease; anesthetics.
- Mismatching of alveolar ventilation and perfusion—most common cause of hypoxemia and occurs with virtually any lung disease: pulmonary thromboembolism; pulmonary parenchymal disease (infectious or neoplastic); lower airway disease; pneumonia; pulmonary contusions; pulmonary edema; also during anesthesia or prolonged recumbency when a large region of lung becomes atelectatic.
- Alveolar–capillary membrane diffusion impairment—rarely clinically important.
- Right-to-left cardiac or pulmonary shunting—tetralogy of Fallot; ventricular septal defect; reversed patent ductus arteriosus; intrapulmonary arteriovenous shunt.

RISK FACTORS

- Move to higher elevation.
- Trauma.
- Bronchopneumonia of any cause.
- Pleural disease.
- Anesthesia.
- Cardiac disease.
- Bronchial disease—chronic bronchitis, feline asthma.
- Diseases associated with risk of embolization, e.g., immune-mediated hemolytic anemia, hyperadrenocorticism, neoplasia, pancreatitis, sepsis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Signs of tachypnea and/or dyspnea.
- Excitement or anxiety.
- Hyperthermia.
- Pyrexia.
- Head trauma.
- Pain.

LABORATORY FINDINGS

Drugs That May Alter Laboratory Results

N/A

Disorders That May Alter Laboratory Results

- Air bubbles in the arterial blood sample—falsely high PaO_2 values.
- Improper packaging of the arterial blood sample—falsely high PaO_2 values after approximately 30 min at room temperature.

Valid if Run in Human Laboratory?

Yes

CBC/BIOCHEMISTRY/URINALYSIS

- Packed cell volume (PCV)—can be high with chronic condition; can be low if inflammatory or neoplastic.
- Liver enzyme elevation common with organ hypoxia.

OTHER LABORATORY TESTS

Arterial Blood Gases

- Collect arterial blood sample in an anaerobic manner, as follows: use enough heparin to coat the needle and the inside of the syringe; collect sample from femoral or dorsal pedal artery; place a rubber stopper on the needle or covering the hub of the syringe, to prevent room air from entering the sample; analyze sample within 15 min if left at room temperature; place sample on ice to extend safe time for analysis to 2–4 hours.
- Bedside or portable blood gas analyzers—several models available; make analysis more convenient.

IMAGING

Thoracic radiographs and echocardiography—evaluate intrathoracic disease; differentiate pulmonary and cardiac disease.

DIAGNOSTIC PROCEDURES

Pulse Oximetry

- Indirectly determines saturation of arterial blood with oxygen (SaO_2); relation between PaO_2 and SaO_2 based on oxyhemoglobin dissociation curve: $\text{SaO}_2 > 90\%$ when $\text{PaO}_2 > 60$ mmHg.
- $\text{SaO}_2 < 95\%$ —considered abnormal, indicates $\text{PaO}_2 < 80$ mmHg.
- Best results when probe used on animal's tongue; thus may be limited to anesthetized, heavily sedated, or seriously ill patients with low level of consciousness; keep tongue moistened for most accurate readings.
- Other potentially successful probe sites—lip, ear, vulva (female), prepuce (male); skin between toes; thin skin in the flank area. Interpret values with caution.
- Poor results—using sites that have hair or poor perfusion; least accurate in low-flow states such as hypotension (global low flow) or hypothermia (low flow to skin); falsely low values (usually <85%) during carboxyhemoglobinemia (smoke inhalation).
- Rectal probes will allow readings in awake patients.

Endoscopy or Lung Biopsy

Airway sampling often required to determine primary abnormality resulting in hypoxemia.

(CONTINUED)

HYPOXEMIA**TREATMENT**

Must identify and correct the primary cause.

Oxygen Therapy

- Most common supportive treatment.
- Corrects low-inspired oxygen, hypoventilation, and alveolar–capillary membrane diffusion defects; may not fully correct mismatching of ventilation and perfusion; does not correct right-to-left cardiac or pulmonary shunts and low cardiac output.
- May not be completely beneficial until adequate blood volume is established or alveolar contents are removed (e.g., pulmonary edema, purulent material).
- Delivery—directly from an oxygen source from the anesthetic machine via a face mask placed securely around the muzzle or from an E-tank fitted with an oxygen regulator through a face mask, intranasal catheter placed in the oropharynx, or oxygen cage.
- Increase in FIO_2 —determined by the oxygen flow rate and the amount of oxygen mixed with room air.
- Positive pressure ventilation—may be needed for severe hypoxemia of any cause.
- High flow oxygen therapy (HFOT) has been shown to increase arterial oxygen in dogs with severe hypoxemia.

Fluid Therapy

- Low cardiac output—fluid administration and inotropic support (e.g., pimobendan, dobutamine, or dopamine) important.
- Cardiac failure—requires aggressive medical treatment; diuretics; afterload and preload reduction; inotropic support; oxygen administration; cautious amounts of fluids may be indicated after institution of primary treatment; use caution with type and rate of fluids after initial stabilization.
- Hypovolemic, hemorrhagic, traumatic, or septic shock—requires end point fluid administration; crystalloids (20–30 mL/kg), hypertonic solutions (7% NaCl, 4 mL/kg), or blood products (packed red blood cells [pRBC], whole blood, plasma), or a combination.
- Severe pulmonary contusion—hypertonic fluids or low dose crystalloids (5–10 mL/kg).

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

For bronchospasm—bronchodilators; terbutaline (0.01 mg/kg SC/IM/IV q8h) or albuterol inhaler.

CONTRAINDICATIONS

- Aggressive fluid administration—not indicated for cardiac failure and pulmonary edema.
- Diuretics—not indicated for shock, low PIO_2 , alveolar–capillary membrane diffusion defects, mismatching of alveolar ventilation and perfusion, and right-to-left shunts.

PRECAUTIONS

- Inotropic drugs—arrhythmias may develop.
- Oxygen toxicity—prolonged (>12 hour) exposure to high-concentration (>70%) oxygen can result in pulmonary edema, seizures, and death.

POSSIBLE INTERACTIONS

N/A

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

- Decrease in respiratory effort and decrease in cyanosis (if initially noted)—check efficacy of treatment and support.
- Arterial blood gas—determine resolution.
- Pulse oximetry—alternative; interpret results cautiously with hypotension, hypothermia, smoke inhalation, and non-tongue probe site. Trend in the actual number being produced is important.

POSSIBLE COMPLICATIONS

- Brain damage—depends on severity and duration of hypoxemia; partial or complete loss of neuronal function; dementia; seizures; loss of consciousness.
- Arrhythmias—may develop secondary to myocardial hypoxia; may be very difficult to treat effectively.
- Respiratory arrest requiring intubation and positive pressure ventilation.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

May adversely affect fetuses, especially during first trimester of pregnancy.

H**SEE ALSO**

- Cyanosis.
- Dyspnea and Respiratory Distress.
- Panting and Tachypnea.

ABBREVIATIONS

- FIO_2 = fraction of oxygen in inspired air.
- HFOT = High flow oxygen therapy.
- PaCO_2 = partial pressure of carbon dioxide in arterial blood.
- PaO_2 = partial pressure of arterial oxygen.
- PCV = packed cell volume.
- PIO_2 = partial pressure of inspired oxygen.
- pRBC = packed red blood cells.
- SaO_2 = saturation of arterial blood with oxygen.

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ICTERUS



BASICS

DEFINITION

Increased total bilirubin concentration causing yellow tissue discoloration.

PATHOPHYSIOLOGY

- Bilirubin—derived from degradation of heme-containing proteins; most (80%) from senescent erythrocytes; remainder from other heme-containing proteins (e.g., P450 cytochromes, myoglobin).
- Unconjugated bilirubin—transported in plasma bound to albumin; diglucuronide conjugated after hepatocellular uptake.
- Conjugated bilirubin—transported in bile, expelled into intestines where most converted to other products, e.g., urobilinogen can undergo enterohepatic circulation, stercobilin colors feces brown.
- Hyperbilirubinemia—caused by increased bilirubin production (increased red blood cell [RBC] destruction; *hemolytic jaundice*); heme exceeding hepatic capacity for uptake, conjugation, or biliary excretion (*hepatocellular jaundice*), or interrupted biliary elimination (*posthepatocellular jaundice*).
- Nonhemolytic jaundice caused by hepatobiliary disease or bile peritonitis.

SYSTEMS AFFECTED

- Skin/exocrine—skin discoloration (jaundice) reflects serum bilirubin >2.5 mg/dL.
- Hepatobiliary—retained bile acids and markedly increased bilirubin may contribute to hepatocellular injury.
- Renal/urologic—extreme hyperbilirubinemia may cause renal tubular injury.
- Nervous—extreme unconjugated hyperbilirubinemia may cause degenerative brain lesions (rare, kernicterus).

SIGNALMENT

Species

Dog and cat.

Mean Age and Range

- Most causes—diseases of adult animals.
- Young, unvaccinated dogs—at risk for infectious canine hepatitis.

Predominant Sex

Adult female pure-bred dogs—at risk for immune-mediated hemolytic anemia.

SIGNS

Historical Findings

Increased Formation: Hemolysis

- Vague signs—lethargy, weakness.
- Gastrointestinal (GI) signs—anorexia, constipation, vomiting, weight loss.
- Jaundice.
- Recent blood transfusion.
- Severe trauma—bleeding into muscle, abdomen, or hematoma formation.
- Rhabdomyolysis (rare cause).

Decreased Elimination: Cholestasis

- Vague GI signs—anorexia, vomiting, diarrhea, change in fecal color: nonobstructive jaundice green, orange; obstructed jaundice acholic.
- Jaundice.
- Change in urine

color—orange.

- Abdominal enlargement—if ascites.
- Polyuria and polydipsia.
- Altered mentation—if hepatic encephalopathy (HE).

Physical Examination Findings

Increased Formation: Hemolysis

- Pallor, tachycardia, tachypnea, weakness, bounding femoral pulses, anemic heart murmur.
- Jaundice.
- Hepatomegaly/splenomegaly—extramedullary hematopoiesis, reticuloendothelial hyperplasia.
- Lymphadenopathy.
- Bleeding tendencies—if thrombocytopenic.
- Orange feces.
- Fever.
- “Gelatinous” feel to skin (vasculopathy).
- Rhabdomyolysis—weakness, pain.

Decreased Elimination: Cholestasis

- Weight loss.
- Jaundice.
- Hepatomegaly/splenomegaly.
- Abdominal effusion/mass/pain.
- Melena, orange, green, or acholic feces.
- Fever.

CAUSES

Prehepatocellular Jaundice

- Hemolytic disorders—immune-mediated hemolysis; certain drugs (propylene glycol carriers in cats, trimethoprim sulfate); systemic lupus erythematosus; infectious disorders; toxins (e.g., oxidative injury: zinc, onions; phenols); severe hypophosphatemia.
- Incompatible blood transfusion.
- Infections—feline leukemia virus (FeLV); *Mycoplasma haemofelis*; heartworm; *Babesia*; *Ehrlichia*; *Cytauxzoon*.
- Large-volume blood resorption—hematomas, body cavities (e.g., hemangiosarcoma, warfarin).

Hepatocellular Jaundice

- Chronic idiopathic or familial hepatitis.
- Adverse drug reactions—e.g., anticonvulsants; acetaminophen; trimethoprim sulfate; carprofen; stanozolol (cats); benzodiazepines (cats); see Hepatotoxins.
- Cholangitis/cholangiohepatitis.
- Infiltrative neoplasia—lymphoma.
- Cirrhosis (dogs).
- Hepatic lipidosis (cats).
- Massive liver necrosis—e.g., aflatoxin, cycad, nonsteroidal anti-inflammatory drugs (carprofen), copper associated injury.
- Systemic illnesses with hepatic involvement—leptospirosis (dogs); histoplasmosis; feline infectious peritonitis; hyperthyroidism (cats); toxoplasmosis (cats).
- Bacterial sepsis—originating anywhere in body; may elaborate bacterial products that impair hepatic bilirubin processing/elimination.

Posthepatocellular Jaundice

Transient or persistent mechanical bile duct obstruction—pancreatitis (transient obstruction); neoplasia: bile duct, pancreas, duodenum; intraluminal duct occlusion: cholelithiasis, sludged bile, liver flukes (cats), immune-mediated duct destruction (sclerosing cholangitis in cats), gall bladder mucocele (dogs); ruptured biliary tree causing bile peritonitis.

RISK FACTORS

- Young unvaccinated dogs—infectious disease, canine infectious hepatitis.
- Breed predisposition for familial hepatic disease—Labrador retriever, Doberman pinscher, Bedlington terrier, cocker

spaniel, Dalmatian.

- Middle-aged, obese dogs—pancreatitis.
- Anorectic, obese cats—hepatic lipidosis.
- Hepatotoxic drugs.
- Blunt abdominal trauma, chronic biliary tract disease, gallbladder mucocele—bile peritonitis.
- Hemolytic anemia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Prehepatocellular jaundice—usually abrupt onset; mucous membrane pallor; mild to moderate jaundice; weakness; tachypnea; cardiac murmur with severe anemia.
- Hepatic jaundice—breed risk for familial hepatitis; variable jaundice; otherwise normal mucous membranes; alteration in liver size (large or small); abdominal effusion (pure or modified transudate); polyuria and polydipsia; behavioral abnormalities of HE; coagulopathy.
- Posthepatocellular jaundice—chronic and/or recurrent bouts of apparent GI signs or pancreatitis with cholelithiasis; moderate or marked jaundice; otherwise normal mucous membranes; diffuse or cranial abdominal pain; cranial abdominal mass; abdominal effusion (septic, nonseptic, or bile peritonitis); bleeding tendencies; acholic feces unless melena.

LABORATORY FINDINGS

- Bilirubin assay—based on diazo reaction; assesses direct-reacting and total serum bilirubin; most yield reasonable total bilirubin results; values for direct bilirubin vary.
- Higher readings in heparinized plasma.
- Sample management—important; total bilirubin may decrease by 50% per hour with direct exposure to sunlight or artificial lighting.
- Hemolysis—variable effects on total bilirubin measured by spectrophotometry.
- Lipemia—falsely increases total bilirubin values measured by endpoint assays.
- Fractionation into conjugated and unconjugated—*unable to define causes of jaundice*, contrary to dogma.

CBC/BIOCHEMISTRY/URINALYSIS

Prehepatocellular Jaundice

- CBC—severe anemia (usually regenerative); blood smear may reveal autoagglutination, spherocytes, Heinz bodies, parasites; hemoglobinemia with intravascular hemolysis, normal to low platelets, normal to high WBCs, with left shift.
- Biochemistry—normal to high alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activity, blood urea nitrogen (BUN) concentration; normal to low albumin; normal to high globulin; normal glucose and cholesterol; high bilirubin.

Hepatocellular Jaundice

- CBC—mild nonregenerative anemia; low mean corpuscular volume (MCV) with chronic liver disease and portosystemic shunting; variable

(CONTINUED)

ICTERUS

- white blood cell (WBC) count. • Biochemistry—mildly to markedly high ALT ± ALP; normal to low albumin, BUN, glucose, cholesterol.
- Urinalysis—normal to dilute urine; bilirubinuria precedes hyperbilirubinemia; bilirubinuria important in cats.

Posthepatic Jaundice

- CBC—± mild nonregenerative anemia; variable WBC count. • Biochemistry—increased ALT, moderate to markedly increased ALP; usually normal albumin, BUN, glucose concentrations; normal to high cholesterol.

OTHER LABORATORY TESTS

- In-saline autoagglutination slide test—with suspected RBC agglutination; may have reported high MCV. • Direct Coombs' test—submit if no evidence of autoagglutination.
- Osmotic fragility test—detects likelihood of RBC hemolysis tonicity challenge. • Blood smears—hemoparasites, spherocytes, schistocytes, anisocytosis (regenerative). • Plasma zinc—if hemolytic anemia. • Antinuclear antibodies—with hemolytic anemia. • Serum bile acids—redundant if nonhemolytic jaundice already suspected. • Serology—for infectious diseases (e.g., FeLV, leptospirosis, mycoses) with signs of multisystemic illness and hepatic jaundice. • PCR for acute leptospirosis—within first few days, urine and/or serum; before appropriate antibiotic therapy.
- Abdominal effusion—characterize cell and protein content. • Coagulation tests—prolonged values, esp. proteins invoked by vitamin K absence or antagonism and prothrombin time, with bile duct occlusion; vitamin K₁ responsive. • Microbial culture and sensitivity—blood ± other specimens if inflammatory leukon and suspected bacterial infection (e.g., urinary tract, biliary tract, liver).

IMAGING

- Abdominal radiography—obscured by effusion; may reveal hepatomegaly, mass effect, mineral or gas interface in liver (emphysematous cholecystitis, choleliths); splenomegaly (hemolytic anemia, portal hypertension, abdominal neoplasia); metallic foreign body with zinc-induced hemolysis. • Thoracic radiography—may reveal metastatic disease; sternal lymphadenopathy (reflecting abdominal disease); general lymphadenopathy (lymphosarcoma, systemic infection [fungal]). • Abdominal US—may distinguish parenchymal liver disease from extrahepatic biliary obstruction; characterizes hepatic parenchymal lesions; may disclose abdominal neoplasia; may determine cause of abdominal effusion; used to target lesions, fluid, or cystocenteses sampling (aspirates or needle biopsy).

DIAGNOSTIC PROCEDURES

- Fine-needle aspiration—cytology of mass, lymph node, hepatic parenchyma, bile.
- Liver biopsy—bacterial culture of liver, bile, other specimens obtained via celiotomy, blind

percutaneous, keyhole, laparoscopic, or US-guided techniques. • Surgical intervention—required for diagnosis and treatment of posthepatic disorders.

**TREATMENT**

- Depends on underlying cause.
- Inpatient—for initial medical care. • Cage rest—to facilitate liver regeneration or reduce oxygen requirements if severe anemia.
- Diet—important for hepatic and posthepatic jaundice; nutritionally balanced with maximum protein tolerated; carbohydrate based (dogs) with restricted protein for hepatic encephalopathy; restrict sodium if ascites. • Vitamin supplementation—water-soluble vitamins in all patients; parenteral vitamin K₁ for bile duct obstruction or severe cholestasis.

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

- Prehepatitic jaundice—eliminate inciting cause; see Anemia, Immune-Mediated; whole blood transfusion for life-threatening anemia.
- Hepatic/posthepatitic jaundice—treat specific disorders based on imaging, biopsy, culture.

CONTRAINdicATIONS

- Avoid known hepatotoxic drugs. • Avoid tetracyclines unless clearly indicated—suppress hepatic protein synthesis, promote hepatic lipidosis. • Avoid analgesics, anesthetics, barbiturates—with hepatic failure.

PRECAUTIONS

- Sedatives—may precipitate HE.
- Corticosteroids—for nonseptic inflammation; increase risk for infection; may aggravate ascites (water and sodium retention), promote vacuolar hepatopathy (dogs) and hepatic lipidosis (cats).

POSSIBLE INTERACTIONS

Consider influence of altered hepatic metabolism on drug therapy; hypoalbuminemia influences potency of protein-bound drugs, enhancing effects (may lead to toxicity).

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

- Prehepatitic jaundice—recheck packed cell volume and blood smears as needed; may require repeat transfusions; taper immunosuppressive drugs. • Hepatic and posthepatitic jaundice—recheck serum biochemical profile as dictated by underlying disease; continue

symptomatic and specific treatments until remission, varies with disease process.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Patients with immune-mediated hemolysis treated with immunosuppressive doses of corticosteroids predisposed to thromboembolism, GI ulcers, and infection. • Patients in hepatic failure susceptible to infections, enteric bleeding, ascites. • Patients with reconstructive biliary surgery have risk of recurrent bacterial cholangitis.

SYNONYMS

Jaundice

SEE ALSO

- Anemia, Heinz Body.
- Anemia, Immune-Mediated.
- Anemia, Regenerative.
- Babesiosis.
- Bartonellosis.
- Blood Transfusion Reactions.
- Cholangitis/Cholangiohepatitis Syndrome.
- Cholelithiasis.
- Cirrhosis and Fibrosis of the Liver.
- Copper Associated Hepatopathy.
- Gallbladder Mucocele.
- Hepatic Failure, Acute.
- Hepatic Lipidosis.
- Hepatitis, Chronic.
- Hepatitis, Infectious (Viral) Canine.
- Hepatitis, Suppurative and Hepatic Abscess.
- Hepatotoxins.
- Liver Fluke Infestation.
- Lupus Erythematosus, Systemic (SLE).
- Pancreatitis—Cats.
- Pancreatitis—Dogs.
- Zinc Toxicosis.

ABBREVIATIONS

- ALP = alkaline phosphatase. • ALT = alanine aminotransferase. • BUN = blood urea nitrogen. • FeLV = feline leukemia virus.
- GI = gastrointestinal. • HE = hepatic encephalopathy. • MCV = mean corpuscular volume. • RBC = red blood cell. • WBC = white blood cell.

Suggested Reading

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**Client Education Handout
available online**

ILEUS



BASICS

OVERVIEW

- Adynamic (paralytic, functional) ileus is defined as a transient and reversible intestinal obstruction resulting from inhibition of bowel motility.
- Lack of peristalsis of stomach, small bowel, or large bowel causes functional obstruction, as intestinal contents accumulate in the dependent areas of the gastrointestinal tract instead of being propelled in an aboral direction.
- Ileus is not a primary disease but a secondary complication of a number of disorders.
- Adynamic ileus is thought to occur secondary to electromechanical dissociation of the intestinal musculature due to increased sympathetic tone, release of humoral inhibitory factors (catecholamines, vasopressin, endogenous opiates), impaired release of prokinetic hormones (neurotensin, motilin), or hypokalemia.
- Secondary causes of intestinal pseudo-obstruction have been subclassified into developmental, infectious, inflammatory, autoimmune, metabolic, paraneoplastic, endocrine, and toxic etiologies.
- Lymphocytic leiomyositis represents a visceral myopathic form of chronic intestinal pseudo-obstruction that has been described in humans, dogs, horses, and cats; it is defined as lymphocytic infiltration of the muscularis propria and is thought to represent an autoimmune response to the myofibers of the muscularis propria layer of the bowel by T lymphocytes.
- Systems affected—gastrointestinal; autonomic nervous system.

SIGNALMENT

Cat and dog.

SIGNS

- Anorexia.
- Vomiting.
- Regurgitation.
- Lethargy.
- Diarrhea.
- Weight loss.
- Coughing secondary to aspiration pneumonia from gastroesophageal reflux.
- Mild abdominal distention or discomfort secondary to accumulation of gas in hypomotile bowel.
- Failure to auscultate gut sounds after 2–3 minutes suggests ileus.
- Gut sounds can be increased during initial state (partial loss of motility).

CAUSES & RISK FACTORS

- Surgery (especially gastrointestinal surgery).
- Pain.
- Electrolyte imbalance (hypokalemia, hypomagnesemia, hypocalcemia).

- Acute inflammatory lesions of bowel, peritoneal cavity, pancreas, or other abdominal organs.
- Unrelieved mechanical obstruction.
- Intestinal ischemia.
- Gram-negative sepsis.
- Endotoxemia.
- Shock.
- Retroperitoneal injury.
- Uremia.
- Autonomic neuropathies (dysautonomia, spinal cord injury).
- Visceral myopathies associated with autoimmune disease.
- Use of anticholinergic drugs.
- Intestinal overdistension (aerophagia).
- Lead poisoning.
- Stress (cold and noise).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Adynamic ileus must be differentiated from mechanical obstruction caused by:

- Intestinal foreign bodies.
- Inflammatory bowel disease.
- Intussusception.
- Intramural abscess.
- Incarcerated or strangulated hernia.
- Volvulus.
- Mesenteric infarction.
- Parasites.
- Adhesions.
- Postoperative stricture.
- Impaction.
- Congenital malformation.
- Inflammatory or traumatic lesions.
- Neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram changes depend on primary cause of ileus.
- Serum chemistry profiles and urinalysis help assess electrolyte disturbances (especially hypokalemia) and presence of azotemia.

OTHER LABORATORY TESTS

- Measurement of pancreatic lipase concentration (Spec or SNAP cPL or fPL) to assess for pancreatitis.
- Fecal parvovirus ELISA test in puppies with ileus and diarrhea.

IMAGING

Abdominal Radiographic Findings

- Stomach and/or intestinal loops are distended with gas and fluid.
- Common radiographic patterns include:
 - Generalized gas ileus—consider aerophagia, smooth muscle paralyzing drugs, generalized peritonitis, or enteritis.
 - Generalized fluid ileus—consider enteritis, diffuse intestinal neoplasia.

- Localized gas ileus—consider localized peritonitis (pancreatitis), early bowel obstruction, disruption of arterial supply.
- Localized fluid ileus—consider foreign body, neoplastic obstruction, intussusception.

Ultrasonography

- Differentiate adynamic ileus from mechanical intestinal obstructions.
- Identify pancreatitis or peritonitis.
- Ultrasound has been used to assess frequency and contraction of pyloric antrum in dogs.
- Careful evaluation of intestinal layers for loss of normal layering associated with infiltrative neoplasia, thickening of muscularis propria layer and/or submucosal layer associated with inflammatory bowel disease or small cell lymphoma, and attenuation of muscularis layer associated with fibrosis secondary to leiomyositis.

DIAGNOSTIC PROCEDURES

Barium-Impregnated Polyethylene Spheres (BIPS)

- Confirm adynamic ileus.
- Delayed gastrointestinal transit along with retention of BIPS in the stomach.
- Scattering of BIPS throughout the upper gastrointestinal tract.

Upper Gastrointestinal Series

- Upper gastrointestinal series can be performed to help assess for presence of partial intestinal obstructions or delayed gastric and intestinal motility.
- Gastric and intestinal transit times must be interpreted cautiously following administration of liquid barium in light of marked variation in emptying times from animal to animal, and the stress of hospitalization can delay gastric and intestinal transit times.

Other Procedures to Consider

- Noninvasive electrogastrography is used experimentally to assess gastric myoelectrical activity in dogs.
- Abdominocentesis with peritoneal effusion to confirm peritonitis.
- Gastrointestinal endoscopy or exploratory laparotomy to rule out mechanical obstruction.
- Full-thickness intestinal biopsies are necessary to diagnose intestinal leiomyositis because the disorder affects the muscularis propria layer of the bowel, which is typically not accessible via endoscopic biopsy.
- Spinal radiographs, myelogram, spinal MRI, CT, cerebrospinal fluid (CSF) analysis to identify spinal cord injury.
- Ocular response test with 0.1% pilocarpine and 0.25% physostigmine for dysautonomia.



TREATMENT

- Identify and treat primary underlying cause.
- Correct electrolyte abnormalities (especially hypokalemia) if present.

(CONTINUED)

ILEUS

- Use of prokinetic drugs such as cisapride, metoclopramide, or erythromycin should be considered, depending on underlying cause.
- Gastrointestinal decompression of stomach via nasogastric tube is beneficial in select cases.
- Fat-restricted diets should be implemented in dogs with delayed gastric emptying because higher-fat diets can delay gastric emptying in this species.

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

- Metoclopramide is most effective when administered as CRI (1–2 mg/kg/24h); bolus injections (0.4 mg/kg IV q6h) are less effective in light of relatively short half-life (90 min) in dogs; metoclopramide does not affect colonic motility and should be avoided in animals with colonic ileus or megacolon.
- Cisapride (0.5–0.75 mg/kg q8–12h) is a far more potent and effective prokinetic compared to metoclopramide and affects gastric, small intestinal, and colonic motility.
- Erythromycin (1–2 mg/kg PO q12h) has prokinetic activity in stomach and small intestine.
- Cyclosporine (5 mg/kg q12–24h) can be administered for management of intestinal leiomyositis or other immune-mediated disorders affecting intestinal tract.
- Prednisone (1 mg/kg q12h with progressive tapering over 10–12 weeks) can be administered for management of leiomyositis or inflammatory bowel disease.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Anticholinergic drugs (e.g., atropine, glycopyrrolate).
- Opiates (e.g., morphine, hydromorphone, oxymorphone, butorphanol).
- Opium antidiarrheals (e.g., paregoric, diphenoxylate hydrochloride/atropine sulfate, loperamide hydrochloride).

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

- Monitor and correct electrolyte imbalance if present.
- Abdominal auscultation to evaluate gastrointestinal motility.
- Survey abdominal radiographs to evaluate gastric and intestinal distension.

PREVENTION/AVOIDANCE

Avoid anticholinergic drugs and opiates if not indicated.

POSSIBLE COMPLICATIONS

Animals with adynamic ileus are predisposed to development of intestinal dysbiosis, bacterial translocation, and sepsis.

EXPECTED COURSE AND PROGNOSIS

Prognosis depends on successful resolution of primary disease process.

**MISCELLANEOUS****SYNONYMS**

- Adynamic ileus—functional ileus, paralytic ileus

- Pseudo-obstruction—chronic, more segmental adynamic ileus.
- Mechanical ileus—generally addressed in current literature as mechanical obstruction.

PREGNANCY/FERTILITY/BREEDING

Ileus has been reported in a lactating bitch with hypomagnesemia and hypocalcemia.

ABBREVIATIONS

- BIPS = barium-impregnated polyethylene spheres.
- CSF = cerebrospinal fluid

Suggested Reading

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INFLAMMATORY BOWEL DISEASE



BASICS

DEFINITION

A group of chronic enteropathies characterized by persistent or intermittent gastrointestinal (GI) signs with histopathologic evidence of intestinal inflammation. Inflammatory bowel disease (IBD) is generally categorized by the predominant mucosal cellular infiltrate, such as lymphocytic-plasmacytic, eosinophilic, or granulomatous enteritis.

PATHOPHYSIOLOGY

- Poorly understood but likely due to complex interplay between mucosal immunity and environmental factors (i.e., dietary and bacterial antigens) in genetically susceptible dogs; aberrant host immune responses are likely triggered by antigens derived from resident microbiota.
- Damage results from elaboration of cytokines, release of proteolytic and lysosomal enzymes, complement activation secondary to immune complex deposition, and generation of oxygen free radicals.
- Host genetic susceptibility involving defects in innate immunity is suspected in dogs, and possibly cats.

SYSTEMS AFFECTED

- GI.
- Hepatobiliary.
- Hemic/lymphatic/immune—rarely.
- Musculoskeletal—rarely.
- Ophthalmic—rarely.
- Respiratory—rarely.
- Skin/exocrine—rarely.

GENETICS

Defects in host susceptibility genes have been identified in German shepherd dog, boxer, and soft-coated wheaten terrier.

INCIDENCE/PREVALENCE

IBD is most common histopathologic diagnosis in dogs and cats with chronic GI signs in which other causes have been eliminated through clinical trials and diagnostic testing.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Increased risk in German shepherd, boxer, and soft-coated wheaten terrier, in addition to breed-specific forms described elsewhere.
- Siamese cats may be predisposed.

Mean Age and Range

Most common in middle-aged animals, but younger animals may be affected.

Predominant Sex

N/A

SIGNS

Historical Findings

- Intermittent or persistent chronic GI signs (>3 weeks' duration).
- May include vomiting,

small/large bowel diarrhea, decreased appetite, and/or weight loss.

- Severe IBD may cause protein-losing enteropathy (PLE) in dogs.

Physical Examination Findings

- Vary from apparently healthy to a thin, lethargic animal.
- Poor hair coat with chronic disease and nutritional deficiencies.
- Abdominal palpation may reveal pain, thickened bowel loops, and mesenteric lymphadenopathy (especially in cats).
- Ascites may occur in dogs with PLE.
- Hematochezia, fecal mucus, and tenesmus seen with colonic involvement.

CAUSES

Pathogenesis unknown but most likely multifactorial, involving complex interactions between host genetics, mucosal immunity, and environmental (diet, intestinal bacteria) factors.

Infectious Agents

- Adherent and invasive *Escherichia coli* has been associated with granulomatous colitis in dogs.
- Giardia*, *Salmonella*, *Campylobacter*, and resident microbiota have been implicated.

Dietary Agents

Meat proteins, milk proteins, gluten (wheat), and additives are all proposed causative agents, likely playing an important role.

Genetic Factors

- Some forms of IBD more common in certain breeds.
- Defects in innate immunity (e.g., mutations in *TLR2*, *TLR5*, and *nod2* as seen in German shepherd dogs) that perturb mucosal homeostasis may predispose individual to IBD.

RISK FACTORS

Current hypotheses suggest that IBD is multifactorial disorder conditioned by genetic, immunologic, and environmental factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Cats—hyperthyroidism, intestinal neoplasia (especially small cell lymphoma), adverse food reactions, feline infectious peritonitis and other viral infections (e.g., feline leukemia virus [FeLV] and feline immunodeficiency virus [FIV]), renal and hepatic insufficiency, exocrine pancreatic insufficiency, intestinal parasitism, and antibiotic-responsive diarrhea (ARD) are primary differentials.
- Dogs—intestinal neoplasia, motility disorders, adverse food reactions, lymphangiectasia, exocrine pancreatic insufficiency, intestinal parasitism, and ARD are primary differentials.

CBC/BIOCHEMISTRY/URINALYSIS

- Often unremarkable; these tests more often serve to eliminate other differential diagnoses.
- Anemia of chronic disease; mild leukocytosis ± left shift sometimes seen with mucosal disruption (e.g., erosions); mild eosinophilia may be seen with eosinophilic enteritis, food allergy, and intestinal parasites among other causes.
- Cats

may show alterations in serum total protein (i.e., hyperproteinemia) and albumin concentrations, with increased liver enzyme activities.

- Hypoproteinemia more common in dogs than cats.
- Cobalamin deficiency in both dogs and cats with involvement of ileum.

OTHER LABORATORY TESTS

- Useful to eliminate other differentials.
- Dogs—evaluation of exocrine pancreatic function: canine trypsin-like immunoreactivity (cTLI); serology for pancreatitis: canine pancreatic lipase activity (Spec cPL), and serum cobalamin and folate assays to localize small intestinal disease.
- Cats—T₄ and FeLV/FIV serology; fasting serum TLI (if exocrine pancreatic insufficiency suspected); serology for pancreatitis (Spec fPL), and serum cobalamin and folate assays to localize small intestinal disease.

IMAGING

- Survey abdominal radiographs—usually unremarkable.
- Barium contrast studies—may reveal mucosal abnormalities and thickened bowel loops; normal findings do not eliminate possibility of IBD.
- Ultrasonography—may indicate increased intestinal wall thickness (particularly muscularis propria and submucosal layers) and mesenteric lymphadenopathy; however, these abnormalities not specific for IBD.

DIAGNOSTIC PROCEDURES

- Perform elimination dietary trial to rule out adverse food reactions; if GI signs resolve within 2 weeks, then diagnosis of adverse food reaction is made.
- Perform fecal testing for nematode and protozoal parasites; treat for *Giardia* spp. and endoparasitic infection with fenbendazole (50 mg/kg for 5 days).
- Definitive diagnosis of IBD requires intestinal biopsy and histopathology, usually obtained via GI endoscopy; WSAVA guidelines should be used to define severity of mucosal inflammation.
- Laparotomy indicated if GI endoscopy unavailable or to collect full-thickness mucosal specimens; *always be sure to collect ileal biopsies*.
- Use scoring indices (canine inflammatory bowel disease activity index) to define clinical severity and assess response to therapy.

PATHOLOGIC FINDINGS

Morphologic evidence of mucosal inflammation including epithelial changes, architectural distortion (e.g., erosion/ulceration, crypt hyperplasia, fibrosis, loss of colonic goblet cells), and increased lamina propria cellularity. Histopathologic guidelines for defining severity of GI inflammation have been described.



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient, unless patient is debilitated from dehydration, hypoproteinemia, or cachexia.

INFLAMMATORY BOWEL DISEASE

(CONTINUED)

NURSING CARE

- If patient is dehydrated or must have food restricted because of intractable vomiting, any balanced crystalloid fluid is adequate (for a patient without concurrent disease); otherwise, select fluids on basis of secondary diseases.
- If severe hypoalbuminemia from PLE, consider use of colloids.

ACTIVITY

No restrictions.

DIET

- I
- Feed novel intact protein or hydrolysate elimination diet to help reduce intestinal inflammation.
 - Fiber supplementation (e.g., fermentable fiber such as pumpkin, Metamucil®) suggested in dogs and cats with colitis.
 - Fish oil (n-3 fatty acids) as free radical scavenger to reduce inflammation.
 - Probiotics may be of benefit in some animals but clinically unproven at this time; must be given continuously over several weeks for potential benefit to be realized.

CLIENT EDUCATION

- Emphasize that IBD is not cured but is controllable in most instances.
- Relapses are common; clients should be patient during the various food and medication trials that are often necessary to control the disease.

SURGICAL CONSIDERATIONS

Surgery only indicated for collection of intestinal biopsies in dogs and intestinal and/or liver, pancreatic and/or mesenteric biopsies in cats.



MEDICATIONS

DRUG(S) OF CHOICE

- Evidence-based data indicate glucocorticoids are effective drugs for inducing remission in majority of dogs and cats; use prednisone or prednisolone in dogs at 1–2 mg/kg PO daily for 21 days to induce remission, then taper dose by 25% every 2 weeks.
- Dogs weighing >30 kg will require lower steroid dosage to provide comparable clinical efficacy; this will also reduce adverse effects; *dose large dogs by body surface area.*
- Treat cats with oral prednisolone at 1–2 mg/kg for 14–21 days, then taper as above; avoid glucocorticoids in cats with diabetes mellitus and those with history of adverse effects.
- Budesonide may be used to minimize adverse steroid effects and maintain remission in some dogs and cats; dosage ranges dogs: 1–3 mg/m² daily; cats: 1 mg/day.
- Correct hypcobalaminemia by weekly parenteral cobalamin injections for first 6 weeks and thereafter every 2–3 weeks or as needed based on repeat testing of cobalamin concentrations; oral cobalamin therapy requires daily administration; antibiotics (metronidazole, tylosin) generally *not* indicated for treatment of IBD; these drugs may cause significant disruption

to gut microbiota even after administration discontinued.

- Some evidence that oral cyclosporine is of value in dogs with steroid-refractory disease and PLE; dose at 5 mg/kg PO daily for 4–6 weeks or as needed to induce remission.
- Use of other immunosuppressive drugs, including azathioprine, chlorambucil, leflunomide, or mycophenolate, has been reported.
- Empirical deworming with fenbendazole (50 mg/kg PO q24h for 5 days).
- Fecal microbiota transplant anecdotally effective in cases of refractory IBD; however, clinical trial data yet to be reported.

CONTRAINDICATIONS

Based on concurrent disease.

PRECAUTIONS

See Drug(s) of Choice.

POSSIBLE INTERACTIONS

See Drug(s) of Choice.

ALTERNATIVE DRUG(S)

See Drug(s) of Choice.



FOLLOW-UP

PATIENT MONITORING

- Periodic (q2–4 weeks) physical and laboratory evaluations may be necessary until the patient's condition stabilizes; serum albumin provides important prognostic information in dogs; serum cobalamin deficiency will delay complete clinical recovery in both dogs and cats.
- Monitor serum cobalamin concentrations in hypcobalaminemic dogs and cats.
- No other follow-up may be required except yearly physical examinations and assessment during relapse.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

Dehydration, malnutrition, adverse drug reactions, hypoproteinemia, hypcobalaminemia, anemia, and diseases secondary to therapy.

EXPECTED COURSE AND PROGNOSIS

- Generally good to excellent short-term prognosis.
- Poor long-term prognosis in dogs with IBD has been associated with severe clinical disease, marked endoscopic (duodenal) abnormalities, ascites, and hypoalbuminemia; long-term prognosis worse compared to food-responsive diarrhea and ARD, other forms of canine chronic enteropathy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- See discussion under specific diseases.
- Cats may demonstrate concurrent

inflammatory lesions in the liver and/or pancreas ("triaditis").

AGE-RELATED FACTORS

Some differentials more likely in younger individuals (i.e., intestinal parasitism vs. neoplasia).

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Counsel clients about breeding and monitoring for appearance of other diseases.

SYNONYMS

None

SEE ALSO

- Colitis, Histiocytic Ulcerative.
- Diarrhea, Chronic—Cats.
- Diarrhea, Chronic—Dogs.
- Food Reactions (Gastrointestinal), Adverse.
- Gastroenteritis, Eosinophilic.
- Immunoproliferative Enteropathy of Basenjis.
- Protein-Losing Enteropathy.
- Small Intestinal Dysbiosis.
- Vomiting, Chronic.

ABBREVIATIONS

- ARD = antibiotic-responsive diarrhea.
- cPL = canine pancreatic lipase.
- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- fPL = feline pancreatic lipase.
- GI = gastrointestinal.
- IBD = inflammatory bowel disease.
- PLE = protein-losing enteropathy.
- TLI = trypsin-like immunoreactivity.

INTERNET RESOURCES

<http://www.vin.com/VIN.plx>

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Client Education Handout
available online

INFLUENZA



BASICS

OVERVIEW

- An acute to subacute contagious viral disease with an almost exclusive respiratory manifestation caused by influenza viruses.
- Canine influenza viruses (CIV) are influenza type A viruses that developed from equine (H3N8, USA) or avian (H3N2; East Asia) influenza viruses. Although the viruses originated in other species, the H3 viruses are considered “canine influenza viruses” as they are now transmissible dog to dog. Influenza H7N2 is an avian influenza A virus that was documented in shelter cats. H1N1 human pandemic influenza is also capable of infecting dogs and cats, but there is no evidence of transmission.
- Natural route of infection is airborne particles or oral contact with contaminated surfaces. Replication of the virus appears to be restricted to epithelial cells of the upper and lower airways, with possible involvement of alveolar macrophages. Antibody response detectable by 8 days post infection and titers remain detectable for >1 year. Protective immune responses have not been defined.
- H3N8 CIV activity was first detected in racing greyhounds in the United States in 2004 and has subsequently been identified in dogs across the country.
- H3N2 CIV was detected in South Korea in 2007, but existed in China several years earlier; genetic lineage is of avian origin and probably arose in East Asia.
- H3N2 CIV infection causes more severe clinical signs, is more easily transmissible, and is shed for a longer period than H3N8 CIV.

SIGNALMENT

- Natural infections of H3N8 CIV currently limited to dogs; H3N2 virus is capable of infecting dogs and cats; H7N2 has infected shelter cats.
- All dogs and cats are susceptible to infection; there are no known age, breed, or sex restrictions on susceptibility.

SIGNS

- 60–80% of infected dogs develop clinical signs.
- Incubation period 2–4 days post infection.
- Modest febrile response 39.4–40 °C (103–104 °F) 3–6 days post infection.
- Clear nasal discharge, which can progress to thick, mucoid discharge, most frequently caused by secondary bacterial colonization.
- More severe form of disease shows higher body temperatures with development of pneumonia and tachypnea 6–10 days post infection.
- Many dogs develop a cough that can last for several weeks.

CAUSES & RISK FACTORS

- Respiratory infection caused by influenza viruses.

- Most cases have a history of group housing in kennels, day care centers, and rescue shelters, or contact with animals that have recently been in group housing or social settings such as dog shows.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- On an individual basis, early signs of influenza are indistinguishable from signs of kennel cough complex.
- Distinction from typical respiratory pathogens of dogs is found in group settings in which 60–80% of dogs can show clinical signs.
- Later in disease course—pneumonia may develop with or without secondary bacterial infections.

CBC/BIOCHEMISTRY/URINALYSIS

- Generally unremarkable.
- CBC may reflect stress initially, then bacterial pneumonia later in disease (leukocytosis, left shift).

OTHER LABORATORY TESTS

N/A

DIAGNOSTIC PROCEDURES

- Matrix gene reverse transcriptase polymerase chain reaction (RT-PCR) test—most reliable and preferred test; can detect agent in acute phase of disease (1–7 days post onset of clinical signs) in nasal swab.
- Viral isolation—possible early (~first 3 days) in infection.
 - PCR and viral isolation can be negative if collected too late in infection.
 - Serologic tests for H3N8 will not detect H3N2 and vice versa; must test for each separately.
- Hemagglutination inhibition test—preferred serologic test; acute and convalescent titers optimal; since most dogs have no circulating CIV antibodies, antibodies detected in serum more than 7 days post onset of clinical signs determine exposure to CIV.
- Antigen-capture ELISA tests gave unacceptable levels of false negatives with H3N8 infections, but higher viral loads with H3N2 give acceptable results if testing done early in course of infection.

PATHOLOGIC FINDINGS

Primary lesion caused by infection is destruction of ciliated epithelial cell layer in upper airways with extension into lungs. Areas of lung consolidation can be found 6–10 days post infection.



TREATMENT

- Infected animals should be isolated to prevent infection of other animals.

- Contagious period for H3N2 CIV extends approximately 2 weeks after onset of clinical signs.
- Continued coughing of affected animal is not a sign of virus shedding.
- Strongly recommend treating uncomplicated cases as outpatients to prevent hospital contamination.
- Only hospitalize those with pneumonia that require IV fluid or oxygen support.
- Enforced rest—for at least 14–21 days (uncomplicated cases); 2 months in cases of pneumonia.



MEDICATIONS

- Antiviral drugs have not been tested for efficacy.
- Antibiotics to control secondary bacterial infections recommended if fever, lethargy, or inappetence accompany mucopurulent nasal discharge—amoxicillin, amoxicillin-clavulanic acid, and doxycycline are empiric first-line options for mild cases.
- Clinical pneumonia—first-line recommendations include parenteral administration of fluoroquinolone and penicillin (ampicillin) or clindamycin initially until antimicrobial culture and sensitivity available.
 - Resistant bacteria—important to culture and establish bacterial sensitivity; consider inherent resistance of Mycoplasma to penicillins and cephalosporins; for organisms resistant to first-choice antibiotic therapies above, consider aminoglycosides (gentamicin or amikacin, contraindicated in animals with renal dysfunction, dehydration), cephalosporins (cephalexin, cefazolin, cefadroxil, cefoxitin, ceftiofur); see Suggested Reading.
 - In absence of controlled studies on efficacy, inhalational antimicrobial therapy not recommended.
- In animals treated for pneumonia—recheck patient and radiographs after 10–14 days to decide whether continued antibiotic therapy indicated; optimal duration of therapy for pneumonia unknown; shorter courses of antibiotics (as used in humans with pneumonia) than traditionally recommended 4–6 weeks may be effective.
- Cough suppressants (butorphanol or hydrocodone bitartrate)—often effective in suppressing dry nonproductive cough; cough suppression counterproductive in animals with pneumonia.
- Bronchodilators (theophylline or aminophylline)—may relieve wheezing.



FOLLOW-UP

- If infection established in a kennel, evacuate kennel for 1–2 weeks and disinfect with sodium hypochlorite (1 : 30 dilution), chlorhexidine, or benzalkonium; influenza virus can live on hard surfaces for up to 24 hours.

INFLUENZA

(CONTINUED)

- Uncomplicated cases should resolve within 10–14 days; if patient continues to cough beyond 14 days, further diagnostics indicated.
- Mortality rate highly variable and likely linked to degree of secondary bacterial infection, strain of virus, and intensity of veterinary care.
- Currently there are licensed influenza vaccines for use in dogs that cover H3N8, H3N2, or both. There are no licensed vaccines for cats.

I



MISCELLANEOUS

ZOONOTIC POTENTIAL

- Risk thought to be low; however, influenza viruses mutate rapidly and outbreaks in dogs

and cats monitored for this potential; one person documented to develop infection with H7N2 working with cats in shelter outbreak.

- Cats can be experimentally infected with H3N8 CIV; H7N2 virus was isolated from cats in an animal shelter.
- H3N2 virus can also infect ferrets, guinea pigs, and mice.

ABBREVIATIONS

- CIV = canine influenza virus.
- RT-PCR = reverse transcriptase polymerase chain reaction.

INTERNET RESOURCES

<https://www.avma.org/resources-tools/animal-health-and-welfare/canine-influenza>

Suggested Reading

- Dubovi EJ, Njaa BL. Canine influenza. *Vet Clin Small Anim* 2008, 38:827–836.
Lappin MR, Blondeau J, Boothe D, et al. Antimicrobial use guidelines for treatment of respiratory tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. *J Vet Intern Med* 2017, 31:279–294.

Author Edward J. Dubovi

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INTERVERTEBRAL DISC DISEASE—CATS



BASICS

OVERVIEW

- Disc extrusion or protrusion causing myelopathy is more common in dogs; both Hansen's type I and type II disc disease, and acute, noncompressive nucleus pulposus extrusion (ANNPE) are reported in cats.
- Type I disc disease is secondary to chondroid metaplasia and mineralization of the nucleus pulposus. • Type II disc disease is secondary to fibroid degeneration and protrusion of the annulus fibrosus. • With ANNPE, normal nucleus pulposus is extruded through a tear in the dorsal annulus, resulting in a concussive or contusive injury, with minimal to no ongoing compression of the spinal cord.

SIGNALMENT

- For all reported cats with myelopathy secondary to disc disease—mean age 8.4 years, range: 1.5–17 years. • Cats with mineralized type I disc disease—mean age 7.3 years, range: 2–13 years. • Predominantly domestic breeds, several purebred (Oriental) breeds reported; rare exotic large cat (tiger) reported. • No sex predisposition.

SIGNS

- Majority of cats have thoracolumbar or lumbosacral disc disease—clinical signs confined to pelvic limbs; cervical disc disease also described, in which case all four limbs may be affected; sacrocaudal disc disease can result in urinary and/or fecal retention or incontinence, lower lumbar pain. • Signs frequently acute or peracute, but may be chronic. • Paresis/paralysis. • Ataxia. • Gait abnormality, lameness, reluctance to jump. • Spinal/back pain. • Urinary/fecal incontinence.
- Abnormalities of tail carriage or tone. • Loss of pain perception (if severe lesion).
- Hypoventilation (if severe cervical lesion).

CAUSES & RISK FACTORS

- Majority of cats reported had type I disc degeneration, with extrusion of mineralized nucleus pulposus into vertebral canal resulting in spinal cord trauma and compression.
- Unlike dogs, where chondrodystrophic breeds (e.g., dachshunds) predisposed to type I disc disease and subsequent extrusion, no obvious risk factors apparent in cats. • Most cats reported had clinically significant disc protrusions or extrusions between T11 and S1; similar to dogs, presence of the intercapitulum ligament from T1 to T10 may make disc protrusions in that region less likely.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Trauma. • Vascular—ischemic neuromyopathy ("saddle thrombus"), ischemic myelopathy. • Neoplasia, especially lymphoma. • Vascular—ischemia to spinal cord. • Infectious—feline infectious peritonitis (FIP), *Cryptococcus*, etc.

CBC/BIOCHEMISTRY/URINALYSIS

USUALLY NORMAL.

IMAGING

- Vertebral column radiographs—narrowed disc space(s), mineralized discs in situ, mineralized disc material within vertebral canal or overlying intervertebral foraminae.
- Myelography—extradural compressive lesion at affected disc. • CT—extradural compression; mineralization of compressive material may be apparent. • MRI—T2 hyperintensity within injured cord; mineralized disc material appears hypointense on all imaging sequences; extradural compression may be apparent; with ANNPE, decreased T2 intensity of nucleus pulposus of likely extruded disc, hyperintensity in overlying spinal cord with minimal to no compressive epidural material.

DIAGNOSTIC PROCEDURES

- Cerebrospinal fluid—unremarkable or contaminated with blood in most cats; neutrophilic pleocytosis noted in three cats.
- Histopathology of material removed at surgery—consistent with degenerative disc material (type I or II).



TREATMENT

- Surgical spinal cord decompression likely most effective treatment for compressive disc disease; cats with noncompressive disc extrusions had successful outcomes with physical rehabilitation alone. • Risks of spinal surgery should be discussed with owner—hemorrhage, iatrogenic injury to spinal cord, instability. • Hemilaminectomy, ventral slot, lateral corpectomy, and lumbosacral dorsal laminectomy surgeries are described in the cat. • Postoperative care—good recumbent patient care, pain management, bladder management if incontinent cat (indwelling urinary catheter or manual expression), and appropriate physical therapy. • Fenestration

of adjacent mineralized discs should be considered to avoid recurrence. • Medical management (cage rest, pain management) may be considered in ambulatory cats, but more aggressive diagnostics and treatment should be considered in nonambulatory cats and those with progressive neurologic signs.



MEDICATIONS

DRUG(S) OF CHOICE

- Pain management, preferably opiates, if cat tolerates them. • Efficacy of corticosteroids in feline disc disease has not been evaluated.



FOLLOW-UP

- Repeat neurologic examinations (at least 1–2 times/day) during hospitalization to monitor postoperative and medically managed patients for improvement or decline in neurologic status. • Strict cage rest for medically managed and postoperative patients for 4–6 weeks, then gradual increase in activity and physical therapy, as needed.
- Unknown whether long-term activity restriction beneficial. • Because disc disease uncommon in cats, possible recurrence rate unknown, but in one cat that recovered well after hemilaminectomy, additional mineralized disc extrusion caused paraplegia and necessitated second surgery (unpublished data). • A few cats had persistent urinary retention in spite of good recovery of ambulation, requiring routine bladder expression by owner. • Majority of cats managed surgically (even two without pain perception) had good to excellent outcome.



MISCELLANEOUS

ABBREVIATIONS

- ANNPE = acute, noncompressive nucleus pulposus extrusion.
- FIP = feline infectious peritonitis.

Suggested Reading

Rayward RM. Feline intervertebral disc disease: a review of the literature. Vet Comp Orthop Traumatol 2002, 15:137–144.

Author Marguerite F. Knipe

INTERVERTEBRAL DISC DISEASE, CERVICAL



BASICS

DEFINITION

Degeneration of the cervical intervertebral discs that may result in protrusion or extrusion of disc material into the spinal canal. The protruded or extruded disc material causes spinal cord compression (myelopathy) and/or nerve root compression (radiculopathy), as well as concussive spinal cord injury in varying degrees.

PATHOPHYSIOLOGY

- Traditionally classified as acute disc herniation (Hansen type I disc) or chronic disc protrusion (Hansen type II disc); other types include extrusion of apparently healthy, hydrated nucleus pulposus with or without spinal cord compression, the latter termed acute noncompressive nucleus pulposus extrusion (ANNPE).
- Hansen type I—degeneration of the nucleus pulposus and acute rupture of the annulus fibrosus with extrusion of the nucleus pulposus into the spinal canal.
- Hansen type II—fibrinoid degeneration and protrusion of the dorsal annulus fibrosus into the vertebral canal (can involve a dynamic component).
- Disc extrusion or protrusion into the spinal canal causes focal compression of the spinal cord (myelopathy) and/or focal compression of a nerve root (radiculopathy) in addition to a variable degree of contusion injury; ANNPE primarily results in a contusion injury.
- Consequences of spinal cord compression are ischemia and demyelination.
- Consequences of spinal cord contusion include axonal and vascular injury as well as secondary cellular injury.
- Disc extrusion may be secondary to trauma, but this rarely occurs aside from those patients with hydrated disc herniations.
- Surgical fusion of cervical vertebrae may alter the biomechanics of adjacent vertebral bodies and therefore predispose discs to protrusion or extrusion; this is termed the domino effect.

SYSTEMS AFFECTED

Nervous system—either focal myelopathy or focal radiculopathy.

GENETICS

- Not known.
- Chondrodystrophic breeds (e.g., dachshund) are most commonly affected with Hansen type I disc extrusion.
- Large-breed dogs are most commonly affected with Hansen type II disc extrusion.

SIGNALMENT

Species

Dogs, rarely cats.

Breed Predisposition

- Hansen type I—dachshund, poodle, beagle, cocker spaniel, French bulldog, shih tzu; chondrodystrophic breeds.
- Hansen type II—Doberman pinscher, Labrador retriever.

Mean Age and Range

- Hansen type I—3–6 years of age.
- Hansen type II—8–10 years of age.

Predominant Sex

None recognized.

SIGNS

- Severity of clinical signs and spinal cord injury is dependent on several factors, including the rate and volume of disc protrusion or extrusion, spinal cord diameter relative to vertebral canal diameter, and the velocity of disc material that is extruded.
- Herniation in the cervical region can result in fewer neurologic deficits compared to similar lesions in the thoracolumbar region, because the spinal canal area is greater and can accommodate more disc material before spinal cord compression.

Historical Findings

- Neck pain—most common owner complaint.
- Stiff, stilted gait, lameness, or reluctance to move the head and neck.
- Lowered head stance and muscle spasms of the head, neck, and shoulder.
- Inability to rise or fall forward frequently.

Physical Examination Findings

- Neck pain—elicited upon slow manipulation of the neck or by deep palpation of the cervical muscles.
- Apparent forelimb lameness or nerve root signature (e.g., a thoracic limb that knuckles, appears lame, or is held in partial flexion).
- Paresis with or without general proprioceptive deficits involving one or both thoracic and pelvic limbs may be present.
- Pelvic limb paresis may be more severe than thoracic limb paresis.
- Pelvic limb spinal reflexes may be normal to exaggerated.
- Thoracic limb spinal reflexes may be normal to exaggerated when lesions are located in the C1–C6 spinal cord segment, and may be normal to decreased when the C6–T2 spinal cord segment is affected, although this finding is not reliable in some patients.
- Severity of clinical signs and degree of compression are not always correlated.
- Bladder function may be upper motor neuron in nature or normal.

CAUSES

- Degeneration of the intervertebral disc material and subsequent herniation or protrusion.
- Trauma may lead to extrusion of healthy material or otherwise degenerative material.

RISK FACTORS

Obesity and repeated traumatic events in those breeds predisposed to intervertebral disc disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Neoplasia.
- Atlantoaxial instability.
- Spinal fracture/luxation.
- Discospondylitis.
- Meningitis.
- Fibrocartilaginous embolism.
- Cervical vertebral instability.
- Systemic illness—hypoadrenocorticism, hypothyroidism.
- Spondylomyelopathy.

CBC/BIOCHEMISTRY/URINALYSIS

Often performed in anticipation of medication administration, general anesthesia, and/or surgery.

OTHER LABORATORY TESTS

- Cerebrospinal fluid (CSF) analysis—performed under general anesthesia (prior to myelography if performed).
- CSF analysis reveals nonspecific changes such as mild to moderate elevation in protein levels and mild to moderate pleocytosis, which is more pronounced in Hansen type I disc extrusion.
- Electromyography may be useful if the underlying cause is associated with denervation.

IMAGING

Cross-sectional Imaging

- MRI and CT are most sensitive for diagnosis of cervical intervertebral disc disease and intervertebral disc herniation (IVDH) as well as for surgical planning.
- MRI is the best available method for early recognition of intervertebral disc degeneration (IVDD) in dogs and is capable of the most complete evaluation of the spinal cord parenchyma.
- CT is also useful in diagnosis of spinal cord compression, especially by degenerative disc material; the spinal cord parenchyma is not as well assessed with this modality compared with MRI.

Cervical Spinal Radiography

- Well-positioned lateral and ventrodorsal survey radiographs of the cervical spine aid in excluding other differentials (i.e., discospondylitis, fracture/luxation, atlantoaxial instability, or lytic vertebrae suggestive of a bone tumor), but are not reliable for many patients with IVDH.
- Classic findings include narrowed intervertebral disc space or disc space wedging, collapse of the articular facets, or calcified disc material present in the

INTERVERTEBRAL DISC DISEASE, CERVICAL

(CONTINUED)

intervertebral foramen or in the spinal canal, although many of these findings can be seen without clinical signs, especially in overrepresented breeds.

- Hansen type II disc disease may be associated with spondylosis deformans.

Myelography

• Survey cervical radiographs may be misleading; therefore, myelography is more sensitive compared to survey radiographs, although cross-sectional imaging has replaced this modality in most practices.

- Lateral radiographs reveal dorsal deviation of the ventral contrast column over the intervertebral disc space consistent with extradural compression; intraforaminal or dorsolateral disc herniation is best seen on an oblique views.
- Acute cases with spinal cord swelling can cause blockage of contrast material and prevent it from flowing past the obstruction, limiting the diagnostic capabilities of the image.

DIAGNOSTIC PROCEDURES

CSF analysis.

PATHOLOGIC FINDINGS

Gross Findings

- Hansen type I disc—white extruded disc material that has a granular consistency and is usually easily removed from the spinal canal.
- Hansen type II disc—firm protrusion of the dorsal annulus fibrosus that is adherent to the floor of the spinal canal and to the dura of the spinal cord; type II discs are much more difficult to remove from the spinal canal.
- Spinal cord—in acute disc extrusion the spinal cord may appear bruised or swollen or may appear grossly normal; in chronic disc protrusion, the spinal cord may appear to be atrophied but is often normal in appearance.

Histopathologic Findings

- Hansen type I disc—shifting concentration of glycosaminoglycans, loss of water and proteoglycan content, and increased collagen content; the disc becomes more cartilaginous and undergoes dystrophic calcification.
- Hansen type II disc—a gradual fibroid metaplasia leaves the disc with increased glycosaminoglycan levels and lower collagen content; the nucleus does not undergo cartilaginous metaplasia.
- Spinal cord—dependent on the severity of the disease and type of disc disease; Hansen type II: demyelination and gliosis are seen; Hansen type I: hemorrhage and edema can be seen; with severe disease, myelomalacia can be observed.



TREATMENT

APPROPRIATE HEALTH CARE

- Conservative or surgical management dependent on patient's history and presenting neurologic status.

- In general, conservative management can be considered with a gradual onset of clinical signs or clinical signs that are limited to hyperesthesia or mild ataxia.

- Surgical management is often indicated in patients with repeated episodes of neck pain, severe neck pain and neurologic deficits, or a lack of response to conservative management.
- Patients with hydrated intervertebral disc herniations may perform similarly with conservative and surgical treatment.
- ANNPE is treated conservatively as there is no compression to address surgically.

NURSING CARE

- Level of nursing care needed depends on the severity of the injury; if unable to be cared for at home, patients should be monitored as inpatients.
- Minimal manipulation of the head and neck to avoid worsening discomfort.
- Urination—monitor patients for complete emptying of the bladder; patients may need to have bladder manually expressed or intermittent bladder catheterization; in some cases, indwelling urinary catheter may need to be placed.
- Defecation—patients typically defecate normally, although frequent cleaning and management of any soft stool are important.
- Recumbent patients—should be kept on a well-padded mat and turned frequently (often every 4 hours); should be checked for pressure sores over bony prominences; should be diligently cleaned and kept dry.
- Physical therapy—passive range of motion of all joints should be performed as often as possible to prevent severe muscle atrophy, especially in patients with minimal voluntary motor ability; hydrotherapy can be considered in tetraparetic patients as well.

ACTIVITY

- Activity should be very limited; no running or jumping, and confined to a crate-sized space; when patients are being walked, a harness should be used instead of a collar.
- With conservative or postoperative management, patients should be strictly confined to cage rest for 4 weeks, followed by a gradual return to normal activity over the course of another 4 weeks.

DIET

For obese patients, a decrease in caloric intake should be instituted.

CLIENT EDUCATION

- Appropriate expectations for clinical improvement or signs of worsening should be discussed.
- Confinement is very important for recovery.
- Weight loss if the animal is obese.

SURGICAL CONSIDERATIONS

- The goal of surgery is to remove disc material from the spinal canal and therefore decompress the spinal cord and/or nerve root.
- Surgery usually provides rapid pain relief and significantly improved motor function.

- A ventral cervical slot is the most common surgical approach for the removal of disc material; disc material that has extruded dorsolaterally into the intervertebral foramen or dorsally is removed via a lateral approach or through a dorsal laminectomy.
- Fenestration alone for dogs with neck pain usually does not resolve clinical signs and is no longer recommended.



MEDICATIONS

DRUG(S) OF CHOICE

- Anti-inflammatory therapy (low-dose glucocorticoid or nonsteroidal anti-inflammatory drugs [NSAIDs]) is often beneficial in order to decrease the pain in animals that are being treated conservatively as well as those recovering from surgery; use of high-dose glucocorticoids is not well supported by the literature and is generally not recommended.
- Analgesic medications such as gabapentin and muscle relaxants such as methocarbamol can also be used in conjunction with anti-inflammatories to improve pain control in both conservative as well as surgical treatment.

CONTRAINDICATIONS

Systemic status should be considered when choosing medications.

PRECAUTIONS

Anti-inflammatories or analgesic medications given to animals without simultaneous strict cage confinement could exacerbate disc extrusion by encouraging activity.

POSSIBLE INTERACTIONS

Using glucocorticoids with NSAIDs can cause severe gastrointestinal irritation and possibly intestinal perforation.



FOLLOW-UP

PATIENT MONITORING

- Weekly evaluations should be performed until resolution of clinical signs or until clinical progress plateaus.
- All patients should be fitted with a harness, and neck collars should be avoided.

PREVENTION/AVOIDANCE

- Inherent in particular breeds.
- Keeping patients at an ideal weight may help.

POSSIBLE COMPLICATIONS

- Complications are uncommon.
- Conservative management—continued neck pain, deteriorating motor status.
- Surgical management—hemorrhage, infection, neurologic deterioration,

(CONTINUED)

respiratory compromise, subluxation/luxation of vertebral bodies, collapse of intervertebral disc space, and foraminal collapse.

EXPECTED COURSE AND PROGNOSIS

- Prognosis for patients treated surgically or conservatively depends on neurologic signs at the time of presentation; lack of nociception leads to a poor prognosis for recovery of function long term (<50%) and duration of clinical signs beyond days likely worsens the prognosis.
- Prognosis is generally favorable for most patients; surgical treatment often leads to rapid improvement in pain control, especially in patients undergoing a ventral slot procedure.
- Some patients treated conservatively have recurrence of disease or deterioration and may require surgical intervention.

INTERVERTEBRAL DISC DISEASE, CERVICAL

- Patients who experience IVDH may be predisposed to IVDH at other sites in the future due to the underlying pathology (IVDD).



MISCELLANEOUS

ASSOCIATED CONDITIONS

Animals predisposed to cervical disc disease are also the same breeds that are predisposed to thoracolumbar disc disease.

SEE ALSO

Intervertebral Disc Disease, Thoracolumbar.

ABBREVIATIONS

- ANNPE = acute noncompressive nucleus pulposus extrusion.
- CSF = cerebrospinal fluid.
- IVDD = intervertebral disc degeneration.
- IVDH = intervertebral disc herniation.

- NSAID = nonsteroidal anti-inflammatory drug.

Suggested Reading

Jeffery ND, Levine JM, Olby NJ, Stein VM.

Intervertebral disc degeneration in dogs: consequences, diagnosis, treatment and future directions. J Vet Intern Med 2013, 27(6):1318–1333.

Lorenz MD, Coates J, Kent M. Handbook of Veterinary Neurology, 5th ed. St. Louis, MO: Saunders, 2011.

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Acknowledgment The author and book editors acknowledge the prior contribution of Otto I. Lanz



Client Education Handout
available online

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR



BASICS

DEFINITION

Intervertebral disc disease (IVDD) is an acute traumatic or chronic degenerative condition that causes loss of normal neurologic function to the pelvic limbs, bladder, and anal sphincter. Intervertebral discs chronically degenerate by loss of water, cellular necrosis, and dystrophic calcification. In the chronic condition, biomechanical properties of the disc deteriorate, and subsequently protrusion (Hansen type II) or extrusion (Hansen type I) of disc material occurs.

PATHOPHYSIOLOGY

- Intervertebral disc degeneration is initiated by one or more factors including trauma, chronic overload, decreased spinal mobility, age-related deterioration in collagen and cartilage, and hypermobility.
- Hansen type I refers to acute extrusion of nucleus pulposus through the annulus fibrosus into the vertebral canal; Hansen type I lesions typically occur in chondrodystrophic dogs, but may occur in larger nonchondrodystrophic dogs as well; onset of neurologic signs is usually acute and often severe; acute disc extrusion results in extruded material causing direct trauma to the spinal cord and residual disc mass leading to extradural spinal cord compression; trauma and spinal cord compression results in ischemia and spinal cord changes that vary from mild demyelination to necrosis of both gray and white matter; events at the cellular level include release of vasoactive substances, increased intracellular calcium, and increased free radical formation and lipid peroxides.
- Hansen type II lesions involve gradual protrusion (bulging) of the dorsal annular fibers into the vertebral canal associated with fibroid degeneration of the disc; Hansen type II lesions typically occur in nonchondrodystrophic dogs; the most common case presentation is of gradual onset of neurologic dysfunction and slow progression.
- Hansen type III injuries occur when the nucleus pulposus herniates with such force as to enter the spinal cord by penetration of the dura; Hansen type III injuries are rare, but carry a poor prognosis because they are commonly associated with subsequent myelomalacia and loss of deep pain response.
- Affected animals exhibit pain due to dural irritation, nerve root impingement, or possibly discogenic (annular pain receptors) in origin.
- Disc herniation is rare between T3 and T10 owing to the barrier of the intercapital ligament between dorsal annulus and spinal cord.

SYSTEMS AFFECTED

- Nervous.
- Neuromuscular.
- Renal/urologic (loss of voluntary urethral sphincter control).
- Digestive (loss of voluntary anal sphincter control).
- Musculoskeletal (muscle atrophy in chronic disease).

GENETICS

Early studies suggest a polygenic model with no dominance or sex linkage.

INCIDENCE/PREVALENCE

- Most common neurologic dysfunction in small animals; affects 2% of the canine population.
- Occurs less commonly in cats, but the exact incidence is unknown, and the disease is likely underdiagnosed or reported due to lack of suspicion as a differential diagnosis.
- In specific breeds, such as dachshunds, affected prevalence as high as 20% has been reported.
- Thoracolumbar disc disease comprises 85% of all disc herniations; 70% occur from T11 to L3.

SIGNALMENT

Species

Dog and occasionally cat.

Breed Predilections

- Type I—dachshund; shih tzu, Lhaso apso; Pekingese, cocker spaniel, Welsh corgi; toy and miniature poodle.
- Type II—large breeds, but may occur in any breed.
- Type III—active agility, racing, or working breeds; greyhound; border collie; Australian shepherd.

Mean Age and Range

- Type I—3–6 years of age.
- Type II—8–10 years of age; cats: mean age of 10 years.
- Type III—any age; occurs during exertion or trauma.

SIGNS

General Comments

The severity of clinical signs depends on the type of herniation, velocity of disc contact with the spinal cord, amount and duration of cord compression, location (upper motor neuron [UMN] or lower motor neuron [LMN]), and regional spinal canal/spinal cord diameter ratio (cervical vs. thoracolumbar).

Historical Findings

- Onset may be peracute or acute in chondrodystrophoid dogs (type I disease) and may occur during vigorous activity.
- Larger dogs or smaller dogs with type II disease have a more insidious onset and tend to worsen with time.
- Dogs with type III disease have a history of active exertion followed by sudden loss of function, or of severe traumatic origin such as vehicular trauma or racing injury.

Physical Examination Findings

- Thoracolumbar pain is a common finding in dogs; reluctant to ambulate and hunched posture; careful palpation of spinous

processes and epaxial musculature produces distinct localized pain; often some degree of paraparesis with decreased or absent proprioception or decreased motor ability in the pelvic limbs.

- Myotactic spinal reflexes in the pelvic limbs are exaggerated (hyperreflexive) when the lesion is between T3 and L3; reflexes are decreased (hyporeflexive) when lesion is caudal to L3.
- Superficial and deep pain perception may be decreased or absent in the pelvic limbs.
- Presence of deep pain sensation is the single most reliable prognostic factor for return to acceptable function; pain perception should be conscious in nature and not confused with a withdrawal reflex (local spinal reflex); in animals with diminished conscious deep pain response, observation of mydriasis or tachycardia may be useful in confirming the presence of deep pain.
- Forelimb function is normal with thoracolumbar disc rupture; occasionally Schiff-Sherrington phenomena may cause increased muscle tone in the forelimbs, but this clinical sign is location related only and does not indicate a poor prognosis.
- Urinary incontinence or retention is common when the lesion affects motor function.
- Pain is less obvious in cats; the site of herniation is often lumbar.

CAUSES

- Chondroid or fibroid degeneration of the thoracolumbar intervertebral discs.
- Acute trauma that overloads the capacity of the intervertebral disc to absorb force and ruptures the dorsal annulus.
- 15% of animals with spinal fractures have been reported to have disc extrusions in addition to the fracture/luxation.

RISK FACTORS

- Type I disease most often affects chondrodystrophic breeds.
- Racing and breeds used for agility competition are at risk for Type III disk disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Type I—trauma causing fracture/luxation, neoplasia, discospondylitis, fibrocartilaginous embolism; differentiated by history, survey radiography, myelography, CT, or MRI.
- Type II—degenerative myelopathy, spinal neoplasia, discospondylitis, orthopedic disease; differentiated by history, radiographic modalities, and careful orthopedic and neurologic examination.
- Type III—trauma causing spinal fracture or subluxation/luxation of vertebrae in the thoracolumbar region, fibrocartilaginous embolism, or Type I disk disease; differentiated by survey radiography, myelography, CT, or MRI.

(CONTINUED)

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR

CBC/BIOCHEMISTRY/URINALYSIS

- Elevation of liver enzymes is common if the patient has received previous corticosteroids for pain or neurologic disease.
- Urine retention/incontinence increases risk of urinary tract infection characterized by leukocytes, protein, and bacteriuria on urinalysis.

OTHER LABORATORY TESTS

Cerebrospinal fluid (CSF) analysis performed routinely in conjunction with myelography if there is high suspicion of another disease process; may be normal, but more typically shows mild to moderate increase in protein with or without pleocytosis when IVDD occurs.

IMAGING

- Thoracolumbar spinal radiography with the patient anesthetized; unanesthetized radiographs can be used to rule out neoplasia and other processes, but can be misleading for thoracolumbar disc disease.
- Survey radiographs rule out some other disease processes.
- Diagnostic radiographs taken under general anesthesia may reveal a narrowed or wedged disc space, collapsed articular facet space, and small intervertebral foramen with increased or mineralized density within the spinal canal.
- Accuracy and sensitivity of survey radiographs for determining a specific site of disc herniation are low; in conjunction with careful neurologic examination, the exact location can often be narrowed down to a small vertebral area, but the extent of herniation and pressure on the meninges from herniation of disc material may extend over more than one space.

DIAGNOSTIC PROCEDURES

- MRI is now considered the diagnostic mode of choice when available due to the noninvasive nature and superior information regarding location and extent of disease; presence of a hyperintense spinal cord lesion as long as the body of L2 on a T2-weighted image in deep-pain-negative dogs is associated with a poorer prognosis.
- CT with or without contrast is often diagnostic in chondrodystrophic dogs; dystrophic calcification of extruded material is easily visualized and lateralization can be easily determined; contrast enhancement can differentiate disc disease from neoplastic or granulomatous processes.
- Myelography performed with iohexol was previously the method of choice and is still indicated when CT or MRI is not available; the contrast agent is usually introduced at L5–L6; positive diagnosis is an extradural mass lesion causing spinal cord compression adjacent to the affected disc; spinal cord swelling may be evidenced by thinning of contrast columns over several intervertebral spaces.
- Lateralization is more consistent when

determined from both oblique and dorsoventral myelogram views.

- CSF analysis is an important addition when alternative causes of neuropathy are likely differential diagnoses or when imaging findings are equivocal or nondiagnostic.

PATHOLOGIC FINDINGS

Gross

- Extruded disc material (type I disease)—white to yellow and “toothpaste” consistency seen on laminectomy; if chronic, may be hardened and adhered to surrounding structures; extradural hemorrhage is usually present and mixed with extruded disc material; the ventral sinus may be ruptured and actively bleeding; subdural hemorrhage may be visible.
- Protruded disc material (type II disease)—usually firm, grayish-white, and may be adherent to surrounding structures; compression of the spinal cord is apparent, but usually without evidence of recent hemorrhage or trauma visible.
- Extradural or intradural hemorrhage without or with minimal extruded disc material (type III disease); the dural membrane may be penetrated and extruded material may be present within the spinal cord parenchyma; myelomalacia may be detectable as loss of dural and parenchymal integrity at the affected site.
- Spinal cord may appear normal or be swollen and discolored in acute severe disease.

Histopathologic

- Degenerated discs have decreased amounts of proteoglycans, glycosaminoglycans, and water; discs may become mineralized or cartilaginous.
- Spinal cord lesion depends upon type and severity of disc extrusion or protrusion; acute, severe disease may cause hemorrhage, edema, tissue necrosis; chronic disease demyelination of white and in some cases gray matter.



TREATMENT

APPROPRIATE HEALTH CARE

Guidelines for Therapy Based on Classification of Clinical Condition

- Class 1—back pain only, first episode.
- Class 2—recurrent back pain, ataxia, mild paraparesis, motor ability good.
- Class 3—severe paraparesis, proprioceptive deficits, motor ability affected but still present; voluntary control of urination may be diminished; bladder may be easy to manually express or difficult due to detrusor dysfunction.
- Class 4A—complete paralysis (no motor ability) with deep pain perception present; voluntary control of urination and defecation absent, bladder usually easy to

express manually.

- Class 4B—complete paralysis, no deep pain perception present.

Treatment Recommendations Based on Classification of Clinical Condition

- Class 1—treated medically unless pain persists.
- Class 2—treated medically initially with serial neurologic exam; surgery is performed if patient remains static or condition declines.
- Classes 3 and 4A—immediate surgical decompression recommended; prognosis good.
- Class 4B—surgical decompression and fair prognosis if within the first 12–48 hours of occurrence or for slower onset of clinical signs (clinical signs progressive over 12 hours); poor prognosis if deep pain perception has been absent for >48 hours or if the clinical signs progressed rapidly (<6 hours) from normal to loss of deep pain.
- Serial neurologic examination important for all affected animals.

NURSING CARE

- Absolute restricted confinement for 2–4 weeks or until ambulatory.
- Minimize spinal manipulation and support spine when handling patient.
- Ensure ability to urinate or consider bladder expression, intermittent catheterization, or indwelling urinary catheter for patients in classes 3–4B.
- Recumbent patients should be kept clean on padded bedding placed on elevated cage racks and turned frequently to prevent formation of decubital ulcers.
- Manual evacuation of the bowel or enemas may be necessary to promote defecation.
- Physical therapy with passive manipulation of pelvic limbs begun early followed by more intense therapy (hydrotherapy) for animals with neurologic deficits but regaining motor function; rehabilitation protocols are not contraindicated, but recent research suggests that they may not be beneficial in improving the speed of return to function.
- Carts useful in many patients in promoting return to function; patient tolerance is limiting factor.

ACTIVITY

- Restricted movement most important part of medical management.
- Cage rest in hospital or enforced cage rest as an outpatient for 2–4 weeks for class 1 patients or postoperative animals.

DIET

Weight reduction if patient is obese.

CLIENT EDUCATION

- Some degree of restricted activity may be important for the remainder of the animal's life since it has disc disease.
- Most animals in classes 1–4A have a good to excellent prognosis for return to function, i.e., ambulation with bowel and bladder continence; patients in class 4B have a poorer but not hopeless prognosis;

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR

(CONTINUED)

percentages vary, but up to approximately 50% may regain deep pain and some function, especially if appropriate surgical decompression occurs early in the disease process.

SURGICAL CONSIDERATIONS

• Surgery strongly indicated for animals in classes 3 and 4, also within the first 12–48 hours for class 4B dogs; also indicated for static or worsening class 1 and 2 dogs. • Primary surgical goal is to relieve spinal cord compression by disc mass removal via hemilaminectomy, dorsal laminectomy, or pediculectomy; disc fenestration alone is not effective for treating acute disc extrusions, but is frequently recommended as an adjunct to decompression at the primary site. • Hemilaminectomy on the side of predominant disc extrusion is the surgical procedure of choice for most thoracolumbar discs; studies indicate improved return to function, minimized spinal destabilization, and decreased formation of compressive laminectomy scars in the long-term postoperative period. • Foramenotomy and pediculectomy are similar to hemilaminectomy and may allow a more limited approach and decreased cord manipulation. • Dorsal laminectomy is the procedure of choice for disc herniation in the region of the lumbosacral plexus or where extensive examination of the spinal cord is necessary. • Recurrence of clinical signs in animals in the immediate postoperative period may be due to further extrusion of disc from the original site if fenestration is not adjunctively performed at the site of disc disease during hemilaminectomy or dorsal laminectomy; later recurrence of clinical signs after recovery is usually due to protrusion/extrusion at adjacent sites; several studies document approximately 8% long-term recurrence of clinical signs in dogs after initial hemilaminectomy and active site fenestration due to protrusion/extrusion at other sites. • Controversy remains over the efficacy of multiple site prophylactic disc fenestrations performed during the decompressive surgery, because evidence that fenestration prevents recurrence of clinical signs is not definitive and fenestration causes osteoarthritis to form at the intervertebral space of each site of fenestration, leading to potential chronic patient discomfort and pain.



MEDICATIONS

DRUG(S) OF CHOICE

- Nonsteroidal anti-inflammatory drugs (NSAIDs) or narcotics may be used as analgesics in class 1 cases to alleviate patient discomfort during recovery; use of analgesics is not a substitute for the cage rest period required of all patients.
- Narcotic analgesics may be necessary postoperatively; hydromorphone (0.05–

0.2 mg/kg IV/IM/SC q4h) or similar narcotic injectable used at appropriate doses are the treatment of choice in the immediate postoperative period; oral narcotics such as codeine (1–2 mg/kg PO q8h) or tramadol (5–8 mg/kg PO q8h) are useful to alleviate patient discomfort within the first week after decompression; transdermal lidocaine or fentanyl may be useful modes of analgesic administration in some animals, particularly those intractable to frequent dosing of injectable or oral agents.

- Gabapentin (5–10 mg/kg PO q12h), an NMDA receptor antagonist in dogs with chronic pain sensitization, is not an appropriate analgesic used alone in the immediate postoperative period.
- Methocarbamol (25–45 mg/kg q8h) may be useful in cases where muscle spasm is contributing to pain; more applicable with cervical disease.
- Bethanechol (5–15 mg/dog PO) and phenoxybenzamine (0.25 mg/kg PO q8–12h) or prazosin (1 mg/15 kg PO q8–12h) are variably helpful in managing bladder dysfunction associated with spinal cord lesion.
- Previous indications for methylprednisolone sodium succinate for treatment of acute pain are now controversial for efficacy; the high potential for side effects may outweigh the small gains from the drug.
- Corticosteroids are no longer commonly recommended in the treatment of acute intervertebral disc disease due to lack of demonstrated clinical efficacy.

PRECAUTIONS

- Glucocorticoid use is discouraged in cases of IVDD where drug side effects such as gastrointestinal hemorrhage and intestinal perforation often far outweigh benefits; potent glucocorticoids such as dexamethasone should never be used.
- Glucocorticoids are contraindicated within 48 hours of using an NSAID in dogs.
- Use of glucocorticoids without cage confinement may decrease pain, thereby encouraging excessive activity and leading to further disc herniation and deterioration of clinical condition.

ALTERNATIVE DRUG(S)

Alternative Therapies

- Acupuncture use has been described, but consistent efficacy has not been demonstrated.
- Chiropractic therapy has no proven benefits for IVDD and may potentially be harmful to the animal.
- Percutaneous therapeutic lasers do not reach the site of inflammation and are not efficacious; one recent study did demonstrate slightly more rapid recovery from IVDD if laser therapy regimens occurred as an adjunct to surgical decompression procedures.
- Discolysis by enzymatic injection or laser ablation has been described but is not proven therapy in dogs.



FOLLOW-UP

PATIENT MONITORING

- Patients treated medically should be reevaluated two to three times daily for worsening neurologic signs for the first 48 hours after onset.
- If stable, reevaluate daily, then weekly, until clinical signs have resolved.
- Patients treated surgically are evaluated twice daily until improvement is noted; urinary bladder function or awaiting development of an autonomic bladder are the limiting factors for hospitalization.

POSSIBLE COMPLICATIONS

- Recurrence of signs associated with disc herniation at original or at new site.
- Deterioration of clinical signs with or without surgery; continued inflammatory processes initiated by the initial extrusion may result in myelomalacia or diminished function.
- Rarely, development of ascending or descending myelomalacia; occurs in class 4A or 4B dogs 3–5 days following injury and is characterized by variable and progressive neurologic deterioration, possible fever, possible dyspnea, and extreme pain, with the cranial movement of the inflammation; careful monitoring of the anatomic position of detection of the panniculus reflex is recommended; cranial movement of the reflex can indicate ascending myelomalacia and provide early warning of a grave condition; such animals are often euthanized when diagnosed.

EXPECTED COURSE AND PROGNOSIS

- Overall prognosis for dogs in classes 1–4A good to excellent (85–95%); those treated conservatively may experience recurrence of clinical signs.
- Recurrence rates of dogs without fenestration at the time of laminectomy range from 5–30%.
- Dogs in class 4B have a variable (10–75%) chance of recovery; overall a guarded but seemingly favorable prognosis if surgery is performed within 48 hours and the animal is allowed sufficient time to recover.
- Dogs with type III disc extrusions often exhibit severe initial clinical signs and carry a grave prognosis for full recovery.



MISCELLANEOUS

ABBREVIATIONS

- CSF = cerebrospinal fluid.
- IVDD = intervertebral disc disease.
- LMN = lower motor neuron.
- NSAID = nonsteroidal anti-inflammatory drug.
- UMN = upper motor neuron.

(CONTINUED)

INTERVERTEBRAL DISC DISEASE, THORACOLUMBAR*Suggested Reading*

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**Client Education Handout
available online**

KERATITIS, EOSINOPHILIC—CATS



BASICS

OVERVIEW

- Presumed immune-mediated inflammation of the cornea characterized by perilimbal corneal vascularization, white-pink corneal infiltrate, and corneal edema.
- Synonym—proliferative keratitis.

SIGNALMENT

Young adult to middle-aged cats.

SIGNS

- Unilateral or bilateral.
- Variable ocular pain, often minimal.
- Serous to mucoid ocular discharge.
- Limbal superficial corneal vascularization 90–360° (temporal or inferior nasal quadrants are first affected).
- White to pink, flat or raised granular corneal infiltrate.
- Multifocal, small, white gritty corneal deposits.
- Corneal edema.
- Corneal ulceration may be present.
- Conjunctival and third eyelid hyperemia, chemosis, and thickening with possible cobblestone surface texture.

CAUSES & RISK FACTORS

- Feline herpesvirus-1 (FHV-1) may be associated, but exact role is unclear.
- Exact etiopathogenesis unknown; proposed theories are: (1) type I hypersensitivity with IgE-mediated mast cell and eosinophil degranulation, (2) type IV reaction where sensitized T-lymphocytes stimulate eosinophil-mediated corneal damage.
- Bacterial and fungal infection are not consistent etiologic causes, although secondary bacterial keratitis may occur.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Chronic corneal ulceration with secondary corneal vascularization (granulation tissue).
- FHV-1 stromal keratitis—appears similar, but lacks proliferative component, with more severe ocular pain and corneal ulceration.
- Corneal neoplasia: (1) lymphoma—concurrent conjunctival and/or uveal infiltration is common, (2) squamous cell carcinoma—rarely involves cornea in cats.
- *Chlamydia psittaci* or *Mycoplasma felis*—usually conjunctival diseases without corneal involvement.

CBC/BIOCHEMISTRY/URINALYSIS

Peripheral eosinophilia may be present.

OTHER LABORATORY TESTS

- PCR for FHV-1 has limited diagnostic value since healthy cats may have positive results.

- Immunofluorescent antibody test (IFA) testing for *Chlamydia psittaci*.

DIAGNOSTIC PROCEDURES

- Corneal cytology provides definitive diagnosis and should be done first. Typically numerous eosinophils, free eosinophil granules and/or mast cells, neutrophils, lymphocytes, plasma cells, and epithelial cells are seen.
- Cytology helps rule out chlamydia and mycoplasma.
- Fluorescein staining to evaluate for corneal ulceration.
- Keratectomy and histopathology may confirm diagnosis in chronic or nonresponsive cases.



TREATMENT

Outpatient



MEDICATIONS

DRUG(S) OF CHOICE

- Topical corticosteroids—1% prednisolone acetate or 0.1% dexamethasone sodium phosphate q6–12h for 5–7 days, then gradually taper to the lowest effective frequency of application or discontinue.
- Topical 1–2% cyclosporine A q8–12h, then tapered to lowest effective frequency of application or discontinued. Can use in cats in which oral megestrol acetate and topical corticosteroids are contraindicated. May be irritating or cause blepharitis.
- Topical 0.5% megestrol acetate q8–12h initially, then tapered to lowest effective frequency or discontinued.
- Adjunctive topical or systemic antiviral therapy may be warranted in cases with history or clinical signs compatible with FHV-1 infection.
- Subconjunctival corticosteroids—triamcinolone acetonide (0.1–0.2 mL q3–7 days); only in cats that are difficult to treat with topical medications.
- Systemic prednisolone—2.2 mg/kg PO q12h and taper. Use only if a cat will not tolerate topical therapy or oral megestrol acetate.
- Megestrol acetate—2.5 mg PO q24h for 3–5 days, then 2.5 mg PO q48h for 3–5 days, then gradually decrease frequency to the lowest effective frequency or discontinue.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Topical corticosteroid administration may be associated with recrudescence of FHV-1 keratoconjunctivitis and should be used and monitored carefully. Client should be advised to immediately report any adverse change in

the condition of the eye (blepharospasm, corneal edema, increased ocular discharge, etc.).

- Megestrol acetate causes adrenal cortical suppression and may result in diabetes mellitus, polyphagia, temperament change, mammary gland hyperplasia, or neoplasia and pyometra. It should not be used in cats with hepatic disease or other illness.



FOLLOW-UP

- Response to therapy is usually rapid.
- Complete resolution may take several days to months. May require long-term therapy.
- Corneal vascularization and infiltrate may resolve completely with minimal corneal scarring.
- Recurrences in both the short and long term are common.



MISCELLANEOUS

Not typically associated with dermatologic eosinophilic granuloma complex.

ABBREVIATIONS

- FHV-1 = feline herpesvirus-1.
- IFA = immunofluorescent antibody test.

Suggested Reading

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KERATITIS, NONULCERATIVE



BASICS

DEFINITION

An inflammatory disorder of the cornea that does not retain fluorescein stain.

PATHOPHYSIOLOGY

A pathologic response resulting in reduced corneal clarity secondary to edema, inflammatory cell infiltration, vascularization, pigmentation, lipid or calcium deposition, or scarring.

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- No proven genetic basis in dogs or cats.
- Chronic superficial keratitis (pannus)—inherited predisposition in German shepherd dogs.

INCIDENCE/PREVALENCE

Common in dogs and cats.

GEOGRAPHIC DISTRIBUTION

Chronic superficial keratitis is more common in regions of high UV light exposure.

SIGNALMENT

Species

- Dog—chronic superficial keratitis (pannus); pigmentary keratitis; pigmentary keratopathy of pugs; nodular granulomatous episcleritis (NGE; see Episcleritis); keratoconjunctivitis sicca (KCS; see Keratoconjunctivitis Sicca).
- Cat—eosinophilic keratitis (see Keratitis, Eosinophilic—Cats); herpesvirus (stromal form); corneal sequestrum; KCS uncommon, usually secondary to chronic herpesvirus infection.

Breed Predilections

Dogs

- Chronic superficial keratitis (pannus)—highest prevalence in German shepherd dogs and sighthounds.
- Pigmentary keratitis—notably brachycephalic breeds with exposure keratopathy from lagophthalmia, tear film deficiencies, and trichiasis.
- Pigmentary keratopathy of pugs—suspected genetic condition that results in progressive corneal pigmentation, cause currently unknown.
- NGE—prevalent in cocker spaniels, collies, and Shetland sheepdogs.
- KCS—brachycephalic breeds, cocker spaniels, English bulldogs, West Highland white terriers, cavalier King Charles spaniels.

Cats

- Eosinophilic keratitis—most prevalent in domestic shorthair.
- Corneal sequestration—most prevalent in brachycephalic breeds.

Mean Age and Range

- Dogs: chronic superficial keratitis—any age, usually between 3–6 years (younger in

sighthounds); pigmentary keratitis and pigmentary keratopathy of pugs may occur at any age; NGE—any age, mean 3.8 years in Collies; KCS—middle-aged to older dogs.

- Cats: herpesvirus, eosinophilic keratitis, and corneal sequestrum—any age.

Predominant Sex

- Dogs—female predisposition reported for pannus and KCS.
- Cats—castrated male predisposition reported for eosinophilic keratitis.

SIGNS

Historical Findings

Corneal discoloration and ocular discomfort.

Physical Examination Findings

Dogs

- Chronic superficial keratitis—usually bilateral, corneal vascularization range from superficial vessels to dense granulation tissue with variable pigmentation; lateral or ventrolateral cornea (entire cornea affected in advanced cases); thickened and depigmented third eyelids; white deposits (corneal degeneration) may be present at the leading edge of corneal lesion; may lead to blindness.
- Pigmentary keratitis—Focal to diffuse brown discolored cornea; often with corneal vascularization or scarring.
- Pigmentary keratopathy of pugs—brown corneal pigmentation originating from medial cornea and progressing towards central cornea.
- NGE—bilateral or unilateral; raised, fleshy masses affecting the lateral limbus and cornea; corneal deposits, edema, and vascularization may occur in adjacent corneal stroma; slow to rapidly progressive; third eyelids may appear thickened.
- KCS—unilateral or bilateral; mucoid ocular discharge, conjunctival hyperemia, corneal vascularization, pigmentation, and scarring; corneal ulceration may occur.

Cats

- Herpesvirus (stromal form)—unilateral or bilateral; stromal edema, infiltrates, deep vascularization and scarring; ulceration may occur; severe scarring may threaten vision.
- Eosinophilic keratitis—usually unilateral; raised vascularized lesion with pink-white infiltrates forming gritty plaques; may retain fluorescein stain at the lesion's periphery.
- Corneal sequestrum—usually unilateral (can be bilateral); amber, brown, or black plaques on the central or paracentral cornea; vary in size and depth; edges may appear raised; corneal vascularization is variable; may retain fluorescein at periphery of lesion.

CAUSES

Dogs

- Chronic superficial keratitis—presumed to be immune-mediated; high altitude (increased UV radiation exposure) increases

the prevalence and severity of disease.

- Pigmentary keratitis—secondary to chronic corneal irritation; evaluate for primary underlying ocular conditions; frequently associated with exposure keratopathy and KCS.
- Pigmentary keratopathy of pugs—unknown, may have genetic basis.
- NGE—presumed to be immune mediated.
- KCS—bilateral: usually immune-mediated or drug-induced; unilateral: congenital, iatrogenic, neurogenic.

Cats

- Herpesvirus (stromal form)—immune-mediated T-cell lymphocyte reaction to herpesvirus antigen (vs. cytopathic effect of the virus).
- Eosinophilic keratitis—possible hypersensitivity reaction; high incidence of animals PCR positive for feline herpesvirus type 1 (FHV-1); fewer positive for *Chlamydia*-like agents.
- Corneal sequestrum—unknown; likely due to chronic corneal irritation or ulceration; suggested relationship with herpesvirus.

RISK FACTORS

Dogs—chronic superficial keratitis more likely to occur at high altitudes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Infectious keratitis is usually ulcerative and painful; cytology of the cornea reveals white blood cells, infectious organisms. In cats, stromal herpesvirus may be associated with ulcerative keratitis and secondary bacterial infection.
- Neoplasia—rare involvement of sclera or cornea; distinguish based on color, age of animal, breed predilection; usually unilateral; lack of response to topical anti-inflammatory therapy. Very rare in cats.

DIAGNOSTIC PROCEDURES

Dogs

- Schirmer tear test—values <15 mm/min suggest KCS but should be interpreted with breed and ocular findings.
- Cytologic examination of corneal or conjunctival scrapings—chronic superficial keratitis characterized by lymphocytes, plasma cells, and mast cells.
- Biopsy of episcleral nodular mass or cornea (superficial keratectomy)—for NGE diagnosis, can be considered for patients with chronic superficial keratitis.

Cats

- Conjunctival or corneal scraping—PCR most successful for diagnosis for herpesvirus (IFA or viral culture of limited value).
- Eosinophilic keratitis: eosinophils on cytology.
- Superficial keratectomy—consider for diagnosis of eosinophilic keratitis or sequestrum but usually unnecessary.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—generally sufficient.
- Inpatient—cases that warrant surgery due to inadequate response to medical therapy.

CLIENT EDUCATION

Dogs

Typically lifelong treatment; disease is controlled rather than cured.

Cats

• Herpesvirus—ocular discomfort and keratitis often recur. • Eosinophilic keratitis—disease controlled rather than cured. • Corneal sequestrum—may slough spontaneously, however cornea may rupture; clinical course often protracted without surgery; removal of sequestrum by superficial keratectomy may be curative, although recurrence possible.

SURGICAL CONSIDERATIONS

Dogs

• Chronic superficial keratitis—superficial keratectomy for severe disease in which vision is impaired due to corneal pigmentation; patients still require indefinite medical treatment to prevent recurrence; β -irradiation with a strontium-90 probe is noninvasive and may be performed in severe cases. • Pigmentary keratitis—superficial keratectomy may be performed only after initial underlying cause is corrected; only in severe cases that threaten vision. • Pigmentary keratopathy of pugs—high likelihood of recurrence after superficial keratectomy. • NGE—superficial keratectomy is diagnostic; medical treatment is still required. • KCS—parotid duct transposition or permanent partial tarsorrhaphy to reduce exposure.

Cats

• Eosinophilic keratitis—superficial keratectomy is diagnostic but not curative; medical treatment is preferred. • Corneal sequestrum—superficial keratectomy may be curative; recurrence is possible.



MEDICATIONS

DRUG(S) OF CHOICE

Dogs

• Chronic superficial keratitis—topical corticosteroids (1% prednisolone or 0.1% dexamethasone q6–12h); topical 0.2–2% cyclosporine, 1% pimecrolimus, or 0.03% tacrolimus q8–12h; agents can be used alone or in combination for more severe cases; subconjunctival corticosteroid injection

(triamcinolone acetonide, 2–8 mg) can be used as an adjunct to topical therapy in severe cases. • Pigmentary keratitis—treatment directed at underlying cause; topical corticosteroids if primary cause is inflammatory; lubricants and cyclosporine or tacrolimus if primary condition is KCS; cyclosporine or tacrolimus may reduce pigmentation in all cases. • Pigmentary keratopathy of pugs—topical cyclosporine 0.2–2% or tacrolimus 0.02–0.03% may arrest progression of corneal pigmentation; topical corticosteroids may temporarily reduce density of corneal pigment. • NGE—topical corticosteroids and/or cyclosporine as described above; systemic azathioprine (2 mg/kg/day PO, initially, then gradually reduce) may be effective when used alone or in combination with topical medications. • KCS—topical 0.2–2% cyclosporine, or 0.02–0.03% tacrolimus q8–12h (see Keratoconjunctivitis Sicca).

Cats

• Herpesvirus—topical antiviral agents recommended: cidofovir 0.5% q12h or trifluridine q4–6h for 2 days, then taper. Systemic antiviral agents include: famciclovir 90 mg/kg PO q12h. For inflammation, topical nonsteroidal anti-inflammatory drugs or cyclosporine q12h may be used. • Eosinophilic keratitis—topical corticosteroids (1% prednisolone or 0.1% dexamethasone) q6–12h; patient monitored for ulceration or worsening of clinical signs; topical antivirals can be used in combination with corticosteroids if concurrent herpesvirus; use of topical cyclosporine reported (0.2–1.5%) with variable results; megestrol acetate (5 mg PO q24h for 5 days, then 5 mg PO q48h for 1 week, then 5 mg PO weekly for maintenance) is highly effective, but associated with side effects. • Corneal sequestrum—topical antibiotic (terramycin or erythromycin) q8–12h for associated corneal ulceration; artificial tear lubrication may relieve discomfort; topical antivirals can be used if herpesvirus infection is suspected; topical 1% atropine ointment q12–24h for pain from concurrent uveitis if present.

CONTRAINdicATIONS

Topical corticosteroids contraindicated with corneal ulcers; topical atropine contraindicated with KCS, glaucoma, or lens luxation. Topical neomycin and polymixin may cause anaphylactic reactions in cats.

PRECAUTIONS

• Azathioprine may cause gastrointestinal signs, pancreatitis, hepatotoxicity, and myelosuppression. • Megestrol acetate—not FDA-approved for use in cats; possible side effects include polyphagia, diabetes mellitus, mammary hyperplasia, mammary neoplasia,

and pyometra. • Famciclovir—anorexia, polydipsia.



FOLLOW-UP

PATIENT MONITORING

Periodic ocular examination recommended to evaluate efficacy of treatment; examine at 1–2-week intervals, gradually lengthening the interval with remission or resolution of clinical signs; taper medications based on resolution of clinical signs; complete resolution of pigmentation may not occur. UV light protection (tinted goggles) is recommended for pannus.

K

POSSIBLE COMPLICATIONS

All of the above may lead to continued ocular discomfort, visual defects, or blindness in severe cases.



MISCELLANEOUS

SEE ALSO

- Corneal Sequestrum—Cats.
- Episcleritis.
- Keratitis, Eosinophilic—Cats.
- Keratitis, Ulcerative.
- Keratoconjunctivitis Sicca.

ABBREVIATIONS

- FHV-1 = feline herpesvirus type 1.
- IFA = immunofluorescent antibody test.
- KCS = keratoconjunctivitis sicca.
- NGE = nodular granulomatous episcleritis.

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Acknowledgments The author/editor acknowledges the prior contribution of Amber L. Labelle.



Client Education Handout
available online

KERATITIS, ULCERATIVE



BASICS

DEFINITION

Inflammation of the cornea associated with loss of corneal epithelium (corneal erosion) or loss of variable amounts of underlying corneal stroma (corneal ulcer).

PATHOPHYSIOLOGY

- May be caused by any condition (traumatic or nontraumatic) that disrupts corneal epithelium or stroma.
- Ulcers—superficial or deep, uncomplicated or complicated:
 - Superficial—involves epithelium and possibly superficial stroma.
 - Deep—involves a greater thickness of stroma and may extend to Descemet's membrane (descemetocele), possibly leading to rupture of globe.
 - Complicated—persistence of underlying/inciting cause, microbial infection, or production of degradative enzymes (melting).
 - Epithelial wound healing—adjacent corneal epithelial cells loosen and begin migration over the defect within a few hours; mitosis occurs within a few days to restore normal epithelial thickness; healing process complete in 5–7 days in uncomplicated, superficial ulcers.
 - Stromal wound healing—slower, more complex; can be in an avascular or vascular manner; in shallow wounds, epithelial migration may be sufficient to fill defect; epithelium may cover some deeper ulcers even when epithelium and stromal regeneration are insufficient to restore normal corneal thickness (nonulcerated divot defect is called a facet); stroma usually heals by fibrovascular infiltration, resulting in scarring.
 - Stromal ulcers—often complicated by microbial infection or enzymatic destruction initiated by microbial organisms, host inflammatory cells, or corneal epithelial or stromal cells; enzymatic destruction may result in gelatinous appearance of corneal stroma ("melting" or "malacic" ulcer).

SYSTEMS AFFECTED

Ophthalmic

GENETICS

- No proven basis; breed predilections exist.
- May be secondary to other corneal diseases with breed predispositions and genetic basis, such as corneal epithelial dystrophy in Shetland sheepdogs and corneal endothelial dystrophy in Boston terriers.

INCIDENCE/PREVALENCE

Common

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Dogs—brachycephalic breeds predisposed.
- Spontaneous chronic corneal epithelial defects (SCCED)/indolent erosion—any breed.
- Cats—Persian, Himalayans, Siamese, and Burmese predisposed to corneal sequestra (see Corneal Sequestrum—Cats).

Mean Age and Range

- Age of onset—variable; determined by cause.
- SCCED—middle-aged and older dogs.

SIGNS

Historical Findings

- May be acute or chronic (SCCED).
- Tearing, squinting, rubbing at eyes.
- Owners may report a "film" over the eye (often corneal edema); prolapsed third eyelid.
- Herpetic ulcers (cats)—may have history of respiratory disease.

Physical Examination Findings

- Nonspecific—serous to mucopurulent ocular discharge, blepharospasm, nictitans prolapse, conjunctival hyperemia.
- Superficial—may note one or more circumscribed, linear, or geographic defects in cornea.
- Deep stromal ulcer or descemetocele—may appear as a crater-like defect.
- Depending on cause and duration—may see neovascularization, pigmentation, scarring, inflammatory cell infiltrate (yellow to cream-colored opacity with indistinct margins, often surrounded by corneal edema), collagenolytic activity (melting) of corneal stroma.
- SCCED—loose or redundant epithelial edges; may demonstrate fluorescein stain extending into areas with seemingly intact epithelium (ring of less intense staining).
- Reflex anterior uveitis—mild or severe, secondary to ulceration; severe may result in hypopyon; severe suggests concurrent bacterial infection.

CAUSES

- Trauma—blunt; penetrating; perforating.
- Adnexal disease—ectopic cilia, entropion, ectropion, eyelid mass, distichiasis.
- Lagophthalmos (inability to close eyelids completely)—results in exposure keratitis; may be breed-related in brachycephalic dogs and cats; may be caused by exophthalmos, buphthalmos, or may be neuroparalytic from facial nerve paralysis.
- Tear-film abnormality—quantitative tear deficiency (keratoconjunctivitis sicca [KCS]); qualitative tear film deficiency caused by mucin deficiency or some other unidentified tear abnormality.
- Infection—usually secondary in dogs; can be primary herpesvirus infection in cats.
- Primary corneal disease—endothelial dystrophy; other endothelial disease.
- Miscellaneous—foreign body (corneal or conjunctival), chemical burns, neurotrophic keratitis (loss of trigeminal sensation), immune-mediated disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of a red and painful eye—conjunctivitis, uveitis, KCS, glaucoma (see Red Eye).
- May develop concurrently with other causes of a red eye (e.g., secondary to KCS).

OTHER LABORATORY TESTS

- Corneal culture and sensitivity—aerobic culture; particularly for complicated, deep, or rapidly progressive corneal ulcers.
- Herpesvirus (cats)—PCR or immunofluorescent antibody test (IFA) for herpesvirus available; negative test does not rule out herpesvirus infection.

DIAGNOSTIC PROCEDURES

Fluorescein Staining

- Homogeneous stain uptake—superficial or stromal ulcer; may be circular to geographic, linear, or combination; location and shape may help determine cause (e.g., linear may indicate foreign body or rubbing of ectopic cilia); interpretation of depth subjective.
- SCCED—may have leakage of stain under surrounding loose epithelium.
- Descemetocele—crater-like defect that retains stain at periphery but is clear at center; may see Descemet's membrane bulging if large defect.
- Previous stromal ulcer that has epithelialized (facet)—crater-like defect with transient pooling of stain that is easily rinsed; must distinguish from descemetocele.

Other

- Cytologic evaluation of cornea and Gram, Giemsa, or Wright staining may reveal microbial or fungal organisms and help direct initial antimicrobial therapy.
- Schirmer tear test may identify ulceration associated with KCS; contraindicated in very deep ulcers or descemetoceles.

PATHOLOGIC FINDINGS

- Ulcers—suppurative inflammation, possibly neovascularization, loss of epithelium and basement membrane; possibly organisms.
- SCCEDs—superficial hylanized zone in stroma; epithelial lipping around erosions; varying degrees and types of leukocytic infiltrate and fibrosis.



TREATMENT

APPROPRIATE HEALTH CARE

Hospitalize deep or rapidly progressive ulcers; these may require surgery and/or frequent medical treatments.

(CONTINUED)

NURSING CARE

Keep facial hair out of eyes and clean.

ACTIVITY

- Restrict with deep stromal ulcer or descemetocele to prevent rupture.
- Prevent self-trauma with Elizabethan collar.

CLIENT EDUCATION

- Instruct client to wait at least 5 minutes between medications if more than one ophthalmic drop is prescribed; wait longer between ointments.
- Advise client to contact veterinarian if patient appears more painful or the eye markedly changes in appearance.
- SCCED—discuss protracted course with client; usually achieve healing within 2–6 weeks but may require weekly rechecks and multiple procedures.

SURGICAL CONSIDERATIONS

- Superficial ulcers do not usually require surgery if inciting cause has been eliminated.
- Ulcer that extends one-half or greater corneal thickness and particularly to Descemet's membrane may benefit from surgery.
- Descemetocele or full-thickness corneal laceration—surgical emergency, possible referral.

Procedures

- SCCED—debridement of loose epithelium with a dry, sterile, cotton-tipped swab after application of topical anesthesia (50% success rate); punctate or grid keratotomy easily performed after epithelial debridement with topical anesthesia (80% success rate); superficial keratectomy is more invasive and may cause more scarring but has 100% success rate; application of a contact lens or nictitans flap after any of these procedures may improve comfort and aid healing.
- Diamond burr keratotomy for SCCED/indolent erosion only; use gently over surface of erosion; may be associated with increased risk of infection.
- Rotational pedicle conjunctival flap, corneoscleral transposition, corneal transplant—surgical procedures for ulcers >50% stromal thickness and descemetoceles.
- Cyanoacrylate repair (corneal glue)—can be used for deep ulcers; promotes corneal vascularization and stabilizes cornea, but has lower success rate compared to other corneal surgeries.

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

- Topical agents—indicated for all patients.
- Frequency of application—determined by severity and preparation; ointments have relatively long contact time and are applied q6–12h; solutions are applied more

frequently (q2–6h) in initial treatment of complicated ulcers; solutions probably more appropriate in deep ulcers.

- Commonly used agents—erythromycin (cats); triple antibiotic, gentamicin, and tobramycin.
- Uncomplicated ulcers or superficial erosions—combination of neomycin, polymyxin B, and bacitracin an excellent first choice; broad spectrum of antimicrobial activity; often used 2–3 times/day for prophylactic therapy.
- Complicated ulcers—often use combination therapy of cefazolin (use IV solution to make 33–50 mg solution in saline or artificial tears for topical use) with a fluoroquinolone (ciprofloxacin, ofloxacin); particularly in rapidly progressive, deep, or melting ulcers; frequency depends on severity but usually a minimum of q3–4h.

Atropine

- 1% ointment or solution.
- Indicated for reflex anterior uveitis; frequency—usually q8–24h to effect (mydriasis).

Antiviral Agents

- Indicated for herpetic ulcers in cats.
- Trifluridine (Viroptic) solution—q4–6h until clinical response is observed; then reduce for 1–2 weeks after clinical signs have subsided.
- Famciclovir—90 mg/kg PO q12h for 2–4 weeks.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Flurbiprofen, diclofenac.
- For anti-inflammatory and analgesic properties.

CONTRAINDICATIONS

- Topical corticosteroids—contraindicated with any corneal erosion or ulcer.
- Topical NSAIDs—contraindicated with herpetic ulcers.
- Topical atropine—contraindicated with glaucoma, KCS.

PRECAUTIONS

- Topical NSAIDs may delay corneal healing, may potentiate corneal melting.
- Trifluridine, neomycin—may be irritating.
- Topical cyclosporine can be used safely in KCS patients with uncomplicated ulcers.

POSSIBLE INTERACTIONS

Combining antibiotics in solution may inactivate some antibiotics.

ALTERNATIVE DRUG(S)

- Acetylcysteine—anticollagenolytic agent used for treatment of melting ulcers; efficacy is controversial; dilute 20% stock solution to 5–10% with artificial tears; apply q2–4h.
- Serum—anticollagenolytic agent; keep refrigerated; avoid contamination; discard after 48 hours.

KERATITIS, ULCERATIVE**FOLLOW-UP****PATIENT MONITORING**

- Superficial ulcers—repeat fluorescein stain in 3–6 days; if it persists 7 days or longer, either inciting cause has not been eliminated or patient has an SCCED.
- Deep stromal or rapidly progressive ulcers—assess every 24 hours initially if outpatient until improvement is seen; many of these patients are hospitalized or undergo surgery; decrease frequency of antibiotic therapy as condition improves.

PREVENTION/AVOIDANCE

- Brachycephalic dogs—lubricant ointment administration, permanent partial tarsorrhaphy surgery, or both may prevent recurrent ulceration.
- KCS-related ulcers—lifelong treatment of KCS (cyclosporine) or parotid duct transposition surgery.
- Herpesvirus (cats)—oral lysine (250 mg PO q12h) may prevent viral replication; may decrease severity and/or frequency of outbreaks.

POSSIBLE COMPLICATIONS

Progressive corneal ulceration—rupture of globe, endophthalmitis, secondary glaucoma, phthisis bulbi, blindness, blind and painful eye (may require enucleation).

EXPECTED COURSE AND PROGNOSIS

- Uncomplicated superficial ulcer—usually heals in 5–7 days.
- SCCED—may persist for weeks to months; may require multiple procedures.
- Deep corneal ulcer treated medically—may require several weeks for fibrovascular repair of defect; does not always granulate satisfactorily; continued deterioration of ulcer and globe rupture are possible.
- Deep ulcer treated with conjunctival flap—frequently results in more comfort within a few days after surgery; blood supply to flap can be cut in 4–6 weeks to decrease scarring.

**MISCELLANEOUS****ABBREVIATIONS**

- IFA = immunofluorescent antibody test.
- KCS = keratoconjunctivitis sicca.
- NSAID = nonsteroidal anti-inflammatory drug.
- SCCED = spontaneous chronic corneal epithelial defect.

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Client Education Handout
available online

KERATOCONJUNCTIVITIS SICCA



BASICS

OVERVIEW

- Deficiency of the aqueous layer of precorneal tear film.
- Causes corneal/conjunctival drying and resultant surface inflammation.

SIGNALMENT

- Common in dog; rare in cat.
- Predisposed dog breeds—many brachycephalic and spaniel breeds, miniature schnauzers, poodles, bloodhounds, Samoyeds, West Highland white terriers, and Yorkshire terriers.
- Inheritance—undefined.
- Age of onset—variable and depends on inciting cause.

SIGNS

- Conjunctival hyperemia.
- Mucoid to mucopurulent ocular discharge—intermittent to persistent depending on severity.
- Blepharospasm.
- Corneal changes—dryness, superficial vascularization, pigmentation, fibrosis, ulceration.
- Blepharitis due to ocular exudates.
- Severe disease—impaired vision or blindness.
- Cats are less symptomatic than dogs.

CAUSES & RISK FACTORS

- Immune-mediated/idiopathic—most common, possibly associated with other immune-mediated diseases (e.g., atopy).
- Infectious—canine distemper virus; leishmaniasis; chronic blepharoconjunctivitis (e.g., feline herpesvirus).
- Iatrogenic—removal of third eyelid gland (especially in at-risk breeds), radiation therapy.
- Congenital—Yorkshire terriers overrepresented.
- Neurologic—loss of parasympathetic innervation to lacrimal gland, trigeminal nerve deficit, or dysautonomia; neurogenic parasympathetic loss may have ipsilateral dry nose.
- Traumatic—after ocular proptosis or orbit inflammation.
- Systemic disease—diabetes mellitus, hyperadrenocorticism, hypothyroidism, or any debilitating disease.
- Drug-induced—systemic sulfonamides (e.g., trimethoprim-sulfadiazine).
- Transient—general anesthesia and atropine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Often confused with allergic or bacterial conjunctivitis.
- Dogs with keratoconjunctivitis sicca (KCS) may have concurrent bacterial overgrowth.
- Differentiate with Schirmer tear test.

DIAGNOSTIC PROCEDURES

- Schirmer tear test—normal value at least 9 mm/min (cat) or 15 mm/min (dog) of wetting; symptomatic patients usually <10 mm/min of wetting; lower values combined with clinical signs suggest KCS.
- Fluorescein staining—may show corneal ulcers.
- Conjunctival cytology—may demonstrate bacterial overgrowth.



TREATMENT

- Outpatient—unless severe corneal ulceration.
- Instruct client to use solution(s) before ointment(s) and wait 5 minutes between treatments.
- Advise client to call at once if ocular pain increases (patients are predisposed to corneal ulceration).
- Parotid duct transposition—surgical option for dogs and cats that reroutes parotid duct to deliver saliva to ocular surface if KCS is refractory to lacrimostimulant therapy.
 - More common with congenital KCS.
 - Saliva can irritate cornea and result in mineral deposits; some patients require ongoing topical therapy.
- Episcleral cyclosporine implant—for dogs responsive to topical cyclosporine but with poor owner compliance.



MEDICATIONS

DRUG(S) OF CHOICE

- Lacrimostimulants—cyclosporine 0.2% ointment or 1–2% solution; tacrolimus 0.02–0.03% solution or ointment—therapy q12h recommended (q8h if severe or refractory).
 - For neurogenic KCS—pilocarpine 0.1–0.2% topically q8h or very careful oral pilocarpine (narrow therapeutic window; see Suggested Reading).
 - For feline KCS—antiviral therapy (see Conjunctivitis—Cats); hyaluronate-based artificial tear in short term; consider lacrimostimulant therapy.
 - Lacrimomimetics—artificial tears to moisten ocular surface to improve comfort; use viscous solutions or gels q2–12h depending on severity and ointment before bedtime; can reduce frequency once patient responds to lacrimostimulants.
 - Broad-spectrum antibiotics—topical ointment q6–8h for 3–4 weeks; indicated for secondary bacterial overgrowth or concurrent corneal ulceration.

- Ocular cleansing—use eye wash to remove discharge and debris prior to administering medications; if mucoid discharge is very tenacious, 5% *N*-acetylcysteine can be used q6–12h as a mucinolytic agent prior to eye rinsing.

- Corticosteroids—topical; minimize inflammation; can reduce corneal vascularization and pigmentation once aqueous tears improve; not commonly used (corneal ulcer risk).

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

- Topical cyclosporine or tacrolimus—rarely irritating, but if noted consider compounded aqueous preparation.
- Pilocarpine—initially irritating topically; systemic side effect risk.
- Topical corticosteroids—avoid with ulcerative keratitis or severe KCS (corneal ulcer risk).



FOLLOW-UP

- Regular rechecks—monitor response and progress.
- Schirmer tear test—4–6 weeks after initiating cyclosporine or tacrolimus (patient should receive drug as prescribed on day of visit).
- Usually requires life-long treatment.
- Good prognosis but refractory cases may require more aggressive therapy (e.g., up to 1% tacrolimus) or surgery (e.g., parotid duct transposition).



MISCELLANEOUS

ABBREVIATIONS

- KCS = keratoconjunctivitis sicca.

Suggested Reading

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LEPTOSPIROSIS



BASICS

DEFINITION

- Caused by pathogenic members of genus *Leptospira*; each serovar has own virulence factors, infectious dose, route of exposure.
- Acute and chronic diseases of dogs (mainly nephritis and hepatitis) and rarely cats.
- Dogs—serovars causing disease vary by geographic area; recent serovars of concern in the United States are *L. grippotyphosa*, *L. autumnalis*, and *L. pomona*; vaccines should include regional serovars.

PATOPHYSIOLOGY

- *Leptospira* penetrate intact/cut skin/mucous membranes; rapidly invade bloodstream (4–7 days); disseminated spread (2–4 days).
- Invasion leads to transient fever, leukocytosis, mild hemolysis and hemoglobinuria, albuminuria. • Capillaries—endothelial cell damage. • Liver—hepatitis.
- Kidney—leptospiuria; *Leptospira* localize in damaged renal tubules; organism replicates in tubular epithelium. • Serum antibodies appear as bacteremia decreases. • Death—usually due to interstitial nephritis, vascular damage, renal failure; may result from septicemia, disseminated intravascular coagulopathy (DIC), respiratory failure.

SYSTEMS AFFECTED

- Cardiovascular—endothelial cell damage, hemorrhage. • Hepatobiliary—hepatitis, necrosis. • Nervous—meningitis. • Renal/urologic—focal interstitial nephritis, hemoglobinuric nephrosis, tubular damage/failure.
- Respiratory—vasculitis, interstitial pneumonia, leptospiral pulmonary hemorrhage syndrome (LPHS).

Chronic Disease

- Ophthalmic—anterior uveitis. • Renal/urologic—chronic kidney disease.
- Reproductive—abortion; weak puppies; linked to feline stillbirth.

INCIDENCE/PREVALENCE

- Reported incidence (dogs)—falsely low due to inapparent and undiagnosed infections.
- Prevalence (dogs)—Increasing in urban dogs; hospital prevalence increasing since 1990s.

GEOGRAPHIC DISTRIBUTION

- Worldwide, especially in warm, wet climates. • Standing water, neutral or slightly alkaline soil promote presence in environment. • *L. canicola* most common worldwide; *L. icterohaemorrhagiae* most common in Australia. • *L. bratislava* has yet to be confirmed by culture as a serovar in dogs in the United States.

SIGNALMENT

Species

Dogs, rarely cats.

Mean Age and Range

- Young dogs without maternal antibodies and unvaccinated older dogs more likely to exhibit clinical disease. • Dogs with adequate antibody titers seldom exhibit clinical disease unless exposed to serovar not in vaccine.

Predominant Sex

N/A

SIGNS

General Comments

Signs vary with age/immune status, virulence of infecting serovar, host response.

Historical Findings

Peracute to Subacute Disease

- Fever. • Sore muscles/stiffness. • Weakness, lethargy. • Anorexia, vomiting. • Diarrhea—with/without blood. • Icterus. • Cough, dyspnea. • Polyuria/polydipsia (PU/PD) progressing to anuria. • Death.

Chronic Disease

- No apparent illness. • Fever. • PU/PD.

Physical Examination Findings

Peracute to Acute Disease

- Tachypnea. • Tachycardia, weak pulses.
- Hematemesis. • Hematochezia, melena.
- Epistaxis. • Injected mucous membranes.
- Widespread petechial and ecchymotic hemorrhages. • Reluctance to move, paraspinal hyperesthesia, stiff gait. • Conjunctivitis.
- Rhinitis. • Hematuria. • Mild lymphadenopathy.

CAUSES

- Dogs—*L. canicola*, *L. icterohaemorrhagiae*, *L. pomona*, *L. grippotyphosa*, *L. copenhagenii*, *L. australis*, *L. autumnalis*, *L. ballum*, and *L. bataviae*.
- Cats—*L. canicola*, *L. grippotyphosa*, *L. pomona*, and *L. bataviae*.

RISK FACTORS

Transmission

- Direct—via urine, post-abortion discharge, fetus, sexual contact (semen). • Indirect—exposure (via urine) to contaminated environment (vegetation, soil, food, water, bedding). • Disease in companion animals is often result of spillover from diseased wildlife maintenance hosts.

Host Factors

- Vaccine—protection is serovar-specific; may not prevent kidney colonization and urine shedding; new vaccines available of “subunit” type; newer panvivalent antigen may cross-protect against many serovars. • Outdoor animals, hunting dogs—exposure of abraded or water-softened skin increases risk of infection.

Environmental Factors

- Warm, moist environment (low-lying areas, rainy season of temperate regions).
- Temperature range—44.6–50°F (7–10°C)

to 93–96°F (34–36°C). • Organism survives best in stagnant water with neutral or slightly alkaline pH: o 180 days in wet soil; longer in standing water. • Dense animal population—kennels or urban settings. • Exposure to rodents, other wildlife (e.g., deer).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Subacute to Acute Disease

- Dogs—heartworm disease; hemolytic anemias; septicemia; viral infections (canine hepatitis, canine herpesvirus); neoplasia; trauma; lupus; tick-borne disease; toxoplasmosis; postrenal obstruction; renal toxins (e.g., ethylene glycol, aminoglycosides); causes of pulmonary interstitial/alveolar disease. • Cats—hemotropic mycoplasmosis; toxins (e.g., acetaminophen); septicemia; feline immunodeficiency virus (FIV)- and feline leukemia virus (FeLV)-associated diseases; cholangitis; toxoplasmosis; feline infectious peritonitis (FIP); neoplasia; trauma; postrenal obstruction.

Reproductive/Neonatal Disease

- Dogs—brucellosis, canine distemper, herpesviruses. • Cats—FIP, FeLV, panleukopenia, herpesvirus, toxoplasmosis, salmonellosis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—leukocytosis with left shift; leukopenia during leptospiremic phase; thrombocytopenia. Hematocrit variable with hemoconcentration, bleeding, or hemolysis.
- Chemistry—azotemia; electrolyte alterations—depend on degree of renal and gastrointestinal dysfunction (hyponatremia, hyper/hypokalemia, hypochloremia, hyper/hypophosphatemia); hypoalbuminemia; elevated hepatic enzyme activities; hyperbilirubinemia. • Prolonged prothrombin and partial thromboplastin times; increased d-dimer concentrations.
- Urinalysis—isosthenuria; proteinuria; glucosuria.

OTHER LABORATORY TESTS

Serology (Microscopic Agglutination)

Test [MAT]

- Test serum in acute stage and 3–4 weeks later (convalescent). • Unvaccinated patients—titers initially low (1:100–1:200), higher in convalescent sample (1:800–1:1,600 or higher) if homologous *Leptospira* serovar is tested; several serovars may cross-react in MAT test, especially if high titers to one serovar. • Vaccinated patients—high titers for up to 12–16 weeks post vaccination, then drop to <1:400; new subunit vaccines—titers rise to ≥1:1,600 for

(CONTINUED)

12 weeks for serovars *L. canicola* and *L. icterohaemorrhagiae*; titers for other serovars (*L. pomona* and *L. grippotyphosa*) variable.

- Run acute and convalescent samples at same time, if possible.

Darkfield Microscopy of Urine

Fresh urine, often inconclusive.

Fluorescent Antibody Test of Urine

- Leptospira* viability not required; submit urine to lab on ice by overnight courier.
- More conclusive than microscopy.

PCR Test of Urine and Tissue

Only indicates genus *Leptospira*; may be useful with refinement and validation.

DIAGNOSTIC PROCEDURES

Culture (body fluids or tissues) not practical due to fastidiousness of leptospiroses; require special culture/transport medium.

PATHOLOGIC FINDINGS

- Degree of kidney and liver disease depends on serovar and host immunity.
- Cats—generally less severe lesions.
- Dogs (acute disease)—lungs may be edematous; kidneys pale and enlarged; liver enlarged, may be friable with multifocal necrosis/hemorrhage; gastrointestinal tract may hemorrhage.
- Warthin–Starry silver stain; immunohistochemistry; fluorescent antibody test on formalin-fixed sections of kidney, liver, fetal/placental tissue.

**TREATMENT****NURSING CARE**

- Shock—IV, balanced, isotonic replacement solution.
- Dehydration—IV or oral maintenance solutions as indicated.
- Severe hemorrhage—blood transfusion may be indicated.
- Oliguria, anuria—restore circulating volume; then give intravenous osmotic diuretics or tubular diuretics; dialysis may be needed.
- LPHS—oxygen supplementation or mechanical ventilation as indicated.

CLIENT EDUCATION

Inform client of zoonotic potential from contaminated urine of affected dogs and environment.

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

- Doxycycline 5 mg/kg PO or IV q12h for 2 weeks; use alone to clear both leptospiremia and leptospiruria.
- Ampicillin 22 mg/kg IV q6–8h (or other penicillins as available); only clears leptospiremia; must be followed by course of doxycycline.

PRECAUTIONS

Doxycycline can cause esophagitis, esophageal stricture.

**FOLLOW-UP****PREVENTION/AVOIDANCE**

- Vaccine (dogs)—whole-cell bacterin vaccines contain serovars *L. canicola/icterohaemorrhagiae* (newer also include *L. pomona/grippotyphosa*): ○ Promotes immunity to homologous serovars and protection from overt clinical disease; may not prevent colonization of the kidneys, resulting in chronic carrier state. ○ Serovar-specific.
- Newer subunit vaccine contains *L. pomona*, *L. icterohaemorrhagiae*, *L. grippotyphosa*, and *L. canicola*; possibly provides protection from clinical disease/prevents kidney colonization.
- Bacteria-induced immunity lasts 6–8 months and is serovar-specific. ○ Revaccinate at least yearly.
- Vaccinate high-risk dogs (hunter, show dogs, dogs with access to water/ponds) every 4–6 months, especially in endemic areas.
- Kennels—strict sanitation to avoid contact with infected urine; control rodents; monitor/remove carrier dogs until treated; isolate infected animals during treatment.
- Activity—limit access to marshy/muddy areas, ponds, low-lying areas with stagnant surface water, heavily irrigated pastures; limit access to wildlife.
- Environmental contamination—leptospira shedding in urine is intermittent; leptospira survive but do not multiply in environment; cells survive until either drying, UV light exposure, or freeze-thaw has killed the leptospires.

POSSIBLE COMPLICATIONS

- DIC.
- Permanent liver/kidney dysfunction.
- Uveitis.
- Abortion.

LEPTOSPIROSIS**EXPECTED COURSE AND PROGNOSIS**

- Most infections subclinical or chronic.
- Prognosis guarded for acute severe disease.

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

Severe clinical disease in young dogs (nonvaccinated or lacking maternal antibody).

ZOONOTIC POTENTIAL

- High—spreads in urine of infected animals.
- Strict kennel hygiene and disinfection of premises.

PREGNANCY/FERTILITY/BREEDING

- Possible abortion.
- Antimicrobial therapy—consider effect of drug on developing fetus.

ABBREVIATIONS

- DIC = disseminated intravascular coagulopathy.
- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIV = feline immunodeficiency virus.
- LPHS = leptospiral pulmonary hemorrhage syndrome.
- MAT = microscopic agglutination test.
- PU/PD = polyuria/polydipsia.

INTERNET RESOURCES

<http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=leptospirosis&lang=en>

Suggested Reading

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Client Education Handout
available online

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LOWER URINARY TRACT INFECTION, BACTERIAL



BASICS

DEFINITION

- Urinary tract infection (UTI)—bacterial adherence, replication, and persistence within the urinary tract associated with clinical signs and/or inflammation.
- Sporadic cystitis (uncomplicated UTI): lower UTI that occurs no more than once every 6 months.
- Recurrent UTI—UTI that occurs ≥ 3 times in a year, or ≥ 2 times in 6 months. Subcategories include:
 - Persistent—UTI that fails to resolve after appropriate antimicrobial therapy.
 - Relapse—UTI that appears to resolve; however, subsequent urine cultures confirm persistence of the original bacterial isolate.
 - Reinfection—UTI resolves with appropriate therapy but abnormal urinary defenses allow for recolonization of different bacterial species.
- Subclinical bacteriuria (asymptomatic bacteriuria)—bacterial presence within the urinary tract not associated with detectable clinical signs and/or inflammation.

PATOPHYSIOLOGY

UTI development is dependent on the interplay between bacterial virulence factors and impairment of the anatomical, functional, environmental, and immunologic competency of the host. Most commonly, uropathogenic bacteria originate from the enteric flora and ascend from the distal urogenital tract into the proximal urethra and urinary bladder. Colonization may elicit a mucosal inflammatory response resulting in dysuria, pollakiuria, pyuria, and hematuria.

SYSTEMS AFFECTED

Renal/urologic.

INCIDENCE/PREVALENCE

- Bacteriuria is not equivalent to UTI. Current data identifies UTI prevalence given predisposing conditions.
- Prevalence of bacteriuria in dogs:
 - With subclinical bacteriuria: 2.1–8.9%.
 - With diabetes mellitus: 37%.
 - With hyperadrenocorticism, at diagnosis: 46%.
 - With thoracolumbar intervertebral disc extrusion: 20.0–38.5%.
 - With indwelling urinary catheters: 63.8%.
- Prevalence of bacteriuria in cats:
 - With subclinical bacteriuria: 0.9–28.8%.
 - With lower urinary tract-associated clinical signs: 3.4–12.0%.
 - With ureteral calculi: 8.4%.
 - With chronic kidney disease: 16.9–29.1%.
 - With diabetes mellitus: 12.2–12.8%.
 - With perineal urethrostomies: 22%.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

More common in dogs than cats.

Breed Predilections

Breed-associated conditions (hyperadrenocorticism, urolithiasis, etc.) may promote bacteriuria.

Mean Age and Range

- UTIs occur at any age, but are more common in older dogs and cats.
- Dogs—female: mean 7.7 ± 0.1 years; male: mean 8.0 ± 0.1 years.
- Cats—female: mean 11.8 ± 4.4 years; male: mean 9.8 ± 4.8 years.

Predominant Sex

- Dogs—female dogs more commonly affected.
- Cats—female cats are slightly overrepresented.

SIGNS

Historical Findings

- Patients may be asymptomatic.
- Pollakiuria, dysuria, hematuria, stranguria, inappropriate elimination, and excessive licking at or discharge from the genitalia may be present.
- Systemic clinical signs (anorexia, fever) are infrequent and suggest complicating factors (e.g., pyelonephritis).

Physical Examination Findings

- Unremarkable in most animals.
- Abnormalities occasionally noted with urinary bladder palpation:
- Stimulation of micturition.
- Pain reactions.

CAUSES

- Uropathogenic bacteria commonly originate from enteric flora with rare hematogenous origins.
- *Escherichia coli* is the most common bacterial isolate in dogs (45–55%) and cats (37.3%).
- Eight species of bacteria (*E. coli*, *Staphylococcus*, *Proteus*, *Streptococcus*, *Klebsiella*, *Enterococcus*, *Pseudomonas*, and *Corynebacterium*) account for approximately 95% of UTIs.

RISK FACTORS

- Immune dysfunction/suppression (e.g., hyperadrenocorticism, feline leukemia virus [FeLV], feline immunodeficiency virus [FIV]).
- Nidus for bacterial adherence and harboring (e.g., indwelling urinary catheters, uroliths).
- Altered urine composition (e.g., persistently dilute urine, glucosuria).
- Abnormal micturition/urine retention (e.g., loss of urethral tone, neurologic disease, urethral obstruction).
- Abnormal anatomy (e.g., ectopic ureters, hooded vulva).
- Disrupted urinary tract mucosal defenses (e.g., mucosal trauma).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- UTI cannot be diagnosed or excluded based on the presence/absence of clinical signs.
- Dysuria, pollakiuria, hematuria, and stranguria occur with lower urinary tract diseases including cystolithiasis, urinary tract neoplasia, prostatitis, obstructive uropathy, and feline idiopathic cystitis.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC and biochemistry are unremarkable.
- Urinalysis:
 - Proteinuria and hematuria indicate inflammation.
 - Urine pH >7.5 may indicate the presence of urease-producing bacteria (*Proteus* spp., *Staphylococcus* spp., *Ureaplasma* spp., or *Corynebacterium* spp.).
 - Pyuria is present in most animals with UTI but is not synonymous with infection.
 - Bacteriuria identification increases UTI suspicion. Using a modified Wright–Giemsa stain (Diff-Quik) or Gram stain can improve bacterial detection.

OTHER LABORATORY TESTS

Urine Culture

- Definitive diagnosis requires aerobic urine culture.
- In female dogs with limited antibiotic exposure forgoing a urine culture can be justified for uncomplicated UTI if the pathogen and local susceptibility patterns are known. In male dogs, cats, and animals with recurrent UTI urine culture is recommended.
- Cystocentesis is the gold standard method for collecting urine culture specimens. Bacterial growth $>10^3$ cfu/mL is diagnostic.
- Urine samples obtained by catheterization are often contaminated by the normal flora of the distal urethra. Bacterial growth $>10^4$ cfu/mL in male dogs, $>10^5$ cfu/mL in female dogs, and $>10^3$ cfu/mL in cats is diagnostic.
- Indwelling catheters may be colonized without concurrent UTI; therefore, sample collection from indwelling urinary catheters should be avoided.
- Culturing voided midstream urine samples should be avoided unless other urine collection techniques are contraindicated or not possible.
- Urine collected from nonsterile surfaces should not be cultured.

Antibiotic Sensitivity Testing

Antibiotic sensitivity is accurately predicted by use of the isolate's "susceptible" vs. "resistant" profiles.

IMAGING

Rarely is imaging necessary for uncomplicated infections. Radiographs, contrast studies, and ultrasound may help to identify recurrent UTI-predisposing causes.

DIAGNOSTIC PROCEDURES

Cystoscopy is used in patients with recurrent UTI to visualize abnormalities within the urinary bladder and urethra including uroliths, masses, polyps, ectopic ureters, etc.

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient treatment is appropriate; inpatient treatment may be necessary with UTI complications or associated conditions (e.g., acute pyelonephritis).

(CONTINUED)

LOWER URINARY TRACT INFECTION, BACTERIAL**NURSING CARE**

N/A

ACTIVITY

Unrestricted

DIET

N/A

CLIENT EDUCATION

N/A

SURGICAL CONSIDERATIONS

Management of uroliths, polypoid cystitis, and infection niduses may require surgical intervention.

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

- Given the morbidity associated with sporadic cystitis, empiric antimicrobial treatment is commonly started before receiving urine culture results. • When susceptibility data is available, the lowest tier antimicrobial should be selected. • “First-line” antimicrobials—should be selected when possible:
 - Amoxicillin (11–15 mg/kg PO q8h).
 - Trimethoprim-sulfadiazine (TMS) (15 mg/kg PO q12h).
 - Amoxicillin/clavulanic acid (12–25 mg/kg PO q12h).
- “Second-line” antimicrobials—reserved for resistant isolates based on culture and sensitivity or when patient factors prohibit the use of “first-line” therapies:
 - Floroquinolones (e.g., marbofloxacin 2.7–5.5 mg/kg PO q24h; enrofloxacin; ciprofloxacin).
 - Cefovecin (8 mg/kg SC).
 - Nitrofurantoin (4.4–5.0 mg/kg PO q8h).
- “Third-line” antimicrobials—reserved for multidrug resistant infections necessitating therapeutic intervention:
 - Amikacin (dogs 15–30 mg/kg IV or SC q24h; cats 10–14 mg/kg IV or SC q24h).
 - Chloramphenicol (dogs 40–50 mg/kg PO q8h; cats 12.5–20 mg/kg [not exceeding 50 mg/cat] PO q12h).
- Antibiotic treatment of uncomplicated infections is recommended for 3–10 days.
- Recurrent UTI treatment requires a urine culture and sensitivity. • Treatment durations are extended for persistent and relapse infections (up to 4 weeks).
- Reinfections are treated as multiple uncomplicated infections, however an attempt to identify an abnormality in host defenses should be pursued.

CONTRAINDICATIONS

N/A

PRECAUTIONS

Pyelonephritis or prostatitis necessitates therapies able to penetrate the respective tissues (see Pyelonephritis; Prostatitis and Prostatic Abscess).

POSSIBLE INTERACTIONS

N/A

ALTERNATE DRUGS

Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used cautiously to reduce clinical signs in dogs with cystitis while awaiting urine culture results. They should not be used in dehydrated patients.

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

- For uncomplicated UTIs clinical improvement should occur within 48 hours. If clinical signs remain for >48 hours, complicating factors should be investigated.
- Complicated UTIs—continue therapy for 7–10 days beyond resolution of clinical signs, pyuria, and bacteriuria. Confirm resolution via urine culture 7–10 days after end of therapy.

PREVENTION/AVOIDANCE

- Diagnosis and control of predisposing conditions is the most effective method for preventing UTIs. • Ancillary therapies can be considered to prevent recurrence:
 - Cranberry extract may inhibit *E. coli* attachment to the bladder mucosa.
 - Methenamine—converted into formalin when urine pH is <7.0. Concurrent administration of ascorbic acid (vitamin C) promotes urinary acidification.
- Prophylactic antibiotics—once-daily administration of antibiotics may lengthen infection-free intervals; however, multidrug resistance is likely in subsequent isolates.

POSSIBLE COMPLICATIONS

UTIs may lead to pyelonephritis, struvite urolith formation, or polypoid cystitis.

EXPECTED COURSE AND PROGNOSIS

Prognosis for patients with uncomplicated UTIs is excellent. The prognosis for patients with complicated infections is determined by successful control or resolution of predisposing conditions.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Struvite urolithiasis.
- Polypoid cystitis.
- Pyelonephritis.
- Prostatitis.
- Emphysematous cystitis.

AGE-RELATED FACTORS

Juvenile animals with recurrent UTIs should be evaluated for urolithiasis or urinary tract malformations.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

L

SYNOMYS

Bacterial cystitis.

SEE ALSO

- Prostatitis and Prostatic Abscess.
- Pyelonephritis.
- Urolithiasis, Struvite—Dogs.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline infectious virus.
- NSAID = nonsteroidal anti-inflammatory drug.
- TMS = trimethoprim-sulfadiazine.
- UTI = urinary tract infection.

Suggested Reading

Weese JS, Blondeau JM, Boothe D, et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Vet J* 2019; 247:8–25.

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Acknowledgment The author and editors acknowledge the prior contribution of Barrak M. Pressler.



**Client Education Handout
available online**

LYMPHOMA—CATS



BASICS

DEFINITION

Malignant transformation of lymphocytes.

PATHOPHYSIOLOGY

Viral (feline leukemia virus [FeLV]) or chemical (tobacco smoke) oncogenesis.

SYSTEMS AFFECTED

- Gastrointestinal
- Hemic/lymphatic/immune
- Nervous—most common spinal cord tumor in cats
- Ophthalmic
- Renal (high rate of relapse in CNS)
- Respiratory—nasal, thoracic cavities

GENETICS

N/A

INCIDENCE/PREVALENCE

- About 90% of hematopoietic tumors and 33% of all tumors in cats
- Prevalence—41.6–200 per 100,000 cats

GEOGRAPHIC DISTRIBUTION

Regional differences may relate to differences in FeLV prevalence.

Breed Predilections

Siamese/Oriental breeds overrepresented in some studies.

Mean Age and Range

- FeLV-positive cats—3 years
- FeLV-negative cats—7 years
- Median age of cats with localized extranodal lymphoma—13 years
- Most cats with Hodgkin's-like lymphoma are older than 6 years

Predominant Sex

None

SIGNS

General Comments

Depend on anatomic form.

Historical Findings

- Mediastinal form—open-mouthed breathing, coughing, regurgitation, anorexia, weight loss
- Alimentary form—anorexia, weight loss, lethargy, vomiting, constipation, diarrhea, melena, hematochezia
- Small cell lymphoma (SCL) typically more chronic signs compared to large cell lymphoma (LCL)
- Renal form—consistent with renal failure
- Nasal form—nasal discharge or epistaxis, facial swelling, ocular signs, respiratory noise, sneezing, anorexia
- Multicentric form—possibly none except for swellings in areas of lymph nodes in early stages; anorexia, weight loss, and depression with progression of disease
- Spinal form—quickly progressing posterior paresis may be seen
- Cutaneous form—pruritic, hemorrhagic, or alopecic dermal masses may be seen

Physical Examination Findings

- Mediastinal form—non-compressible cranial thorax, dyspnea, tachypnea
- Alimentary form—thickened intestines or abdominal masses
- Renal form—large, irregular kidneys
- Nasal form—purulent or mucoid nasal discharge, facial deformity, epiphora, exophthalmos, poor globe retroversion
- Multicentric form—generalized lymphadenomegaly, possible hepatosplenomegaly
- All forms—fever; dehydration; depression; cachexia in some patients

CAUSES

FeLV

RISK FACTORS

- FeLV exposure
- Exposure to environmental tobacco smoke (relative risk 2.4, increases linearly with duration and quantity of exposure)
- Feline immunodeficiency virus (FIV) infection



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Mediastinal form—congestive heart failure; cardiomyopathy; chylothorax; pyothorax; hemothorax; pneumothorax; diaphragmatic hernia; allergic lung disease; thymoma; ectopic thyroid carcinoma; pleural carcinomatosis; acetaminophen toxicity
- Alimentary form—foreign body ingestion; intestinal ulceration; intestinal fungal infection; inflammatory bowel disease; intussusception; lymphangiectasia; other gastrointestinal tumor
- Renal form—pyelonephritis; amyloidosis; glomerulonephritis; chronic renal failure; polycystic kidneys; feline infectious peritonitis
- Multicentric form—systemic mycotic infection; immune-mediated disease; toxoplasmosis; lymphoid hyperplasia; hypersensitivity reaction; plague (specifically if prominent cervical lymphadenopathy as with Hodgkin's-like form)

CBC/BIOCHEMISTRY/URINALYSIS

- May see anemia (negative prognostic factor), leukocytosis, and lymphoblastosis
- May find high creatinine, high serum urea nitrogen, high hepatic enzyme activity, hypercalcemia (rare), and monoclonal gammopathy

OTHER LABORATORY TESTS

FeLV testing—usually negative in older cats and in cats with large granular lymphocyte lymphoma (LGLL), usually positive in younger cats and those with mediastinal (85%) or CNS lymphoma, renal (45% positive), multicentric (20%), intestinal (15%)

IMAGING

- Thoracic radiography—may see mediastinal mass, pleural effusion, abnormal pulmonary parenchymal patterns (rare), perihilar or retrosternal lymphadenomegaly
- Abdominal ultrasonography—may see diffuse echotexture changes in the liver, spleen, and kidneys, focal or diffuse thickening of the intestines and the gastric wall, abdominal lymphadenopathy, intestinal/gastric mass:
 - Hypoechoic subcapsular thickening is associated with renal lymphoma
 - Despite thickening of intestines, layering may be preserved
- Computed tomography—space-occupying mass effect in affected area, especially used for nasal lymphoma

DIAGNOSTIC PROCEDURES

- Aspiration or biopsy of a mass or lymph node
- Aspirate often sufficient to diagnose LCL; biopsy often required for SCL
- Can be challenging to distinguish SCL from inflammatory bowel disease (IBD)
- Immunohistochemistry (IHC) ± PCR for antigen receptor rearrangement (PARR) testing can be done to distinguish between IBD and SCL; sensitivity of IHC for detecting lymphoma 78% vs. 83% for IHC + PARR; sensitivity of PARR for detecting T-cell and B-cell lymphoma is 78% and 50%, respectively
- Staging—CBC/chemistry profile/urinalysis/FeLV/FIV testing, thoracic radiographs, abdominal ultrasound, regional lymph node aspirates for localized lesions, ± bone marrow aspirate depending on CBC findings; serum cobalamin level in SCL

PATHOLOGIC FINDINGS

- Gross—usually white to gray in color with areas of hemorrhage and necrosis
- Cytologic—monomorphic population of intermediate to large sized immature lymphocytes (lymphoblasts) in LCL vs monomorphic population of small mature lymphocytes in SCL
- Histopathologic—vary; several morphologic classification schemes in use:
 - Nasal lymphoma is most often immunoblastic B-cell origin
 - Hodgkin's-like lymphoma is characterized by Reed-Sternberg cells and few neoplastic cells in a background of a reactive T-cell population with histiocytes and granulocytes
 - LGL lymphoma most commonly affects the intestine and mesenteric lymph nodes
 - B-cell most common in stomach (100%) and large intestine (88%); T-cell most common in small intestine (52%)
 - In gastrointestinal (GI) lymphoma, LCL more common than SCL when both cytologic and histopathologic samples are evaluated

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Outpatient whenever possible, supportive care if needed.

NURSING CARE

Fluid therapy, antiemetics, appetite stimulants, analgesia, thoracocentesis, etc. when indicated.

ACTIVITY

Normal

DIET

No change, can add *n*-3 fatty acids to diet (fish oil origin).

CLIENT EDUCATION

- Emphasize that side effects are treatable and should be addressed promptly.
- Inform client that the goal is to induce remission and achieve a good quality of life for as long as possible.

SURGICAL CONSIDERATIONS

- To relieve intestinal obstructions or perforations and remove solitary masses.
- To obtain specimens for histopathologic examination.

RADIATION THERAPY

Possible option for localized lesions, such as nasal cavity or mediastinum, as well as rescue treatment for GI LCL.



MEDICATIONS

DRUG(S) OF CHOICE

- Chemotherapy—there are many variations of similar combination protocols, all with similar efficacy.
- High-grade lymphoma can respond to CHOP-based protocols (cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone) such as the University of Wisconsin–Madison protocol (alternating drugs in repeated sequence) or COP-based protocols (cyclophosphamide, vincristine, prednisone/prednisolone).
- Vinblastine has similar efficacy but less GI toxicity compared to vincristine.
- SCL can respond to oral chlorambucil (either low dose daily/every other day or high dose pulsed) and prednisone/prednisolone.
- Consult a veterinary oncologist for doses, schedules, and to help assess best option(s) for treatment.

CONTRAINDICATIONS

Avoid doxorubicin in cats with preexisting renal failure as high-cumulative dosages have been demonstrated to potentially be nephrotoxic.

PRECAUTIONS

- Myelosuppression secondary to chemotherapy—more in FeLV-positive cats.
- Seek advice before initiating treatment if you are

unfamiliar with cytotoxic drugs. Some drugs such as vincristine and doxorubicin are vesicants and can cause severe tissue sloughing if leaked outside the vein.



FOLLOW-UP

PATIENT MONITORING

- Physical examination and CBC—before each chemotherapy treatment and 1 week after each new drug is administered, or if there are concerns about low cell counts.
- Diagnostic imaging—as necessary depending on location to assess response to therapy.

PREVENTION/AVOIDANCE

Avoid exposure to or breeding FeLV-positive cats.

POSSIBLE COMPLICATIONS

- Leukopenia/neutropenia.
- Sepsis.
- Anorexia, vomiting, weight loss; may need imaging tests to distinguish between chemotherapy side effects and lymphoma progression.

EXPECTED COURSE AND PROGNOSIS

- Depends on initial response to chemotherapy, anatomic type, FeLV status, and tumor burden.
- Median survival according to treatment (overall 50–70% response rate):
 - Prednisone alone—1.5–2 months.
 - COP/CHOP-based chemotherapy—6–9 months.
 - Doxorubicin-based, lomustine, MOMP (mechlorethamine, vincristine, melphalan, prednisone), and DMAC (dexamethasone, melphalan, actinomycin-D, cytarabine) rescue therapy reported for refractory lymphoma.
 - Median survival according to FeLV status:
 - Negative—7 months (17.5 months if low tumor burden).
 - Positive—3.5 months (4 months if low tumor burden).
 - Median survival according to anatomic location:
 - Renal—FeLV-negative, 11.5 months; FeLV-positive, 6.5 months.
 - Nasal—1.5–2.5 years with radiation and chemotherapy.
 - Chemotherapy may not improve survival over radiation alone.
 - Higher radiation doses (>32 Gy) result in longer survival.
 - Mediastinal—about 10% of patients live >2 years.
 - Alimentary—8 months.
- Peripheral multicentric—23.5 months.
- If localized (median remission time)—114 weeks.
- Median survival according to histology (tumor grade or subtype):
 - SCL of GI tract with or without additional visceral involvement—95% overall response to chlorambucil and prednisone for median survival of approximately 2 years (longer in complete vs. partial remission).
 - LGLL—30% response for median survival 57 days.
 - Cats with Hodgkin's-like lymphoma can do well for extended periods of time, even without

LYMPHOMA—CATS

treatment (months to years).

- Weight loss during first month of treatment of LCL associated with shorter survival.
- Clinical response after 1 cycle of COP chemotherapy associated with longer survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Hypoglycemia (rare).
- Monoclonal gammopathy (rare).
- Hypercalcemia (10–15%).

AGE-RELATED FACTORS

Young cats with lymphoma are generally FeLV-positive.

L

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Do not use chemotherapy in pregnant animals.

SYNOMYS

- Lymphosarcoma.
- Malignant lymphoma.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- GI = gastrointestinal.
- IBD = inflammatory bowel disease.
- IHC = immunohistochemistry.
- LCL = large cell lymphoma.
- LGLL = large granular lymphocyte lymphoma.
- PARR = PCR for antigen receptor rearrangement.
- SCL = small cell lymphoma.

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Acknowledgment The author and editors acknowledge the prior contribution of Kim A. Selting.



Client Education Handout
available online

LYMPHOMA—DOGS



BASICS

DEFINITION

- Clonal proliferation of B-, T-, or non-B-/non-T-type (null cell) lymphoblasts found primarily in enlarged peripheral lymph nodes.
- Cells can spread systemically to invade bone marrow, peripheral blood, CNS, and visceral organs.

PATHOPHYSIOLOGY

- ~85% of cases are multicentric (involving more than one lymph node).
- ~75% are B-cell in origin and ~25% are T-cell in origin.
- B-cell lymphoma (LSA) includes mainly multicentric B-cell lymphoma (80% of cases) which is an aggressive disease similar to human diffuse, large B-cell lymphoma (DLBCL), and marginal zone lymphoma (MZL, 20% of cases). Follicular lymphoma (FL) is rare.
- Multicentric T-cell LSA includes aggressive (peripheral T-cell LSA—not otherwise specified [PTCL-NOS]) and indolent (T-zone LSA [TZL]) subtypes. T-cell LSAs are most commonly associated with hypercalcemia.
- Aggressive lymphomas respond to treatment quickly, but have shorter overall survivals.

SYSTEMS AFFECTED

- Lymphatic (~85%)—generalized peripheral lymphadenopathy with or without splenic, hepatic, peripheral blood, and/or bone marrow involvement.
- Gastrointestinal (~5–7%)—focal or diffuse infiltration of intestines, and associated lymph nodes.
- Mediastinal (~5%)—proliferation of neoplastic lymphocytes in mediastinal lymph nodes, thymus, or both.
- Skin—divided into cutaneous non-epitheliotropic B- and T-cell LSA and mycosis fungoides (epitheliotropic T-cell LSA).
- Hepatosplenomegaly—liver/spleen sinusoidal infiltration of T-cells with eventual bone marrow infiltration. Erythrophagia commonly seen.
- Intravascular LSA (rare)—typically T- or null cell proliferation in lumen or wall of blood vessel.

GENETICS

- Some chromosome copy number aberrations are shared between human and canine lymphomas.
- Gene expression profiling can be used to separate distinct subtypes of human and canine lymphoma.
- Canine DLBCL and MZL may be a continuum of the same disease.

INCIDENCE/PREVALENCE

- 20–107 LSA cases per 100,000 dogs.
- LSA comprises up to 24% of all canine neoplasms and 83% of all canine hematopoietic malignancies.

SIGNALMENT

Breed Predilections

- Boxer, basset hound, golden retriever, Saint Bernard, Scottish terrier, Airedale terrier, and bulldog—reported high-risk breeds.

- Dachshund and Pomeranian—reported low-risk breeds.
- Breed determines relative risk for B-cell or T-cell disease: ~85% of boxer LSAs are T-cell in origin (>50% are CD3+CD4+ in origin), while golden retrievers develop both B- and T-cell LSA in an ~50:50 ratio.

Median Age

Historically, 6–9 years.

SIGNS

History

- Multicentric—from no clinical signs to anorexia, lethargy, vomiting, diarrhea, weight loss, fever, polydipsia and polyuria secondary to hypercalcemia.
- Gastrointestinal—vomiting, diarrhea, anorexia, weight loss, malabsorption.
- Mediastinal—respiratory distress, pleural effusion, coughing, difficulty swallowing, caval syndrome.
- Skin:
 - Cutaneous LSA—lesions usually generalized or multifocal: nodules, plaques, ulcers, focal alopecia and hypopigmentation.
 - Mycosis fungoides—initial scaling, alopecia, pruritus progressing to thickened, ulcerated, exudative lesions. Later stages include proliferative plaques and nodules with progressive ulceration. Oral mucosa many times involved.
 - Extranodal—vary with the anatomic site: ocular—photophobia and conjunctivitis; CNS—neurologic deficits, paresis, paralysis, seizures; hepatosplenomegaly—lethargy, inappetance, weakness, icterus.

Physical Examination Findings

- Multicentric—generalized, painless, enlarged peripheral lymph node(s) with or without hepatosplenomegaly.
- Gastrointestinal—unremarkable to palpable thickened gut loops and/or abdominal mass, rectal mucosal irregularities, ascites.
- Mediastinal—dyspnea; tachypnea; muffled heart sounds secondary to pleural effusion, pitting edema of head, neck, forelimbs.
- Skin—raised plaques that may coalesce, patch lesions, and erythematous, exudative lesions.
- Extranodal—ocular—anterior uveitis, retinal hemorrhages, and hyphema; CNS—dementia, seizures, and paralysis.

CAUSES

Suggested causes include heritable breed risks, chromosomal aberrations, increased telomerase activity, germline and somatic genetic mutations, epigenetic changes, retroviral infection, Epstein–Barr virus infection, and environmental factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Multicentric—disseminated infections, metastatic disease, immune-mediated disorders, other hematopoietic tumors.
- Gastrointestinal—other GI tumors, foreign body, enteritis, GI ulceration, systemic

- mycosis.
- Mediastinal—other tumors (thymoma, chemodectoma, ectopic thyroid), infectious disease.
- Skin—infectious dermatitis, pyoderma, immune-mediated dermatitis, histiocytic or mast cell disease.
- Extranodal—depends on affected site.

CBC/BIOCHEMISTRY/URINALYSIS

- Anemia of chronic disease, thrombocytopenia, lymphocytosis, lymphopenia, neutrophilia, monocytosis, circulating blasts, hypoproteinemia (GI).
- Hypercalcemia, increased liver enzymes with hepatic involvement, increased creatinine or blood urea nitrogen with renal involvement.
- Urinalysis usually normal.

OTHER LABORATORY TESTS

- Immunohistochemistry (lymph node [LN] biopsy/resection)—to determine immunophenotype.
- Flow cytometry or PCR for antigen receptor rearrangements (PARR) (LN or affected organ fine-needle aspirates)—to determine immunophenotype.

IMAGING

- Thoracic radiography—sternal or tracheobronchial lymphadenopathy, widened mediastinum, pulmonary densities, and pleural effusion.
- Abdominal ultrasonography—abdominal lymphadenopathy, hepatosplenomegaly, involvement, thickened bowel loops, other visceral organ involvement, ascites.

DIAGNOSTIC PROCEDURES

- Fine-needle aspirate cytology of enlarged lymph nodes or other affected organs—for cytopathologic confirmation.
- LN biopsy or resection—for accurate histopathologic classification.
- Bone marrow cytology—for accurate prognosis.
- CSF analysis—if patient has neurologic signs.
- ECG—identify arrhythmias before doxorubicin administration.

PATHOLOGIC FINDINGS

- Multicentric—effacement of LN parenchyma with large, neoplastic CD79a+ B-cells (high-grade DLBCL) or perifollicular proliferation of CD79a+ cells (MZL) or CD79a+ cell proliferation that maintains follicle architecture (FL). Effacement of LN parenchyma with large, neoplastic CD3+ T-cells (PTCL-NOS) or small, CD3+ cell proliferation between fading follicles (indolent TZL).
- Gastrointestinal—infiltration of neoplastic lymphocytes throughout mucosa and submucosa, with occasional transmural infiltration.
- Skin—CD79a+ B-cells infiltrating mucosa and submucosa, but sparing the epidermis (non-epitheliotrophic) LSA or CD3+ T-cells invading the epidermis: Pautrier's microabscesses (mycosis fungoides).
- Hepatosplenomegaly—sinusoidal infiltration of erythrophagocytic CD3+ T-cells.

Staging

- I—one enlarged LN.
- II—regionally enlarged LNs.
- III—generalized LN involvement.
- IV—visceral organ involvement.

(CONTINUED)

- V—blood or bone marrow involvement.
- Substage a—not sick. • Substage b—sick.



TREATMENT

APPROPRIATE HEALTH CARE

- High-grade LSAs are exquisitely sensitive to both chemotherapy and radiation. • Systemic multiagent chemotherapy—therapy of choice.
- Radiation therapy—for refractory lymphadenopathy, large mediastinal masses, and solitary cutaneous areas. Half-body irradiation has been included into some chemotherapy protocols. • Surgery—rarely used unless an acutely obstructive GI mass is identified or to remove a refractory lymphadenopathy. • Autologous and allogeneic bone marrow transplantation (BMT)—after total body irradiation can be considered. • Fluid therapy—for advanced disease to treat clinically ill, azotemic, and/or dehydrated patients. Fluid therapy, steroids, \pm calcitonin—to treat hypercalcemia. • Consider aggressive fluid therapy—to prevent tumor lysis syndrome when inducing dogs with a high tumor burden or dogs with peripheral blood lymphoblasts.

CLIENT EDUCATION

- Canine LSA is a treatable, but rarely curable disease. • Side effects of chemotherapy drugs include reversible GI tract and bone marrow toxicities. • Most dogs will not experience alopecia, but, dogs who need grooming will.
- The vast majority of dogs receiving chemotherapy enjoy an excellent quality of life.



MEDICATIONS

DRUG(S) OF CHOICE

- Consider combination chemotherapy protocols to treat intermediate and high-grade diseases and single-agent protocols to treat indolent diseases. • Most multiagent protocols have superior remission and survival times when compared to single-agent protocols.
- Corticosteroids alone can induce significant multidrug resistance.

Intermediate and High-Grade Lymphomas

- L-CHOP—L-asparaginase 10,000 IU/m², vincristine (Onvcovin) 0.7 mg/m² IV, cyclophosphamide (Cytosan) 250 mg/m² IV or PO, doxorubicin (Adriamycin) 30 mg/m² IV, prednisone 30, 20, 10 mg/m² PO q24h tapering for 3 weeks. Consult a veterinary oncologist concerning the treatment schedule.
- COP—vincristine 0.7 mg/m² IV, cyclophosphamide (Cytosan) 250 mg/m² IV or PO, prednisone 30, 20, 10 mg/m² PO q24h tapering for 3 weeks. Each drug given weekly.

Single Agent

- Any drug of L-CHOP can be used as a single agent, but expect shorter overall survival than multiagent. • Doxorubicin (Adriamycin) 30 mg/m² IV every 3 weeks (1 mg/kg for dog <15 kg) 5–6 treatments.
- CCNU (lomustine) 70 mg/m² PO every 3 weeks, prednisone 2 mg/kg PO daily.
- Tanovea (rabacfosadine) 1 mg/kg IV every 3 weeks, prednisone 1 mg/kg PO EOD.

Low-Grade Lymphomas

- Chlorambucil (Leukeran) 6 mg/m² PO daily for 7–14 days, prednisone 2 mg/kg PO daily. Consider reducing chlorambucil dose to 3 mg/m² for maintenance. • CCNU (lomustine) as above.

PRECAUTIONS

- Doxorubicin—use dexamoxane (Zinecard) in conjunction with doxorubicin or substitute epirubicin for dogs with cardiac issues. Always use a freshly placed catheter when administering IV doxorubicin.
- L-Asparaginase and doxorubicin—pretreat with diphenhydramine 1–2 mg/kg SC, 15 minutes before administration. • Cytosan—pretreat with furosemide 2 mg/kg to prevent sterile hemorrhagic cystitis.

POSSIBLE INTERACTIONS

Most chemotherapy drugs have overlapping GI and bone marrow toxicities. Consider antidiarrheals (metronidazole, loperamide) and antiemetics (metoclopramide, maropitant, ondansetron) to abrogate these effects.

ALTERNATIVE DRUG(S)

- Many published rescue protocols have been reported; therefore, always consult with a medical oncologist. • MOPP—mechlorethamine (Mustargen), vincristine, procarbazine, and prednisone. • DMAC—dexamethasone, melphalan, actinomycin-D, and cytosine arabinoside. • CCNU \pm L-asparaginase, prednisone, or DTIC (dacarbazine). • Mitoxantrone alone or doxorubicin/DTIC.



FOLLOW-UP

PATIENT MONITORING

- Weekly physical examination to assess response and CBC to gauge bone marrow toxicities. • If neutropenia (neutrophils <1,500 cells/mm³) is noted, reduce dosage (20–25%) of drug when given again.

POSSIBLE COMPLICATIONS

- Reversible neutropenia 7–10 days after chemotherapy. • Temporary vomiting, diarrhea, and anorexia 3–5 days after chemotherapy. • Alopecia in certain dog breeds that require grooming (poodle, shih tzu, etc.). • Febrile neutropenia (treated with broad-spectrum antibiotics).

LYMPHOMA—DOGS

EXPECTED COURSE AND PROGNOSIS

- >80% of dogs will go into clinical remission during the first month of induction chemotherapy. • Stage, substage, and immunophenotype are important prognostic indicators.
- Expect median survivals of ~12–14 months and ~6–9 months in dogs with high-grade multicentric B- and T-cell LSA, respectively, when treated with a multiagent protocol. Dogs with indolent disease can live years. GI, mediastinal (T-cell \pm hypercalcemia), and mycosis fungoides are associated with poorer response to treatment and an overall shorter survival time. • Autologous BMT can cure ~33% of dogs with B-cell LSA and ~15% of dogs with T-cell LSA. The cure rate of allogeneic BMT is currently unknown.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

Treatment of pregnant dogs is usually contraindicated.

SYNONYMS

- Lymphosarcoma. • Malignant lymphoma.

SEE ALSO

- Hypercalcemia.
- Leukemia, Chronic Lymphocytic.

ABBREVIATIONS

- DLBCL = diffuse, large B-cell lymphoma.
- FL = follicular lymphoma.
- GI = gastrointestinal.
- LN = lymph node.
- LSA = lymphoma.
- MZL = marginal zone lymphoma.
- PTCL-NOS = peripheral T-cell lymphoma—not otherwise specified.
- TZL = T-zone lymphoma.

Suggested Reading

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



Client Education Handout
available online

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MAMMARY GLAND TUMORS—CATS



BASICS

DEFINITION

Malignant and benign tumors of the mammary glands in cats.

PATHOPHYSIOLOGY

- The majority of mammary gland tumors are malignant (85–95%) and tend to have an aggressive biologic behavior. Most malignant mammary tumors are adenocarcinomas; sarcomas are rare.
- Exposure to ovarian hormones and exogenous progestin increases risk of mammary tumor development. Intact cats have a 7-fold increased risk of developing mammary tumors as compared to spayed cats. Spaying cats prior to 1 year of age greatly reduces risk of mammary tumor development.
- While less common at diagnosis, pulmonary metastasis occurs in up to 80% of cats. Regional lymph node metastasis is common at diagnosis and may occur in up to 45% of cats. At necropsy, metastasis is identified in >90% of cats; other sites of metastasis may include liver, spleen, kidney, adrenal gland, pleura, peritoneum, and bone.
- Inflammatory mammary carcinomas are rare. These are anaplastic carcinomas with considerable inflammatory cell infiltrates, and are associated with extensive local ulceration, edema, and pain, as well as rapid metastasis.

SYSTEMS AFFECTED

- Reproductive—mammary glands.
- Metastasis can affect any organ system, especially the respiratory and lymphatic systems.

GENETICS

The high incidence of mammary tumors in Siamese cats suggests a genetic component to this disease, but specific genes have not been identified to date.

INCIDENCE/PREVALENCE

- Third most common neoplasia in cats (after lymphoma and skin tumors).
- The estimated incidence rate is 12.8–25.4 per 100,000 cats.

SIGNALMENT

Species

Cat

Breed Predilections

- Domestic shorthair and longhair breeds are affected most commonly, but likely reflects the popularity of these breeds rather than a true predilection.
- Siamese cats have twice the risk of other breeds for developing mammary tumors.

Mean Age and Range

- Mean—10–12 years.
- Range—9 months to 23 years; most are >5 years of age.
- Siamese cats tend to be diagnosed with

mammary tumors at a younger age (mean of 9 years).

- Male cats tend to be diagnosed with mammary tumors at an older age (mean of 12.8 years).

Predominant Sex

- Females predominate with only 1–5% of mammary carcinomas occurring in male cats.
- While being intact increases the risk of mammary tumors (see Risk Factors), most cats diagnosed with mammary tumors are spayed.

SIGNS

Historical Findings

- Most cats present for evaluation of a palpable ventral abdominal mass.
- Cats with advanced metastatic disease may present for general signs of illness (e.g., lethargy or anorexia) or for signs attributable to a specific site of metastasis (e.g., dyspnea due to pulmonary metastasis or pleural effusion).
- The duration of clinical signs can vary from days to several months.

Physical Examination Findings

- Mammary masses can be discrete or infiltrative, soft or firm. Smaller masses often are freely moveable, whereas larger masses can adhere to the underlying abdominal musculature.
- The overlying skin is often intact for smaller tumors, but larger tumors may be ulcerated and inflamed.
- The associated nipple may be inflamed and exude serous fluid.
- Any gland can be affected, although the caudal two glands are affected more commonly. Left and right sides are affected with equal frequency.
- Up to 60% of cats will have multiple tumors on the same and/or opposite mammary chain.
- Axillary or inguinal lymphadenopathy (reactive or metastatic) may be present.
- Cats with inflammatory carcinomas present with severe ulceration, erythema, pain, and edema in the ventral abdomen and pelvic limbs.

CAUSES

Unknown

RISK FACTORS

- Compared to intact cats, those spayed at <6 months of age or 6–12 months had a 91% and 86% risk reduction, respectively, for mammary carcinoma development, suggesting that hormonal influence is significant.
- There is no obvious protective effect when cats are spayed at >12 months of age.
- Exogenous progestins (e.g., medroxyprogesterone acetate) increase the risk of benign and malignant mammary tumor development in female and male cats. In one study, 8 of 22 male cats with mammary carcinomas had a history of exogenous progestin therapy.
- Parity has not been shown to affect mammary tumor development.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Fibroepithelial hyperplasia—especially in young (<2 years) intact female cats, and older or spayed cats receiving exogenous progestins.
- Mastitis.
- Other cutaneous or subcutaneous tumors.
- Inguinal or axillary lymphadenopathy (reactive or neoplastic).
- Inguinal hernia.
- Large/prominent inguinal fat pad.

CBC/BIOCHEMISTRY/URINALYSIS

Usually unremarkable.

OTHER LABORATORY TESTS

Coagulation profile recommended for cats with suspected inflammatory carcinomas due to the high incidence of secondary disseminated intravascular coagulopathy.

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IMAGING

- Three-view thoracic radiographs are recommended to screen for pulmonary metastasis, pleural effusion, and/or sternal lymphadenomegaly. Pulmonary metastases commonly appear as ill-defined interstitial nodules or a diffuse pulmonary pattern, although well-defined interstitial nodules are seen occasionally. Malignant pleural effusion is common and can obstruct adequate visualization of pulmonary parenchyma.
- Abdominal ultrasound is recommended to screen the medial iliac lymph nodes and other abdominal viscera for metastases.
- Ultrasound also can be used to visualize nonpalpable axillary or inguinal lymph nodes, as well as to look for additional small masses within the mammary glands.

DIAGNOSTIC PROCEDURES

- Cytology can be useful for ruling out other nonmammary malignancies. However, it is not useful for distinguishing between benign and malignant mammary masses.
- Histopathologic evaluation is needed to reach a definitive diagnosis. Since most mammary tumors are malignant, this is usually performed on tissue removed during radical mastectomy (see Treatment). While not contraindicated, incisional biopsies are routinely recommended only for cats with advanced-stage disease that are not candidates for aggressive local surgery.
- All tissue removed must be submitted for histopathologic evaluation. This allows for the most accurate diagnosis, and also allows for evaluation of surgical margins for completeness of excision.
- The ipsilateral draining lymph nodes (axillary and inguinal) should be removed whenever possible and submitted separately for histopathologic evaluation, even if grossly normal.
- Cytology of pleural fluid

MAMMARY GLAND TUMORS—CATS

(CONTINUED)

can be useful for confirming intrathoracic metastasis.

PATHOLOGIC FINDINGS

- The most common histologic subtypes are tubulopapillary, cribriform, and solid carcinomas.
- Histologic subtype has not consistently been shown to affect prognosis, but there is some evidence that tubulopapillary carcinomas carry a better prognosis.
- Tumor grade, based on degree of tubule formation, nuclear and cellular pleomorphism, and mitotic index, is predictive of survival after surgery.
- Vascular and lymphatic invasion is associated with more advanced clinical stage and shorter disease-free interval after treatment.
- Mammary sarcomas are rare but potentially slow to metastasize.
- Benign histologic subtypes are uncommon and may include mammary adenomas, ductal adenomas, fibroadenomas, and intraductal papillary adenomas.



TREATMENT

APPROPRIATE HEALTH CARE

- Surgery is recommended for cats with gross disease confined to the mammary glands with or without regional lymph node involvement.
- Adjuvant chemotherapy is recommended after the cat has recovered from surgery.
- Chemotherapy can be used as a sole treatment modality for cats with nonsurgical local disease and/or distant metastasis, although long-term control would not be expected to be durable.
- Radiation therapy has not been evaluated.
- Palliative pain therapy is recommended for cats with nonresectable local disease or gross metastasis, or when definitive therapy is declined.

CLIENT EDUCATION

- Stress the benefits of early ovariohysterectomy (<6 months of age) in nonbreeding cats.
- Stress the importance of early detection and aggressive treatment as small tumors (<2 cm) have a better prognosis.

SURGICAL CONSIDERATIONS

- Radical mastectomy of the affected mammary chain(s) is recommended. This significantly reduces the risk of local tumor recurrence as well as recurrence in the lymphatic vessels coursing through the mammary tissue.
- Bilateral radical mastectomy, regardless of tumor location, has been shown to lead to decreased rates of local tumor recurrence, new mammary tumor development, and metastasis as well as increased survival time as compared unilateral mastectomy. Mastectomies are usually staged 2–4 weeks apart as performing bilateral mastectomies in a single surgical procedure is associated with increased risk of

incisional dehiscence and/or infections and, less commonly, respiratory difficulty.

- The inguinal and (if possible) axillary lymph nodes should be removed at the same time, regardless if they are normal in size.
- In cats with advanced metastatic disease, palliative local mastectomy can be considered to remove an ulcerated or infected tumor.



MEDICATIONS

DRUG(S) OF CHOICE

- Doxorubicin 25 mg/m² IV every 3 weeks, alone or in combination with cyclophosphamide 100 mg/m² IV or PO divided over 4 days.
- Mitoxantrone, carboplatin, and docetaxel might have activity.
- Consult with an oncologist for current chemotherapy recommendations.
- Palliative analgesics and antibiotics should be considered for cats with tumors that are painful and/or ulcerated.

CONTRAINdications

Use doxorubicin with caution in cats with renal or hepatic insufficiency.

PRECAUTIONS

If you are unfamiliar with chemotherapy, consult an oncologist before administering.



FOLLOW-UP

PATIENT MONITORING

- Thorough physical examination conducted monthly for the first 3 months, then every 2–3 months thereafter is recommended.
- Palpation of the previous incision line, the remaining mammary glands (if only unilateral radical mastectomy performed), and regional lymph nodes should be emphasized during examination.
- Three-view thoracic radiographs every 2–3 months for detection of metastases.
- Consider abdominal ultrasound every 2–3 months to monitor for local lymph node metastasis.

PREVENTION/AVOIDANCE

Ovariohysterectomy prior to 6 months of age is associated with a 91% risk reduction in the development of mammary carcinoma.

POSSIBLE COMPLICATIONS

Malignant pleural effusion may develop rapidly causing life-threatening dyspnea.

EXPECTED COURSE AND PROGNOSIS

- Most cats die from local recurrence and/or metastasis.
- Tumor size is strongly predictive of prognosis. For tumors ≤2 cm in diameter median survival is >4.5 years (14 months in males), for tumors 2–3 cm it is 1–2 years (5–6 months in males), for tumors >3 cm it is

4–6 months (1–2 months in males).

- Radical mastectomy significantly reduces the risk for local tumor recurrence. The impact on survival is not as consistent because of the high metastatic rate associated with this tumor.
- In retrospective studies, adjuvant chemotherapy (doxorubicin with or without cyclophosphamide) has not consistently improved disease-free interval or survival. However, chemotherapy has proven efficacy against nonresectable and metastatic feline mammary tumors (gross disease), and given the high metastatic rate of these tumors adjuvant chemotherapy is still strongly recommended.
- For cats with advanced-stage disease treated with chemotherapy alone, response rates are around 50%. Survival times are 6–12 months for cats that do have a positive response to treatment, <6 months for those that do not.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

- Given the possible genetic contribution to this disease, particularly in Siamese cats, breeding affected cats is not recommended.
- Chemotherapy is not recommended in pregnant queens, particularly during the early stages of pregnancy.

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Dennis B. Bailey.



Client Education Handout available online

MAMMARY GLAND TUMORS—DOGS**BASICS****DEFINITION**

Benign or malignant tumors of the mammary glands in dogs.

PATHOPHYSIOLOGY

- Estrogen can exert direct genotoxic effects on mammary epithelium leading to mutations and aneuploidy.
- Progesterone may increase growth hormone and growth hormone receptor expression by the mammary gland, leading to increased insulin-like growth factor-1 (IGF-1) which is associated with proliferation and survival.
- Most dogs develop multiple tumors due to entire mammary tissue exposed to sex hormones during puberty, i.e., “field carcinogenesis.”
- Mammary gland tumors are a continuum from benign to malignant.
- Obesity decreases sex hormone-binding globulin, leading to increased concentration of free estrogen.

SYSTEMS AFFECTED

- Reproductive.
- Metastasis—lymphatic, respiratory, skeletal, nervous, and other systems.

GENETICS

Germline mutations of *BRCA-1* and -2 and *CDK5RAP2* genes reported in English springer spaniels.

INCIDENCE/PREVALENCE

Constitute 50–70% of all tumors in female dogs; 71% of all female beagles developed at least one mammary neoplasm.

SIGNALMENT**Breed Predilections**

Toy and miniature poodle, English springer spaniel, Brittany spaniel, cocker spaniel, English setter, boxer, English pointer, German shepherd dog, Maltese, Samoyed, schnauzer, Doberman pinscher, shih tzu, and Yorkshire terrier.

Mean Age and Range

Uncommon in dogs <5 years; mean age 9–11 years (malignant) and 7–9 years (benign).

SIGNS

- 70% of patients have multiple tumors.
- Caudal mammary glands more commonly affected.
- Discrete, well-circumscribed mass in systemically healthy patient.
- Inflammatory carcinoma—diffuse edematous, warm, painful mammary chains.
- Inflammatory carcinoma associated with distant metastasis and systemic illness.

CAUSES

Unknown; likely hormonal.

RISK FACTORS

- Age.
- Breed—more common in small breeds than in large breeds.
- Hormone influence (see Prevention/Avoidance).
- Obesity during puberty increases risk. Underweight at 9–12 months of age associated with protective effect.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Lipoma.
- Mast cell tumor.
- Mammary hyperplasia.
- Mastitis.
- Soft tissue sarcoma.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

N/A

IMAGING

- Thoracic radiography may detect metastasis and three views are advised.
- CT is more sensitive for detection of pulmonary metastasis than are plain radiographs.
- CT lymphography could aid in the assessment of sentinel lymph node metastasis.
- Abdominal radiography may detect metastasis to regional lymph nodes or vertebrae.
- Abdominal sonography to evaluate for regional or distant metastasis.

DIAGNOSTIC PROCEDURES

- Fine-needle aspirate cytology—67.5–93% correlation with histopathology; 88% sensitivity and 96% specificity for malignancy.
- Fine-needle aspirate cytology of local lymph node(s).
- Histologic evaluation for definitive diagnosis. Request margin evaluation.

PATHOLOGIC FINDINGS

- There is a wide histologic spectrum of mammary tumors. Dogs may have concurrent benign and malignant tumors. Histologic examination of all excised masses is indicated.
- Histologic grading 1 (well-differentiated) to 3 (poorly differentiated) based on tubule formation, nuclear pleomorphism, and mitotic index valid for epithelial tumors only.
- Stromal invasion, vascular/lymphatic invasion, and lymph node status important.
- Complex carcinoma is more common than simple carcinoma.

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

- Surgery—primary mode of treatment. Completeness of excision is prognostic.
- Chemotherapy—may be effective and indicated for patients with high risk of metastasis or recurrence: histologic high grade or subtype, lymphatic/vascular invasion, stage III or higher.

CLIENT EDUCATION

- Advise client that a mammary lump should be evaluated by a veterinary health professional.
- Inform client that early surgical intervention is best.
- Advise ovariohysterectomy at time of tumor removal.

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SURGICAL CONSIDERATIONS

- Type of surgery determined by therapeutic intent: curative intent with wide excision; preventative with chain mastectomy; palliative intent for advanced disease.
- Consider age, tumor size, number of tumors, history of prior tumors, and clinical stage.
- Most patients with inflammatory carcinoma are poor surgical candidates due to profound diffuse microscopic disease, advanced stage, systemic illness, and local coagulopathies.
- 58% of dogs treated with regional mastectomy will develop a new tumor in the ipsilateral chain; increased risk if initial tumor is malignant (>70%).
- Current recommendations for single tumor of unknown histology: wide excision to achieve complete removal is the adequate surgical “dose,” i.e., 2 cm lateral margins and 1 fascial plane deep.
- Extirpation of the draining lymph node is advised. Immunohistochemistry may be indicated to detect occult metastasis.
- Ovariohysterectomy (OHE) concurrent with tumor removal may decrease the risk of relapse in dogs with grade 2, estrogen receptor-positive tumors, or dogs with increased presurgical serum estradiol.
- Remove tumor following abdominal closure if performing concurrent OHE to avoid tumor seeding of abdomen or incision.

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

- Always consult a veterinary oncologist for updated information.
- Nonsteroidal anti-inflammatory drug (NSAID) as sole adjuvant therapy.
- Doxorubicin 30 mg/m² IV (dogs >15 kg)

MAMMARY GLAND TUMORS—DOGS

(CONTINUED)

every 21 days (maximum 6 treatments).

- NSAID ± chemotherapy for inflammatory carcinoma.

CONTRAINDICATIONS

Doxorubicin—myocardial failure.

PRECAUTIONS

Chemotherapy may be toxic; seek advice before treatment if you are unfamiliar with cytotoxic drugs.

POSSIBLE INTERACTIONS

Doxorubicin—potential side effects include myelotoxicity, vomiting, diarrhea, and cardiac damage.

ALTERNATIVE DRUG(S)

- Carboplatin, mitoxantrone, gemcitabine, fluorouracil (5-FU), cyclophosphamide have been reported with varying impact on clinical outcome.
- Perioperative desmopressin for grade 2–3 carcinoma may improve survival.
- Tamoxifen—helpful in some humans with breast cancer; ineffective in dogs and has serious side effects (e.g., pyometra); do not use in dogs.



FOLLOW-UP

PATIENT MONITORING

Physical examination, abdominal sonography, and thoracic radiographs—1, 3, 6, 9, 12, 15, 18 months after treatment, then every 6 months thereafter.

PREVENTION/AVOIDANCE

- Spayed before first estrous cycle—0.5% lifetime risk of developing tumor.
- Spayed before second estrous cycle—8.0% lifetime risk.
- Spayed after second estrus—26% lifetime risk.
- Spayed after 2.5 years of age—no sparing effect on risk.

POSSIBLE COMPLICATIONS

- Infection or dehiscence with surgery.
- Myelosuppression with chemotherapy.
- Disseminated intravascular coagulation (DIC) with some (especially inflammatory carcinomas) types.

EXPECTED COURSE AND PROGNOSIS

- 50–70% of canine mammary tumors are malignant.
- 50% of malignant tumors metastasize.
- 58–70% of dogs will develop another tumor in the ipsilateral chain.
- Tumor diameter is strong predictor of local recurrence and distant metastasis and is a negative, independent prognosticator of survival.

• Lymph node status, histologic grade, and proposed World Health Organization (WHO) clinical stage (I–V) are most consistent prognostic factors.

- Stage I: Tumor size <3 cm, no regional or distant metastasis—complete excision has excellent prognosis.
- Stage II: Tumor 3–5 cm, no regional or distant metastasis—complete excision has excellent prognosis.
- Stage III: Tumor >5 cm, no regional or distant metastasis—median survival 10 months with surgery alone.
- Stage IV: Any tumor size, lymph node metastasis, no distant metastasis—median survival time 5–10 months with surgery.
- Stage V: Any tumor size, any lymph node status, evidence of distant metastasis—median survival time <6 months.
- Clinical stage, presence of lymphatic invasion, ulceration, and incomplete surgical margins are reported as independent negative prognostic factors.
- Complex carcinoma and simple tubular carcinoma associated with prolonged survival
- Simple tubulopapillary carcinoma, intraductal papillary carcinoma, and malignant myoepithelioma carries 10-fold higher risk of tumor-related death
- Adenosquamous carcinoma may have a high recurrence rate (50%).
- Anaplastic carcinoma and carcinosarcoma carry worst prognosis (<3 months) with >90% metastatic rate.
- Inflammatory carcinoma median survival time <3 months.
- WHO clinical stage may be applicable to noninflammatory epithelial tumors.
- Simple carcinoma and grade 1 tumors more commonly associated with stages I, II, or III.
- Lymph node invasion and less cellular differentiation more common in complex carcinoma than simple carcinoma.
- High COX2/CD31 or high COX2/VEGF coexpression have been associated with a decreased survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Paraneoplastic glomerulopathy and proteinuria.
- Hypertrophic osteopathy.
- Metastasis to lymph nodes, lungs, and CNS.

PREGNANCY/FERTILITY/BREEDING

- Treatment with progestin increases the chance of tumor development at a younger age.
- Treatment with progestin increases risk of development of benign tumor.
- Treatment with progestin and estrogen increases risk of malignant tumor development.

ABBREVIATIONS

- 5-FU = fluorouracil.
- DIC = disseminated intravascular coagulation.
- IGF-1 = insulin-like growth factor-1.
- NSAID = nonsteroidal anti-inflammatory drug.
- OHE = ovariohysterectomy.
- WHO = World Health Organization.

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Client Education Handout
available online

MASTITIS



BASICS

OVERVIEW

- Bacterial infection of one or more lactating mammary glands.
- Result of ascending infection, trauma to the gland, or hematogenous spread.
- *Escherichia coli*, staphylococci, and β -hemolytic streptococci most commonly involved; *Mycobacterium* and blastomycosis reported.
- Potentially life-threatening infection; may lead to sepsis if systemic involvement.

SIGNALMENT

- Postpartum bitch and queen.
- Pseudopregnant lactating bitch or queen (rare).

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SIGNS

Historical Findings

- Anorexia.
- Lethargy.
- Neglect of puppies or kittens.
- Failure of puppies or kittens to thrive.

Physical Examination Findings

- Firm, swollen, warm, and painful mammary gland(s) from which purulent or hemorrhagic fluid can be expressed.
- Fever, dehydration, and shock—with systemic involvement.
- Abscessation or gangrene of gland(s) can result.

CAUSES & RISK FACTORS

- Ascending infection via teat canals.
- Trauma inflicted by puppy or kitten toenails and teeth.
- Poor hygiene.
- Systemic infection originating elsewhere (e.g., metritis).
- Rarely secondary to fibroadenomatous hyperplasia in queens.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Galactostasis—no systemic illness; cytologic examination and culture of milk aid differentiation.
- Inflammatory mammary adenocarcinoma—affected gland does not produce milk; differentiated by biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with left shift, or leukopenia with sepsis.
- Hemoconcentration (increased packed cell volume, total plasma protein concentration), and azotemia from dehydration or prerenal effects.

OTHER LABORATORY TESTS

N/A

IMAGING

Ultrasonography reveals loss of distinct layering of normal tissue in glands, decreased echogenicity, increased heterogeneity, and altered blood vessel density on color Doppler.

DIAGNOSTIC PROCEDURES

- Cytology—neutrophils, macrophages, and other mononuclear cells can be observed in normal milk; the presence of large numbers of free and phagocytosed bacteria and degenerative neutrophils occurs with mastitis.
- Microbial culture—identification and sensitivity of microorganisms from milk of affected glands; screening for methicillin-resistant *Staphylococcus aureus* recommended.



TREATMENT

- Inpatient until stable.
- Puppies and kittens—neonates may be allowed to continue nursing unless glands are necrotic or dam is systemically ill; affects choice of antibiotics; monitor weight gain in neonates: pups should gain 10% of birth weight per day, kittens should gain a minimum of 7–10 g/day.
- IV isotonic crystalloid fluid to treat dehydration, hypovolemia, shock.
- Correct electrolyte imbalances, hypovolemia, hypoglycemia.
- Apply warm compress and milk out affected gland(s) several times daily.
- Cover friable glands to prevent excoriation if nursing is allowed.
- Application of cabbage leaf wraps to affected glands may speed resolution.
- Abscessed or gangrenous glands—require surgical debridement.
- Open wound management or negative pressure wound therapy may be needed after surgery in some cases; negative pressure therapy may also be used for conservatively managed cases.



MEDICATIONS

DRUG(S) OF CHOICE

- Acidic milk—weak bases; erythromycin 10 mg/kg PO q8h, lincomycin 15 mg/kg PO q8h, or trimethoprim-sulfadiazine 15–30 mg/kg PO q12h for 21 days.
- Alkaline milk—weak acids; amoxicillin or cephalosporin 20 mg/kg PO q8h, dogs and cats; amoxicillin/clavulanic acid 13.75 mg/kg PO q12h (dogs); 62.5 mg/cat PO q12h (cats) for 21 days.

- Either alkaline or acidic milk—chloramphenicol 40–50 mg/kg PO q8h or enrofloxacin 5–20 mg/kg/day PO for 21 days.

- May infuse affected gland(s) with 1% betadine solution by lacrimal cannula.
- Cabergoline 5 µg/kg PO q24h for 5–7 days to suppress lactation in unaffected glands in patients with sepsis; neonates must be hand-reared.

CONTRAINdicATIONS/POSSIBLE INTERACTIONS

Patient allowed to nurse—avoid tetracycline and chloramphenicol; may use cephalosporins, amoxicillin, and amoxicillin with clavulanic acid. Enrofloxacin may be used in dogs up to 3 weeks of age.



FOLLOW-UP

PATIENT MONITORING

- Physical examination and CBC.
- Repeated ultrasonographic evaluation helps assess healing—normal distinct layering of tissues will appear with recovery.

PREVENTION/AVOIDANCE

- Clean environment.
- Hair shaved from around mammary glands.
- Toenails of puppies and kittens clipped.
- Ensure neonates nurse from all glands.
- Probiotic administration.

POSSIBLE COMPLICATIONS

- Abscessation or gangrene—may cause loss of gland(s).
- Hand-raising puppies and kittens—requires considerable commitment by the owner; may affect behavioral outcome of offspring.

EXPECTED COURSE AND PROGNOSIS

Prognosis—good with treatment.



MISCELLANEOUS

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Joni L. Freshman.

MEGACOLON



BASICS

DEFINITION

A disorder characterized by persistent, irreversible dilation of the colon that is often the result of chronic constipation/obstipation.

PATHOPHYSIOLOGY

- Idiopathic dilated megacolon is the most common cause of chronic constipation in cats and occurs due to generalized colonic smooth muscle dysfunction. • The diagnosis of idiopathic dilated megacolon is often preceded by chronic, recurrent constipation so it is unclear whether a primary disorder of colonic smooth muscle occurs first or whether smooth muscle dysfunction results from prolonged colonic distension. • Megacolon can also occur secondary to abnormal neurologic function of the colon, including dysautonomia, spinal cord injury or deformities, pelvic nerve injury, and autonomic ganglioneuritis. • Colonic aganglionosis/hypoganglionosis (Hirschsprung's disease in humans) is a congenital absence of ganglia in the colonic smooth muscle; affected segments are unable to relax, resulting in megacolon.
- Hypertrophic megacolon can develop as a consequence of obstructive lesions and will progress to dilated megacolon if the obstruction is not corrected.

SYSTEMS AFFECTED

- Gastrointestinal. • Neuromuscular—concurrent neurologic abnormalities may be seen when megacolon has a neurogenic cause.
- Musculoskeletal—megacolon can occur secondary to pelvic fractures. • Endocrine/metabolic—megacolon can result in electrolyte derangements due to prolonged vomiting. Electrolyte and endocrine abnormalities (hypercalcemia, hypokalemia, hypothyroidism) can promote constipation and possibly lead to or exacerbate megacolon.

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Cat > dog.

Breed Predilections

Possible increased risk in Manx cat.

Mean Age and Range

- Idiopathic megacolon—young adult cats most commonly (mean 6 years) although cats of any age can be affected. • Acquired megacolon—none.

Predominant Sex

Male

SIGNS

Historical Findings

- Idiopathic megacolon—typically a chronic/recurrent problem; signs often present for months to years. • Acquired megacolon—signs may be acute or chronic. • Constipation/obstipation. • Tenesmus with small or no fecal volume. • Hard, dry feces. • Infrequent defecation. • Small amount of diarrhea (often mucoid) may occur after prolonged tenesmus.
- Occasional vomiting, anorexia, and/or lethargy with chronic fecal impaction.
- Weight loss.

Physical Examination Findings

- Abdominal palpation reveals an enlarged colon with hard feces. • Digital rectal examination may indicate an underlying (obstructive) cause and confirms fecal impaction. • Dehydration. • Unkempt hair coat. • Weight loss with chronicity.
- Neurologic examination may reveal underlying neurologic disease.

CAUSES

- Mechanical obstruction—pelvic fractures, neoplasia, rectal foreign body, rectal stricture, atresia ani, prostatomegaly. • Neurologic disease—dysautonomia, sacral spinal cord deformities (Manx cat), cauda equina syndrome, pelvic nerve injury or dysfunction. • Endocrine/metabolic—hypercalcemia, hypokalemia, hypothyroidism, severe dehydration. • Drugs—opioids, anticholinergics, phenothiazines.

RISK FACTORS

- Chronic constipation. • Conditions leading to obstruction or difficulty defecating, including prior trauma and spinal cord injury or deformity. • Possible association with low physical activity and obesity as well as consumption of bone meal in dogs.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of palpable colonic masses (e.g., lymphoma, carcinoma, intussusception)—distinguish on the basis of texture, rectal examination, imaging, and mucosal biopsy.
- Dysuria/stranguria—exclude by palpation of the bladder and colon, and by urinalysis.
- Tenesmus due to inflammation of the colonic mucosa (colitis)—exclude by palpation, rectal examination, and colonoscopy with mucosal biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- Often normal. • May show evidence of dehydration and stress leukogram. • Electrolyte abnormalities may develop; may be prerenal azotemia with dehydration. • Urinalysis—typically unremarkable.

OTHER LABORATORY TESTS

Total thyroxine (T_4) to assess thyroid function.

IMAGING

- Abdominal/pelvic radiographs to identify underlying causes. • Can easily visualize an enlarged, fecal-filled colon on survey abdominal radiographs. • Abdominal ultrasound may identify mural or obstructive masses.

DIAGNOSTIC PROCEDURES

Rarely need colonoscopy to rule out mural or intraluminal obstructive lesions.

PATHOLOGIC FINDINGS

- Feline idiopathic megacolon has no defining histologic changes. Smooth muscle typically appears normal with evidence of normal innervation. Mucosal and submucosal ulceration, fibrosis, and inflammation can be variably present and are secondary to chronic fecal impaction. • Megacolon resulting from other etiologies may have features such as abnormalities in or reduced numbers of ganglia (ganglioneuritis or hypoganglionosis), or smooth muscle hypertrophy (hypertrophic megacolon).

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TREATMENT

APPROPRIATE HEALTH CARE

- If administration of laxatives or enemas fails to resolve fecal impaction, inpatient management and manual evacuation of feces will be necessary.
- For manual evacuation of feces, the patient should be placed under general anesthesia and intubated to prevent aspiration should manipulation of the colon trigger vomiting or regurgitation:
 - Warm water combined with a water-based lubricant can be administered during the procedure to help facilitate removal of feces. Feces are then removed manually while providing gentle assistance with abdominal palpation of the colon.
 - Periprocedural administration of an IV antibiotic with a good anaerobic spectrum can be considered in case manipulation of the compromised colon results in bacterial translocation.
 - This procedure may need to be repeated if the impaction is too severe to safely accomplish removal of all feces under one anesthetic event.
 - Trickle administration of polyethylene glycol 3350 via nasogastric tube for 24–48 hours prior to manual extraction will result in better fecal hydration and may facilitate stool removal.

NURSING CARE

- Most patients require parenteral fluid support to correct dehydration. • IV administration of balanced electrolyte solutions is the preferred route. • Control nausea and vomiting with antiemetic medications.

ACTIVITY

- Encourage activity and exercise.
- Restriction indicated postoperatively if surgery is performed.

MEGACOLON

(CONTINUED)

DIET

- Many patients require a low-residue producing diet; bulk-forming fiber diets can worsen or lead to recurrence of colonic fecal distension.
- A soluble fiber-rich diet may be helpful.
- A maintenance-type diet can be supplemented with fiber-enriched foods (pumpkin) or products containing fermentable fiber such as Metamucil.

CLIENT EDUCATION

- Following treatment for constipation, medical therapy, including dietary management, laxatives, and/or colonic prokinetics, may be required long term and has the potential to fail.
- Subtotal colectomy is indicated in cases of medical treatment failure.

SURGICAL CONSIDERATIONS

- An underlying obstructive cause should be surgically corrected, if possible. Alternatively, subtotal colectomy has been described in the successful management of megacolon occurring secondary to pelvic fracture malunion.
- For patients that do not respond favorably to medical treatment, subtotal colectomy is the treatment of choice.
- Subtotal colectomy may be required with obstructive megacolon even if the obstruction is corrected if irreversible changes in colonic motility have already occurred.
- Avoid enema administration or attempts at colonic evacuation prior to surgery. These efforts result in increased likelihood of fecal contamination of the abdomen during surgery.
- Subtotal colectomy can be performed with either ileorectal or colorectal anastomosis. Preservation of the ileocolic junction is recommended as this results in more formed stool compared to cats in which it is excised.



MEDICATIONS

DRUG(S) OF CHOICE

- Colonic prokinetic agents—cisapride (5-HT receptor agonist) has been shown to stimulate colonic smooth muscle motility in cats and dogs with constipation. The dose is 0.1–0.5 mg/kg PO q8–12h, but may be increased up to 1 mg/kg if well tolerated. Metoclopramide is not effective for constipation.
- Hyperosmotic laxatives—polyethylene glycol 3350 powder (Miralax[®]) 1/8–1/4 tsp with food q12h; lactulose 0.5 mL/kg PO q8–12h to effect. In cats with severe constipation, polyethylene glycol electrolyte solution (GoLyteley[®], Colyte[®]) can be given via nasogastric or nasoesophageal feeding tube at 6–10 mL/kg/h for 12–48 hours in a 24-hour care hospital setting to facilitate passage of feces, either as an alternative to or in preparation for manual evacuation of feces.
- Enemas—5–10 mL/kg warm water or a 50–50 mixture of warm water and water-soluble lubricant administered slowly via a lubricated 10–12 Fr red rubber catheter gently passed into the rectum. Lactulose can also be administered as an enema at a dose of 5–10 mL/kg.

CONTRAINDICATIONS

- Sodium phosphate retention enemas (e.g., Fleet by C.B. Fleet Co., Inc.)—because of their association with severe hypocalcemia.
- Mineral oil and white petrolatum—because of danger of fatal lipid aspiration pneumonia due to lack of taste.

PRECAUTIONS

Common hairball laxatives (e.g., Laxatone, Cat-a-Lax) are typically ineffective.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Docusate sodium can be used as a stool softener in place of lactulose.
- Psyllium can be added to food at a dose of 1/4–1 tsp twice a day. Fiber may be beneficial in early stages but may exacerbate clinical signs in cats with loss of colonic muscle function.
- Diocetyl sodium sulfosuccinate (Colace[®]) is an emollient laxative that can be given as an alternative to lactulose or polyethylene glycol.
- Ranitidine, a member of the H₂-receptor antagonist drug class, may stimulate colonic motility and can be given if cisapride is unavailable. The dose is 1–3 mg/kg PO q12h.
- One recent pilot study using multistrain probiotic SLAB51[™] showed clinical improvement in some cats with chronic constipation and idiopathic megacolon.



FOLLOW-UP

PATIENT MONITORING

- Following colonic resection and anastomosis—for 3–5 days check for signs of dehiscence and peritonitis.
- Clinical deterioration warrants abdominocentesis and/or peritoneal lavage to detect anastomotic leakage.
- Continue fluid support until the patient is willing to eat and drink.

PREVENTION/AVOIDANCE

- Repair pelvic fractures that narrow the pelvic canal.
- Avoid exposure to foreign bodies and feeding bones.
- Encourage physical activity.

POSSIBLE COMPLICATIONS

- Recurrence or persistence—most common.
- Potential surgical complications include peritonitis, persistent diarrhea, fecal incontinence, stricture formation, and recurrence of obstipation.
- Traumatic perforation of the colon is a serious complication of overzealous fecal evacuation.

EXPECTED COURSE AND PROGNOSIS

- Historically, medical management has been unrewarding for the long term.
- Cisapride appears to improve the prognosis with medical management in some patients, but may not suffice in severe or long-standing cases.
- Postoperative diarrhea—expected; typically resolves within 6 weeks (80% of cats

with idiopathic megacolon undergoing subtotal colectomy) but can persist for several months; stools become more formed as the ileum adapts by increasing reservoir capacity and water absorption.

- Subtotal colectomy is well tolerated by cats; constipation recurrence rates are typically low.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Perineal hernia.

AGE-RELATED FACTORS

Concurrent medical conditions (e.g., chronic renal insufficiency, hyperthyroidism) may occur with idiopathic megacolon, because many cats are old.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

- The effect of cisapride on the fetus is unknown.
- Patients would be at increased risk for dystocia if they carried a pregnancy to term.

SYNOMYNS

None

SEE ALSO

- Constipation and Obstipation.
- Dyschezia and Hematochezia.
- Perineal Hernia.

ABBREVIATIONS

- T₄ = thyroxine.

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Client Education Handout
available online

MEGAESOPHAGUS



BASICS

DEFINITION

A focal or generalized, diffuse dilation of the esophagus with decreased to absent peristalsis.

PATHOPHYSIOLOGY

- In the normal esophagus, the presence of a food bolus in the proximal esophagus stimulates afferent sensory neurons. • Signals are transferred centrally, via the vagus and glossopharyngeal nerves to the tractus solitarius and nucleus ambiguus. • Motor impulses travel back via the efferent neurons of the vagus nerve to stimulate striated muscle (canine) and striated and smooth muscle (feline) esophageal contraction. • Lesions anywhere along this pathway may lead to megaesophagus and resultant retention of food and liquids.
- Approximately 60% of dogs with megaesophagus have an “achalasia-like” syndrome of the lower esophageal sphincter (LES), that is a well-documented cause of megaesophagus in people.
- Functional obstruction of the LES results in esophageal dilatation, retention of ingesta, loss of esophageal motility, and associated clinical signs of esophageal dysphagia. • Dogs with evidence of esophageal achalasia may respond to targeted therapy with subsequent improvement in esophageal dysphagia.
- Focal megaesophagus is typically caused by esophageal obstruction secondary to strictures or a vascular ring anomaly with dilation of the esophagus proximal to the obstruction.

SYSTEMS AFFECTED

- Gastrointestinal—dysphagia, regurgitation, weight loss. • Musculoskeletal—weakness, weight loss, exercise intolerance, dysphonia.
- Nervous—possible manifestation of systemic neurologic/neuromuscular disorder.
- Respiratory—aspiration pneumonia, coughing.

GENETICS

- Congenital form—megaesophagus can be inherited in smooth fox terriers (autosomal recessive) and miniature schnauzers (autosomal dominant or 60% penetrance autosomal recessive). In addition, Jack Russell terriers, springer spaniels, long-haired miniature dachshunds, golden retrievers, Labrador retrievers, and Samoyeds are predisposed to the congenital form of myasthenia gravis.
- Other breeds in which acquired megaesophagus is more commonly reported include German shepherd dog, Great Dane, Irish setter, Labrador retriever, pug, and Chinese Shar-Pei.
- Acquired form—many diseases, especially neuromuscular diseases, may have an association with megaesophagus. Genetic

predispositions for such diseases are listed under each disease separately.

INCIDENCE/PREVALENCE

- Congenital forms—relatively uncommon.
- Acquired disease—increasingly recognized in the dog and rare in the cat.

SIGNALMENT

Species

Dogs are more commonly affected than cats.

Breed Predilections

- Dogs—see Genetics. • Cats—Siamese and Siamese-related cats.

Mean Age and Range

- Congenital cases present soon after birth or at weaning during transition from liquid diets to solid foods. • Acquired cases may be seen at any age, depending on the etiology.

SIGNS

Historical Findings

- Owners often report vomiting; the veterinarian must differentiate vomiting from regurgitation. • Regurgitation (considered the hallmark sign); dysphagia; coughing/nasal discharge with aspiration pneumonia; ravenous appetite or inappetence; weight loss or poor growth; ptalism, and halitosis. Dysphonia may occur secondary to neuromuscular disease. • Other signs depend upon underlying etiology.

Physical Examination Findings

- Cervical swelling may be noted, representing a distended cervical esophagus; ptalism; halitosis; increased respiratory noises, nasal discharge, and fever (if concurrent pneumonia); cachexia; weakness; weight loss. • Assess for concurrent neurologic deficits that may indicate generalized disease. Special attention should be paid to cranial nerves IX, X, and XI. Muscle atrophy (if present) may be focal or generalized.

CAUSES

Congenital

Idiopathic megaesophagus; congenital myasthenia gravis (MG) (rare).

Acquired/Adult Onset

- Idiopathic (most common).
- Neuromuscular disease—MG, focal or generalized (25% of cases in dogs); systemic lupus erythematosus (SLE); myositis/myopathic disease; dysautonomia (more common in cats); botulism; vagal dysfunction/damage (bilateral); a possible association between laryngeal paralysis and esophageal dysmotility secondary to polyneuropathy has been identified. • Brainstem disease—disease involving cranial nerves IX, X nuclei or peripheral nerves. • Esophageal obstruction—vascular ring anomaly; esophageal or periesophageal neoplasia (e.g., lymphoma,

thymoma, leiomyoma); stricture; foreign body; granuloma. • Toxicity—lead, thallium, anticholinesterase; acrylamide. • Endocrine disease—hypoadrenocorticism, hypothyroidism (controversial). Thymoma is associated with MG and megaesophagus in approximately 25% of cats. • Miscellaneous—gastric dilatation volvulus, hiatal hernia, gastroesophageal intussusception; esophagitis (gastroesophageal reflux, parasitic infection).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must distinguish regurgitation from vomiting. • Regurgitation—passive; little to no abdominal effort; no prodromal phase; regurgitated material has increased amounts of thick mucus. Regurgitation often occurs many hours after a meal has been consumed due to retention of the food bolus within the esophagus. • Vomiting—active process; prodromal phase; vomited material may have increased bile staining. • The shape of the expelled material, presence of undigested food, and length of time from ingestion to regurgitation or vomiting are less helpful to differentiate.

CBC/BIOCHEMISTRY/URINALYSIS

- May be unremarkable. • Inflammatory leukogram may be seen with pneumonia.
- Other changes may identify underlying etiology—basophilic stippling on red blood cells with lead toxicity; electrolyte disturbances with hypoadrenocorticism, although lack of electrolyte changes does not rule out hypoadrenocorticism; hypercholesterolemia with hypothyroidism; elevated creatine kinase with myopathic disease, particularly during the acute phase.

OTHER LABORATORY TESTS

- Acetylcholine receptor (AchR) antibody titer in all cases of acquired megaesophagus (screen for MG). Approximately 2% of dogs with generalized MG are seronegative; testing should be repeated 2–3 months later, particularly if initial antibody titer is only slightly below the reference interval. Dogs with congenital MG do not have an autoimmune disorder associated with circulating AchR antibodies, but instead have a deficiency of the AchR receptor itself. Serologic testing of antibodies to the AchR in puppies or dogs suspected of the congenital form of MG is thus of no diagnostic value and is a waste of money. • Adrenocorticotropic hormone (ACTH) stimulation test or baseline cortisol level for hypoadrenocorticism. • Thyroid panel for hypothyroidism (may be affected by concurrent disease). • Blood and urine lead

MEGAESOPHAGUS

(CONTINUED)

levels. • Antinuclear antibody (ANA) titers for SLE. • Blood cholinesterase levels for organophosphate toxicity.

IMAGING

Survey Thoracic Radiographs

- Dilated esophagus filled with air, fluid, or food. Interpret thoracic radiographs in anesthetized animals and anxious or painful animals with caution in light of aerophagia that can cause distention of the esophagus with air.
- Evidence of aspiration pneumonia may be evident.
- Ventral displacement of the trachea on lateral radiographs.
- Ventrodorsal radiographs may show lateral tracheal displacement.
- Evidence of underlying etiology: mediastinal mass (thymoma), hiatal hernia, neoplasia, etc.
- Radiographs do not differentiate dogs with megaesophagus due to MG from dogs with megaesophagus due to other etiologies.

Contrast Esophagram and Videofluoroscopy

- Barium liquid and barium meal may demonstrate abnormal pooling, poor motility, or structural lesions. Iohexol may be used if perforation is a concern.
- Use with caution in animals with megaesophagus due to risk of aspiration of contrast material.
- Exercise extreme caution in animals with radiographic evidence of pneumonia.
- Monitor animals closely after radiographs for signs of aspiration.
- Videofluoroscopy—may be used to assess primary and secondary esophageal peristalsis. May help determine the best food consistency for long-term management. Videofluoroscopy commonly demonstrates marked retention of the food bolus within the esophagus for hours, despite gravity-assisted feeding in a Bailey chair. A bird-beak effect of the lower esophageal sphincter may be evident due to esophageal achalasia.

DIAGNOSTIC PROCEDURES

- Esophagoscopy—may be used for foreign body retrieval, evaluation of suspected obstructive lesions, neoplasia, or esophagitis. Distal esophageal neoplasia or stricture of the lower esophageal sphincter may mimic idiopathic megaesophagus and may require endoscopy for diagnosis.
- Electrophysiology—in cases of suspected neuromuscular disease, may be used in conjunction with muscle and nerve biopsies.
- Additional tests—may be indicated in cases of CNS disease: CSF analysis, distemper titers, brain CT or MRI.
- Fecal exam—may indicate *Spirocerca lupi* infection.

PATHOLOGIC FINDINGS

Depend upon underlying etiology and presence of complicating factors.



TREATMENT

APPROPRIATE HEALTH CARE

- Treat underlying etiology (when applicable).
- Most important aspects are meeting nutritional requirements and treating or preventing aspiration pneumonia.

NURSING CARE

- Aspiration pneumonia may require oxygen therapy, nebulization/coupage, fluid therapy with balanced electrolyte solution.
- These animals may be recumbent and require soft bedding and should be maintained in sternal recumbency or turned to alternate down side every 4 hours.

ACTIVITY

Depending on etiology, restricted activity is not necessary.

DIET

- Calculate precise nutritional requirements, including degree of debilitation.
- Experimentation with different food consistencies is essential (e.g., liquid gruel, small meatballs, blenderized slurries).
- Many cases benefit from gastrostomy tube placement for feeding; however, this does not prevent gastroesophageal reflux and potential aspiration or aspiration of saliva.
- Feeding and drinking should be from an elevated position (45–90° from floor) and the upright position should be maintained for 10–15 minutes after eating or drinking. An upright position may be easier to attain with the use of a specific “chair” (e.g., Bailey chair).

CLIENT EDUCATION

- Most cases of megaesophagus require life-long therapy. Even if an underlying etiology is found and treated, prognosis for resolution of idiopathic acquired megaesophagus is unlikely. Client dedication is important for long-term management.
- Most animals succumb to or are euthanized because of aspiration pneumonia, malnutrition, or progression of underlying disease.

SURGICAL CONSIDERATIONS

- Surgery is indicated for vascular ring anomalies, bronchoesophageal fistula, some foreign bodies and other obstructive lesions, or thymectomy.
- Balloon dilation is indicated for cases of esophageal stricture.
- Surgical management of esophageal achalasia (Heller's myotomy followed by fundoplication) has been well documented in people with acquired megaesophagus

secondary to esophageal achalasia and in a recent publication evaluating acquired megaesophagus in dogs.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics for aspiration pneumonia (ideally based on culture and sensitivity from transtracheal wash or bronchoalveolar lavage).
- Therapy for underlying etiology if indicated—immunosuppressives (use with caution if pneumonia present) for immune-mediated disease; pyridostigmine for MG; prednisone supplementation for hypoadrenocorticism.
- Proton pump inhibitors (PPIs) are superior acid suppressants to H₂-receptor antagonists (H2RAs) for the management of moderate to severe esophagitis, and are not susceptible to tolerance (tachyphylaxis) that has been well documented in people, dogs, and cats within 3–5 days following the implementation of H2RA therapy. PPIs such as omeprazole or pantoprazole must always be given twice daily for optimal benefit (1 mg/kg PO or IV q12h). In addition, PPIs should be gradually tapered before discontinuing to avoid acid rebound hypersecretion.

Prokinetics

The use of prokinetics such as cisapride and metoclopramide in dogs and cats with diffuse megaesophagus is contraindicated and should be avoided because they will tighten the LES (which already has increased tone in most dogs with megaesophagus as a consequence of achalasia) and possibly increase the risk of aspiration pneumonia. Prokinetics such as metoclopramide (1.0–2.0 mg/kg/day IV CRI or PO q6–8h) or cisapride (0.5 mg/kg PO q8–12h) are more effective for minimizing gastroesophageal reflux and subsequent esophagitis in dogs that do not have megaesophagus. Cisapride is more potent and effective than metoclopramide for increasing LES tone and enhancing gastric emptying, and can be used in animals with evidence of esophagitis but no evidence of megaesophagus, or in cats with esophageal dysmotility affecting the smooth muscle in the distal 1/3 of the esophagus.

PRECAUTIONS

- Absorption of orally administered drugs may be compromised.
- Injectable forms should be used when applicable.
- Immunosuppression, if indicated, must be used with caution due to risk of aspiration pneumonia.

(CONTINUED)



FOLLOW-UP

PATIENT MONITORING

- Thoracic radiographs when aspiration pneumonia is suspected (fever, cough, lethargy).
- Cases of pneumonia may require CBC, blood gas analysis, and bronchoalveolar lavage. Repeat thoracic radiographs in animals with congenital megaesophagus as spontaneous resolution may occur.
- Examine and weigh patients regularly to evaluate disease progression and ensure adequate nutritional intake.

PREVENTION/AVOIDANCE

If an esophageal foreign body is identified, remove as quickly as possible.

POSSIBLE COMPLICATIONS

- Aspiration pneumonia.
- Others, depending on etiology.

EXPECTED COURSE AND PROGNOSIS

- Congenital cases have a guarded prognosis (20–46% recovery).
- Miniature schnauzers may have better prognosis.
- Prognosis may be improved with identification and treatment of specific etiology (e.g., hypoadrenocorticism, vascular ring anomaly).
- Roughly 50% cases of MG respond to therapy; however, megaesophagus may persist even if other signs of MG resolve.
- Prognosis for idiopathic,

adult-onset disease is poor.

- Owner dedication is crucial.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Aspiration pneumonia.

AGE-RELATED FACTORS

- Signs of regurgitation in very young animal or at weaning may indicate congenital lesion.
- Prognosis may be better in young animals.

ZOONOTIC POTENTIAL

- None for megaesophagus.
- Rabies vaccination status should be determined in any animal with possible neurologic disease.

SYNOMYMS

- Esophageal aperistalsis.
- Esophageal dilatation.

SEE ALSO

- Dysphagia.
- Esophageal Foreign Bodies.
- Myasthenia Gravis.
- Pneumonia, Aspiration.
- Pneumonia, Bacterial.
- Regurgitation.

ABBREVIATIONS

- AchR = acetylcholine receptor.
- ACTH = adrenocorticotropic hormone.
- ANA = antinuclear antibody.

- H2RAs = H₂-receptor antagonists.
- LES = lower esophageal sphincter.
- MG = myasthenia gravis.
- PPI = proton pump inhibitor.
- SLE = systemic lupus erythematosus.

INTERNET RESOURCES

- <https://www.marvistavet.com/megaesophagus.pml>
- <http://www.baileychairs4dogs.com/>

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Client Education Handout
available online

M

METRITIS



BASICS

OVERVIEW

- Bacterial uterine infection that develops in the immediate postpartum period (usually within the first week); occasionally develops after an abortion or nonsterile artificial insemination—rarely after natural breeding.
- Bacteria—ascend through the open cervix to the uterus; postpartum uterus provides an ideal environment for growth; Gram-negative bacteria (e.g., *Escherichia coli*) commonly isolated.
- Potentially life-threatening infection; may lead to septic shock.
- Can become chronic and lead to infertility.

M SIGNALMENT

- Postpartum bitch and queen.
- No age or breed predilection.

SIGNS

Historical Findings

- Malodorous, purulent, sanguinopurulent, or dark green vulvar discharge.
- Depression.
- Anorexia.
- Neglect of puppies and kittens.
- Reduced milk production.
- Polyuria/polydipsia.

Physical Examination Findings

- Fever.
- Large uterus on abdominal palpation.
- Dehydration.
- Injected mucous membranes (septic shock).
- Tachycardia, hypotension, other signs of shock.

CAUSES & RISK FACTORS

- Dystocia.
- Obstetric manipulation.
- Retained fetuses or placentas.
- Prolonged delivery (large litter).
- Post abortion, and post natural or artificial insemination (rare).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Subinvolution of placental sites—no sign of infection on cytologic examination of vagina.
- Eclampsia—differentiated by serum calcium concentration.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia with left shift, although neutropenia and leukopenia are occasionally seen, especially in patients with septic shock.
- High packed cell volume and total plasma protein concentration; azotemia secondary to

dehydration/hypovolemia. Normocytic, normochromic nonregenerative anemia may also occur.

- With endotoxemia or sepsis, hypoalbuminemia, elevation of C-reactive protein concentration, and other acute phase changes may occur. Elevated liver enzyme activities may be seen.
- Urine specific gravity may be elevated (from dehydration) or decreased (isosthenuria).
- Urinalysis (obtain via ultrasound-guided cystocentesis) may reveal bacteriuria.

OTHER LABORATORY TESTS

N/A

IMAGING

- Radiography—reveals a large uterus and possibly retained fetus(es).
- Ultrasonography—intratubal fluid accumulation and increased horn width, retained placenta(s), and retained fetus(es); abdominal effusion may be present if uterine rupture.

DIAGNOSTIC PROCEDURES

- Vaginal cytologic examination—detect degenerative neutrophils with intracellular bacteria.
- Guarded anterior vaginal or transcervical culture—aerobes and anaerobes; culture and sensitivity recommended.



TREATMENT

- Inpatient until systemic signs resolve.
- Treat shock—IV balanced electrolyte solution.
- Correct electrolyte imbalances and hypoglycemia.
- Ovariohysterectomy—treatment of choice for uterine rupture or severe sepsis, and if future breeding is not desired; the uterus is friable; pack off and handle gently at surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics—start broad-spectrum agents (oral if patient is stable; IV if patient is in shock); choice confirmed by bacterial culture and sensitivity; continued at least 14 days. Give at separate time from prostaglandin F2 α (PGF2 α) administration due to risk of vomiting.
- Nursing planned—amoxicillin-clavulanic acid 22 mg/kg PO q12h; can administer q8h to treat Gram-negative infections, enrofloxacin 10 mg/kg PO, IV q24h (dogs); 5 mg/kg PO q24h (cats), if puppies <3 weeks of age and susceptibility indicates.

- If ovariohysterectomy not performed and cervix is open—oxytocin 0.5–1 U/kg IM, SC (do not exceed 5 IU total); then repeat in 1–2 hours; may require increased dose to attain similar degree of uterine contraction if >48 hours since parturition.
- PGF2 α 10–50 μ g/kg SC q3–5h for 3–5 days or 100 μ g/kg SC q12h for 3–5 days; to evacuate uterus, ultrasound prior to cessation of treatment to ensure resolution of fluid accumulation in uterine lumen.

CONTRAINdications/POSSIBLE INTERACTIONS

- Prostaglandin—may induce uterine rupture if the tissue is devitalized.
- Oxytocin—reduced efficacy beyond 48 hours post partum.



FOLLOW-UP

PATIENT MONITORING

- Physical exam, CBC, vaginal cytologic examination.
- Ultrasonography—monitor evacuation of uterine fluid.

POSSIBLE COMPLICATIONS

- Ovariohysterectomy—when medical treatment is ineffective.
- Uterine rupture and peritonitis—may occur with medical treatment.
- Owners may need to foster or hand-raise puppies and kittens.

EXPECTED COURSE AND PROGNOSIS

- Ovariohysterectomy—prognosis for recovery good.
- Medical treatment—prognosis for recovery dependent on early recognition of problem by owner; good if early, but may adversely affect future reproduction.



MISCELLANEOUS

ABBREVIATIONS

- PGF2 α = prostaglandin F2 α .

Suggested Reading

Johnston SD, Root Kustritz MV, Olson PNS. Periparturient disorders in the bitch. In: Johnston SD, Root Kustritz MV, Olson PNS, eds., Canine and Feline Theriogenology. Philadelphia, PA: Saunders, 2001, pp. 129–145.

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Acknowledgment The author and editors acknowledge the prior contribution of Joni L. Freshman.

MYOCARDITIS



BASICS

DEFINITION

- Inflammation of the myocardium, definitive identification of which requires histologic examination.
- In humans, the widely accepted Dallas criteria specify that necrosis and/or degeneration of myocytes adjacent to inflammatory infiltrates is a requisite for diagnosis.
- Causes are diverse and include infective (viral, bacterial, protozoal, mycotic) pathogens and noninfective (toxic, possibly immune) disease agents.
- Traumatic myocarditis is a term applied to the syndrome of arrhythmias that sometimes complicates blunt trauma. The term is a misnomer because myocardial lesions (if present) are more likely to take the form of necrosis than inflammation.

PATOPHYSIOLOGY

- Numerous mechanisms, determined partly by the nature of the causative agent, are implicated.
- Microbial agents and toxins can result in direct cellular damage causing cell death, activation of the immune system, and inflammation.
- Though incompletely described in veterinary patients, chronic myocarditis, immune myocarditis and autoreactive myocarditis—the latter occurring in the absence of microbial agents—as well as dilated cardiomyopathy (DCM) are potential sequelae of acute myocarditis.
- The cellular character of inflammation is partly determined by the nature of the pathologic insult; protozoal and mycotic agents result in pyogranulomatous infiltrates, while viral myocarditis is generally lymphocytic.
- Myocardial involvement may be focal or diffuse.
- Canine parvoviral infection can result in myocarditis in pups, and has been implicated as a cause of DCM. The virus has tropism for dividing cells, and adult myocytes do not replicate. Parvovirus myocarditis is most likely to occur in unvaccinated pups from immunologically naïve dams.
- Protozoal myocarditis resulting from *Trypanosoma cruzi* infection causes Chagas disease. Acute phase illness is characterized primarily by electrocardiogram (ECG) abnormalities. Chronic infection can result in myocardial dysfunction and development of heart failure.
- It has been hypothesized that feline endomyocarditis might be a precursor of restrictive cardiomyopathy; recent findings implicate infection by *Bartonella* spp.
- Bacterial myocarditis can be observed in patients with overwhelming sepsis.
- Bacterial, protozoal, and mycotic myocarditis may reflect immunosuppression.
- An apparently rare, as yet idiopathic, atrial myocarditis might be important in the pathogenesis of persistent canine atrial standstill.
- The pathogenetic importance of myocardial inflammation in canine

arrhythmogenic right ventricular cardiomyopathy is unresolved; however, myocarditis is observed in a substantial proportion of cases.

- The pathogenesis of traumatic myocarditis is incompletely defined; direct trauma resulting in necrosis is likely responsible in some cases, but extracardiac factors including electrolyte derangements, hypoxia, acid–base disturbances, and altered function of the autonomic nervous system might contribute.

SYSTEMS AFFECTED

- Systemic involvement depends on the causative agent.
- Cardiovascular—myocardial dysfunction and/or arrhythmias.
- Respiratory—if pulmonary edema develops.

INCIDENCE/PREVALENCE

- Histologically confirmed myocarditis is rarely identified in veterinary patients, therefore epidemiology of myocarditis is incompletely described.
- Viral myocarditis is seemingly rare.
- Chagas disease is uncommon and occurs primarily in the southern United States.
- Fungal myocarditis—primarily seen in association with systemic fungal infection—is rare and occurs regionally, where mycoses are endemic.
- Spirochetal myocarditis and atrioventricular (AV) block resulting from *Borrelia burgdorferi* infection has been reported, but seemingly is rare.
- Infection by *Bartonella* spp. has been associated with canine and feline myocarditis.

GEOGRAPHIC DISTRIBUTION

Myocarditis can result from infectious agents that have distinct geographic distributions.

SIGNALMENT

Species

Dog and cat.

Mean Age and Range

Largely unknown.

SIGNS

General Comments

- Related to the extent and duration of myocardial involvement.
- Signs relating to arrhythmias or heart failure are most common.
- Onset of cardiac dysfunction in association with systemic illness should prompt consideration of myocarditis and, because myocardial disease in veterinary patients is often familial, development of cardiac dysfunction in patients with atypical signalment suggests the possibility of myocarditis.

Historical Findings

- Coughing, exercise intolerance, dyspnea—associated with congestive heart failure (CHF).
- Syncope and weakness—associated with arrhythmias.
- Concurrent manifestations of systemic disease reflective of the etiologic agent.
- Road traffic or other accidents often precede the development of traumatic myocarditis.

Physical Examination Findings

- Gallop sounds or murmurs may be heard.
- Arrhythmias—may be auscultated.
- Fever—potentially observed in patients with infective myocarditis.
- Evidence of injury in those with traumatic myocarditis.

CAUSES

- Virus (e.g., parvovirus, distemper virus, herpesvirus, West Nile virus).
- Protozoa (e.g., *T. cruzi*, *Toxoplasma gondii*, *Neospora caninum*, *Hepatozoon canis*, *Babesia* spp., and *Leishmania* spp.).
- Bacteria (e.g., *Bartonella vinsonii* subsp. *berkhoffii*).
- Fungi (e.g., *Cryptococcus neoformans*, *Coccidioides immitis*, *Blastomycetes dermatitidis*, and *Aspergillus terreus*).
- Algae (e.g., *Prototheca* spp.).
- Blunt trauma can result in the syndrome of traumatic myocarditis.

RISK FACTORS

- Exposure to infectious agents.
- Immunosuppression.
- Debilitating diseases.
- Trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Consider the possibility that preexisting heart disease such as congenital defects, cardiomyopathy, and acquired valvular disease are responsible for clinical findings.
- History of a heart murmur or the presence of arrhythmias before onset of systemic illness helps differentiate from other diseases.
- Extracardiac organ involvement and identification of infectious agents may aid in the diagnosis.
- History of road traffic accident generally makes the diagnosis of traumatic myocarditis obvious.

CBC/BIOCHEMISTRY/URINALYSIS

Abnormalities—vary, depending on organ involvement.

OTHER LABORATORY TESTS

- Serologic tests can be used to detect exposure to infectious agents.
- Cytologic examination of pericardial, pleural, and peritoneal effusions to identify the infectious organism.
- Blood culture to identify bacteremia.
- Troponin—concentrations might be high and reflect myocyte necrosis.

IMAGING

Thoracic Radiography

- Cardiac silhouette may be enlarged if myocarditis has resulted in cardiac dysfunction; potential consequences of cardiac dysfunction include: pulmonary edema and/or pleural effusion.
- Pulmonary granuloma may be found in animals with granulomatous myocardial infection.
- Evidence of trauma potentially including pulmonary contusions or pneumothorax.

MYOCARDITIS

(CONTINUED)

Echocardiography

- Reflects the extent of myocardial damage; may be normal if lesions are small or primarily affect the conduction system.
- Evaluation of systolic myocardial function might reveal minor segmental abnormalities, or global dysfunction associated with chamber enlargement.
- In humans and experimental models, an increase in wall thickness has been associated with inflammatory infiltrates/edema; this observation might be relevant to the syndrome of “transient wall thickening” observed in cats.
- Pericardial effusion in patients with pancarditis.
- In exceptional cases granulomas result in echocardiographically evident masses.

DIAGNOSTIC PROCEDURES

M

ECG

- Arrhythmias of all types—supraventricular tachyarrhythmias, ventricular tachyarrhythmias, and bradyarrhythmias, perhaps particularly AV block—can be observed in association with inflammatory myocardial disease.
- Arrhythmias associated with trauma—ventricular tachyarrhythmias occur in most affected patients; supraventricular arrhythmias and bradyarrhythmias are rare.
- Ventricular rhythms that complicate blunt trauma often have relatively slow rates detected only during pauses in the sinus rhythm; they are most appropriately referred to as accelerated idioventricular rhythms (AIVRs). The QRS complexes are wide and bizarre; the rate is >100 bpm but <160 bpm. Usually, these rhythms are electrically and hemodynamically benign. However, dangerous ventricular tachycardias can complicate blunt trauma and evolve from seemingly benign AIVRs, compromising perfusion and placing the patient at risk for sudden death.

Endomyocardial Biopsy

A minimally invasive technique that is required for definitive ante-mortem diagnosis but rarely performed in veterinary patients.

Pericardiocentesis

- Alleviates tamponade caused by pericardial effusion.
- Submit fluid for cytologic examination and, possibly, bacterial culture.

Holter Monitoring

- To define the burden of arrhythmia in terms of frequency and character over a 24-48 hour period.
- To monitor antiarrhythmic therapy.

PATHOLOGIC FINDINGS

- Dilated cardiac chambers with patchy areas of hyperemia, necrosis, or fibrosis.
- Granulomas seen grossly in some patients.
- Histologic examination of the myocardium or pericardium may reveal inflammatory cells (e.g., lymphocytes, plasma cells, and macrophages), patchy fibrosis, or the infectious agents themselves.



TREATMENT

APPROPRIATE HEALTH CARE

- Hospitalize patients with decompensated heart failure for initial medical management.
- Hospitalize patients with hemodynamically consequential ventricular arrhythmias for initial, parenteral antiarrhythmic therapy.
- Hospitalize patients with severe systemic manifestations for appropriate medical therapy.

ACTIVITY

Restricted

DIET

Sodium restriction if CHF.

CLIENT EDUCATION

- Cardiac manifestations may persist even after resolution of systemic illness.
- Certain arrhythmias (e.g., ventricular tachycardia, third-degree AV block) may predispose to sudden death.
- Antemortem diagnosis may be difficult.
- Some infectious agents may pose a public health risk.

SURGICAL CONSIDERATIONS

Complete AV block may require pacemaker implantation.



MEDICATIONS

DRUG(S) OF CHOICE

- If a specific pathogenetic agent is identified, appropriate, etiologically targeted therapy.
- Tailor antiarrhythmic therapy based on ECG findings.

CONTRAINDICATIONS

N/A.

PRECAUTIONS

- All antiarrhythmic drugs potentially have proarrhythmic properties and their effects should be closely monitored.
- Systemic organ involvement (e.g., renal involvement) may necessitate modifying drug dosages.
- Some agents that result in canine or feline myocarditis can also affect humans, so potentially there are public health considerations.



FOLLOW-UP

PATIENT MONITORING

- Antiarrhythmic therapy—frequent auscultation and ECG.
- Serologic titers when appropriate.
- Auscultation and follow-up radiographs—treatment of heart failure.
- Hemograms and serum biochemical analysis—systemic effects.

PREVENTION/AVOIDANCE

- Avoid breeding animals that have not been immunized.
- Avoid endemic areas if possible.

EXPECTED COURSE AND PROGNOSIS

- Depend on the extent and severity of myocardial involvement.
- Many systemic fungal and protozoal diseases do not respond well to medical management.
- Patients with extensive myocardial inflammation, degeneration, and signs of heart failure have a very poor prognosis.
- Good prognosis if the underlying cause can be treated successfully.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Often accompanies systemic illness.

AGE-RELATED FACTORS

Viral myocarditis—most often seen in animals <1 year old.

ZOONOTIC POTENTIAL

- Varies with infectious agent involved.
- May be high with protozoal and mycotic infections.

PREGNANCY/FERTILITY/BREEDING

Some viral diseases (e.g., canine herpesvirus and parvovirus) have been passed to the fetus during pregnancy.

SEE ALSO

- Aspergillosis, Disseminated Invasive.
- Babesiosis.
- Bartonellosis.
- Blastomycosis.
- Canine Distemper.
- Canine Parvovirus.
- Chagas Disease (American Trypanosomiasis).
- Coccidioidomycosis.
- Cryptococcosis.
- Hepatozoonosis.
- Idioventricular Rhythm.
- Leishmaniosis.
- Neosporosis.
- Protothecosis.
- Toxoplasmosis.
- Ventricular Premature Complexes.
- Ventricular Tachycardia.

ABBREVIATIONS

- AIVR = accelerated idioventricular rhythm.
- AV = atrioventricular.
- CHF = congestive heart failure.
- DCM = dilated cardiomyopathy.
- ECG = electrocardiogram

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Larry P. Tilley.

NASAL DISCHARGE



BASICS

DEFINITION

May be serous, mucoid, mucopurulent, purulent, blood tinged, or frank blood (epistaxis); may contain food debris, from one or both nasal cavity(ies), may be permanent or in variable amount or consistency over time.

PATHOPHYSIOLOGY

- Secretions—produced by mucous cells of the epithelium and submucosal glands; increased production from glandular hypertrophy and hyperplasia owing to irritation of the nasal mucosa by infectious, mechanical, chemical, or inflammatory stimuli.
- Blood from vascular leakage related to infectious, mechanical, chemical, inflammatory, or tumoral stimuli.
- Xeromycteria—“dry nose”; facial nerve damage secondary to middle ear disease may decrease serous secretions from the lateral nasal glands leading to compensatory mucoid secretion; usually unilateral with unilateral nasal planum hyperkeratosis, ± keratoconjunctivitis sicca (KCS).

SYSTEMS AFFECTED

- Respiratory—mucosa of the upper tract, including the nasal cavities, sinuses, and nasopharynx; lower tract disease can also result in secretions from the upper airways.
- Gastrointestinal—signs may be observed with swallowing disorders or esophageal or gastrointestinal diseases when secretions are forced into the nasopharynx.
- Hemic/lymphatic/immune—blood-tinged discharge or epistaxis owing to platelet or hemostatic defects.
- Ophthalmic—may have KCS ipsilaterally if there is nerve damage due to middle ear disease.

SIGNALMENT

- Dogs and cats.
- Young animals—cleft palate; nasal polyp, ciliary dyskinesia; immunoglobulin deficiency.
- Older animals—nasal tumors; primary dental disease (tooth root abscess).
- Hunting dogs—foreign body.
- Dolichocephalic dogs—aspergillosis, nasal neoplasia.

SIGNS

Historical Findings

- Sneezing—often found concurrently.
- Reverse sneezing—can be found concurrently, if nasopharyngeal involvement or passage of nasal secretions through the choanae towards the nasopharynx.
- Important to know both the initial and current character of the discharge as well as whether it originally started unilaterally or bilaterally.
- Stertor—owners frequently report noisy breathing, especially when animal is sleeping.
- Response to previous antibiotic therapy common due to secondary bacterial infection.

antibiotic therapy common due to secondary bacterial infection.

Physical Examination Findings

- Secretions or dried discharge on the hair of the muzzle or forelimbs.
- May note reduction in nasal air flow, particularly with nasal neoplasia.
- Concurrent dental, nasopharyngeal, or lower airway disease.
- Bony involvement—with a tumor or fourth premolar abscess; may be detected as facial or hard palate swelling or as pain secondary to fungal or bacterial osteomyelitis or neoplasia.
- Mucosal depigmentation of the nasal alar cartilage—observed with canine nasal aspergillosis.
- Mandibular lymphadenomegaly—neoplasia, fungal infection, dental disease.
- Polyp—may be visible on otoscopic exam, or pushing the soft palate down on oral exam.
- Chorioretinitis—may be seen with canine distemper or cryptococcosis.
- Eyeball deviation (abscess, sino-orbital aspergillosis in cats, tumors).

CAUSES

- Unilateral—often associated with non-systemic processes; foreign body; dental-related disease; fungal infections; nasal tumor; facial nerve damage leading to xeromycteria, nasopharyngeal stenosis, or atresia.
- Bilateral—infectious agents (e.g., feline viral rhinotracheitis or calicivirus, canine herpesvirus, canine distemper, secondary bacterial infection); IgA deficiency; airborne irritant; allergy; ciliary dyskinesia; lymphoplasmacytic or hyperplastic rhinitis.
- Unilateral progressing to bilateral—*Aspergillus*; nasal tumor.
- Either unilateral or bilateral—epistaxis; foreign body; extranasal disease; nasal parasites, inflammatory rhinitis.
- Extranasal diseases—chronic pneumonia, chronic vomiting, nasopharyngeal diseases.

RISK FACTORS

- Dental disease.
- Foreign bodies.
- Infectious—poorly vaccinated animal; kennel situations, exposure to other animals.
- Nasal aspergillosis.
- Thrombocyte disorder—thrombocytopenia or thrombocytopathy: primary immune or secondary to infectious (i.e., rickettsial) disease or neoplasia.
- Coagulation defect due to rodenticide intoxication.
- Nasal mites—kennel-raised dogs.
- Immunosuppression, chronic corticosteroid use; feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV) infection.
- Chronic, low-grade pneumonia.
- Chronic vomiting.
- Chronic otitis (facial nerve damage).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Important to differentiate nasal discharge, secretions, or crusting from diseases that

occur at mucocutaneous junctions, such as pemphigus, vasculitis, or leishmaniosis.

Differential Diagnosis Causes

- Serous—mild irritation; viral and parasitic (e.g., nasal mites) disorders.
- Mucoid—allergy; nonspecific airborne irritants; early neoplasia.
- Purulent (or mucopurulent)—secondary bacterial or fungal infection, neoplasia.
- Serosanguinous to epistaxis—nasal tumor and aspergillosis; after violent or paroxysmal sneezing episodes; coagulopathy, platelet disorder, angiostrongylosis and systemic hypertension.

CBC/BIOCHEMISTRY/URINALYSIS

Results not specific for any particular cause but can detect concurrent problems; part of a thorough evaluation before general anesthesia for diagnostic procedures.

OTHER LABORATORY TESTS

- Serologic tests—help to diagnose fungal or rickettsial disease.
- Coagulation studies—determine platelet numbers and function, coagulation panel.

IMAGING

Skull Imaging

- Anesthetize and carefully position patient.
- Perform before rhinoscopy and periodontal probing, which may cause nasal bleeding and alter imaging findings.
- Radiography (not performed when CT is available):
 - Lateral view—detect any periosteal reaction; note gross changes in the maxillary teeth, nasal cavity, and frontal sinuses; evaluate air column outlining the nasopharynx for filling defects.
 - Open-mouth ventrodorsal and intraoral views (using sheet film)—excellent for evaluating nasal cavities and turbinates.
 - Rostral-caudal view—evaluate each frontal sinus (periosteal reaction and filling).
- CT and MRI—CT superior to radiography in making diagnosis; CT and MRI help detect the extent of bony changes or CNS involvement associated with nasal tumors, fungal rhinitis, or chronic otitis.

Thoracic Radiography

May reveal areas of alveolar infiltrates in patient with chronic pneumonia, or situs inversus in some dogs with primary ciliary dyskinesia.

DIAGNOSTIC PROCEDURES

- Rhinoscopy—indicated with chronic or recurrent nasal discharge; acute epistaxis; evaluate both anterior and posterior; may be contraindicated with bleeding disorders.
- Nasal cytologic examination—nonspecific inflammation most commonly found.
- Fungal culture—difficult to interpret; false positives and negatives common.
- Bacterial culture may be useful when resistant organisms are suspected, but requires deep nasal sampling under anesthesia.
- Biopsy of

(CONTINUED)

the nasal cavity—indicated with chronic nasal discharge or visualized abnormalities; multiple samples required to ensure adequate representation; may perform electron microscopy for suspected ciliary dyskinesia.

- Bronchoscopy—indicated if there has been a history of coughing with nasal discharge.
- Periodontal probing of all upper teeth—perform after rhinoscopy; the normal gingival sulcus: dogs, ≤4 mm; cats, ≤1 mm.
- Blood pressure, platelets, and coagulation profile for epistaxis.
- Angiostrongylosis rapid detection test or PCR.
- Schirmer tear test, otoscopic exam, or CT—to evaluate for possible facial nerve damage from chronic otitis.
- Tracheal/bronchial scintigraphy and electron transmission microscopy—to confirm primary ciliary dyskinesia.



TREATMENT

• Outpatient—adequate hydration, nutrition, warmth, and hygiene (keeping nares clean)—important with chronic sneezing and nasal discharge. Prioritize local therapy (nasal drops, nasal nebulization).

- Inpatient—any surgical treatment, topical therapy for aspergillosis.



MEDICATIONS

DRUG(S) OF CHOICE

- Secondary bacterial infection—antibiotics; choose a good Gram-positive spectrum of activity (e.g., amoxicillin, clavamox, clindamycin, azithromycin, cephalosporins).
- Attempt to dry up serous nasal secretions—decongestants (dogs: ephedrine at 10–50 mg total PO q8–12h, to a maximum of 4 mg/kg; cats: 2–4 mg/kg q8–12h); topical vasoconstrictors (neosynephrine at 0.25–0.5% q8–24h or oxymetazoline at 0.25% q24h) but for a limited period of time—less than 1 week—since they do not treat any cause and could induce damage to the nasal mucosa.
- Dental-associated rhinitis—antibiotics; dental surgery as indicated.
- Foreign

body—removal, antibiotics.

- Nasal parasites—ivermectin 300 µg/kg PO or SC weekly for 3 weeks or milbemycin 1 mg/kg PO weekly for 3 weeks (in collie and similar breeds) to treat *Pneumonyssoides*; fenbendazole 50 mg/kg PO q24h for 10 days to treat *Eucoleus* (nasal nematode).
- Nonspecific inflammation—prednisolone 1–2 mg/kg PO q12–24h or piroxicam 0.3 mg/kg PO q24–48h.
- Canine nasal aspergillosis—topical treatment with enilconazole or clotrimazole.
- Feline cryptococcosis or sporothricosis—itraconazole 5–10 mg/kg PO q24h or fluconazole 50 mg/cat q12h.
- Feline aspergillosis—topical therapy, itraconazole.
- Canine angiostrongylosis—antiparasitic (e.g., fenbendazole 50 mg/kg PO q24h for 3 weeks).
- Neoplasia—radiotherapy and chemotherapy.
- Xeromycteria—oral administration of ophthalmic pilocarpine in attempt to stimulate nasal secretions.

CONTRAINDICATIONS

- Ephedrine—in cardiac patients.
- Ivermectin—in collies and similar breeds.

PRECAUTIONS

- Itraconazole—anorexia, nausea, vomiting, and high liver enzymes.
- Rebound phenomenon—reported with overuse of topical nasal vasoconstrictors.



FOLLOW-UP

PATIENT MONITORING

- Nasal discharge and sneezing—note changes in frequency, volume, and character.
- Repeat rhinoscopy—indicated to ensure adequate response to treatment of fungal rhinitis.
- Recheck thoracic radiographs or bronchoscopy—monitor response to treatment for chronic pneumonia.

POSSIBLE COMPLICATIONS

- Loss of appetite—especially in cats.
- Extension of primary disease (e.g., fungal infection, tumor) into the mouth, eye, or brain.
- Respiratory distress—with nasal obstruction.
- Involvement of the cribriform plate in dogs with aspergillosis—

NASAL DISCHARGE

CNS damage during topical drug therapy is a risk.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Sinusitis.
- Dental disease.
- Secondary causes—coagulopathy, pneumonia, cricopharyngeal disease, megaesophagus.

AGE-RELATED FACTORS

Middle-aged to old patients—often associated with dental or neoplastic conditions.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

The safety of most recommended drugs has not been established in pregnant animals.

N

SEE ALSO

- Aspergillosis, Nasal.
- Cryptococcosis.
- Epistaxis.
- Nasal and Nasopharyngeal Polyps.
- Nasal tumor chapters.
- Nasopharyngeal Stenosis.
- Primary Ciliary Dyskinesia.
- Rhinitis and Sinusitis.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIV = feline immunodeficiency virus.
- KCS = keratoconjunctivitis sicca.

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Client Education Handout
available online

OBESITY



BASICS

DEFINITION

Obesity is the unhealthy accumulation of body fat. Precise definitions are debated but it is widely accepted that dogs or cats with body condition score (BCS) 6 or 7 on a 9-point scale are overweight, and those with BCS 8 or 9 are obese.

PATHOPHYSIOLOGY

- Animals gain weight when energy intake from food chronically exceeds energy expended to maintain basic homeostatic processes and during exercise.
- Homeostatic neuroendocrine responses ensure food intake meets energy requirements and establish modest energy reserves in case of a period of fasting.
- Energy homeostasis may be disrupted by: ready availability of highly palatable energy-dense food (which elicits hedonic responses that override homeostatic satiation); genetic variation in appetite; neutering; and limits to a pet's ability to exercise.

SYSTEMS AFFECTED

- Endocrine—insulin resistance develops secondary to obesity and can lead to diabetes mellitus in cats.
- Immune—adipose tissue dysfunction in obesity causes a proinflammatory state.
- Other organ systems may be affected by the mechanical effect of increased body fat and/or endocrine and metabolic disruption.

GENETICS

- Breed variation in obesity predisposition suggests obesity susceptibility is in part heritable with a polygenic mode of inheritance.
- Mutations in the genes *POMC* (Labrador and flatcoat retrievers) and *MC4R* (beagles) are associated with obesity and/or food motivation.

INCIDENCE/PREVALENCE

Common. As many as 65% of dogs and 25% cats are overweight or obese.

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Domestic shorthair cats.
- Labrador retriever, Cairn terrier, cavalier King Charles spaniel, Scottish terrier, cocker spaniel.

Mean Age and Range

Obesity prevalence is highest in middle age but can occur throughout life.

Predominant Sex

Neutered pets of either sex are predisposed.

SIGNS

Historical Findings

- Weight gain.
- Change in BCS.
- A full diet and exercise history and understanding of concurrent medical problems is essential to formulating a treatment plan.

Physical Examination Findings

Excess body fat and BCS (see Diagnostic Procedures).

CAUSES

Energy intake chronically exceeding energy output.

RISK FACTORS

- Neutering.
- Middle age.
- Feeding highly palatable, energy-dense foods without adequate restriction.
- Restricted exercise (e.g., following injury, indoor cats, or leash-only exercise).
- High drive for food, driven by genetic variation (e.g. Labrador retriever *POMC* mutation).
- Uncommonly, endocrinopathies can cause obesity (hypothyroidism, insulinoma), or mimic obesity (as with the abdominal enlargement of hyperadrenocorticism).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Abdominal distention from pregnancy, ascites, hyperadrenocorticism, or neoplasia.

CBC/BIOCHEMISTRY/URINALYSIS

Normal or may reflect endocrine disruption (hyperglycemia, dyslipidemia) or concurrent disease.

OTHER LABORATORY TESTS

N/A

IMAGING

Ultrasound, MRI, or dual-energy x-ray absorptiometry can measure body fat more accurately.

DIAGNOSTIC PROCEDURES

- BCS is a semi-quantitative, ordinal measure of body composition. Observation and palpation are used to assign a score based on how findings best match a series of descriptors. The best validated 9-point scale assigns BCS 4–5 as ideal, 6–7 as overweight, and 8–9 as obese.
- Serial measurement of body weight is more sensitive for monitoring.

PATHOLOGIC FINDINGS

N/A



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient.
- Calorie restriction is the mainstay of successful weight loss.
- Changes in owner management behavior are critical to success.
- Energy requirements for maintenance are lower after weight loss so long-term vigilance and food restriction are required to prevent recurrence.

NURSING CARE

N/A

ACTIVITY

- Increasing exercise is ineffective to induce weight loss alone so if owners are reluctant to make management changes, focus should be on food restriction.
- However, exercise is encouraged because it promotes retention of lean mass (muscle) during weight loss.

DIET

- Reducing daily energy intake in food to below maintenance requirements is essential.
- Target weight is estimated from current weight and BCS—every 1 unit increase over BCS 5/9 equates to 10% excess body mass; e.g., to calculate the target weight of a dog in BCS 7, divide current weight by 1.2.
- The amount of food required to promote weight loss can be estimated from calculated maintenance energy requirements (MER) or by reducing current food intake by 10–20%.
- To calculate MER, use estimated target weight (MER (kJ) = $440 \times \text{body weight} [\text{BW}]_{\text{kg}}^{0.75}$) and feed 50–65% of MER as a starting point.
- Feeding recommendations should be altered from baseline to maintain weight loss at 0.5–1% per week until target weight is reached.
- For weight loss of <20% (i.e., starting BCS ≤ 6), food restriction is moderate and a conventional diet is adequate, although specialized diets may be advantageous. Where energy restriction is greater (starting BCS ≥ 7), the density of essential nutrients in maintenance diets may be inadequate so a specialized diet is recommended.
- Specialized diets improve the success of weight loss programs and improve satiety, which itself may improve compliance because owners are subjected to less begging behavior.
- Specialized diets are commonly formulated to provide: high essential nutrient density; low energy density (added water in canned food or air in kibble); high protein (improves satiety and promotes lean mass retention); and high fiber (promotes satiety). Canned (compared to dry) food may improve weight loss in cats.
- Accurate feeding using weighed portions is important. Treats are ideally excluded but if owners feel they are essential, factor them into the diet plan.

CLIENT EDUCATION

- Owners of obese pets often do not follow advice to reduce their pet's weight because they do not recognize obesity, do not see it as a problem, or struggle to follow the advice. By definition, they have already failed to make the small adjustments needed to keep their dog slim; it follows that they are likely to find making the major changes required to reduce their dog's weight difficult.
- Although it might sound simple to "feed less and exercise more," the reality is that owners are being asked to change established habits, spend more time caring for their pets, and perhaps work to motivate other family members.
- Promoting those behavior changes requires us to motivate owners, to understand their barriers to change, and to offer practical and simple advice on

(CONTINUED)

OBESITY

how to overcome those barriers. Information does not automatically lead to motivation; it is more likely if the actions required are consistent with their existing values and beliefs.

- Owners may not recognize obesity. Being overweight is regarded as the norm for some breeds. Regular recording of body weight and BCS can objectively identify a problem early (“I see she’s gained a pound—it would be good to cut the food down before that becomes a problem”).
- Owners may not appreciate that obesity causes health problems. Positive motivation (“slimming him down could really improve his mobility”) is more effective than negative (“if he doesn’t lose weight he’ll never walk properly again”).
- Lack of motivation may be difficult to modify (“his breeder says his weight is fine”) or challenge (“everyone in our family carries a little extra weight—it’s cuddly”).
- Owners often find food restriction difficult. Reducing intake in highly food-motivated animals may require constant vigilance to reduce scavenging, stealing, or hunting. Ignoring begging requires a strong will because of the importance of food-giving in maintaining the human-animal bond.
- Owners may not feel confident in how or what to feed. Practical problems may limit the exercise they offer their pet.
- Practical advice to overcome those barriers should ideally be tailored to each owner. If owners complain their pets are always hungry, a satiety-promoting diet or trickle feeding using toys or frequent small meals may help. If owners insist on treat feeding, suggest low-calorie treats or factor planned treats into the daily ration. If owner mobility restricts dog walks, suggest ball play or longer time in the yard to increase activity.
- Human behavior change is also improved by goal-setting, action planning, and monitoring. For instance, the aim for a weight loss consultation could be that owners leave with written plans formulated in the session: “my goal is to slim her down to 18 kg”; “I have chosen to make these 3 management changes from the list of suggestions...”; and “I will bring her back once a month to be weighed.”
- Fostering a nonjudgmental and supportive veterinary practice culture regarding pet obesity should encourage owners to seek support and act early.

SURGICAL CONSIDERATIONS

N/A

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

No approved medications for use in United States or Europe.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

N/A

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

- Monitoring progress is important. After initiating a diet change, check progress after 2 weeks and alter food ration to aim for 0.5–1% body weight loss per week. Regular monthly visits promote owner compliance and allow ration changes to maintain progress.
- Once target weight is achieved, ongoing monitoring is essential to minimize rebound weight gain. Weighing at veterinary visits is ideally supplemented by owners becoming more adept at noticing weight gain and acting to reverse it.

PREVENTION/AVOIDANCE

- Prevention should be a central aim of routine vet visits. Veterinary teams should work to empower owners to recognize a healthy weight and to intervene effectively when obesity occurs.
- Weight and BCS should be recorded at every practice visit.
- Incorporating weight management advice into waiting room displays will establish the importance of maintaining a healthy weight to the client population.

POSSIBLE COMPLICATIONS

See Associated Conditions.

EXPECTED COURSE AND PROGNOSIS

- Food restriction leads to weight loss in research settings but in client-owned dogs has lower success rates. Compliance is frequently poor and total weight loss often falls short of the target. Rebound weight gain is common.
- Encouragingly, however, even modest weight loss (of approximately 10%) can produce clinically significant improvement.

**MISCELLANEOUS****ASSOCIATED CONDITIONS*****Endocrine and Metabolic***

- Dyslipidemia.* • Insulin resistance (dogs and cats), diabetes mellitus (cats).* • Hepatic lipidosis (cats).* • Hypothyroidism.**
- Insulinoma.**

Orthopedic

- Osteoarthritis. • Humeral condylar fractures. • Cranial cruciate ligament rupture.
- Intervertebral disc disease.

Cardiorespiratory Disease

- Tracheal collapse.* • Brachycephalic obstructive airway syndrome.* • Laryngeal paralysis.* • Increased blood pressure.*

Urogenital System

- Urethral sphincter mechanism incompetence.*
- Feline lower urinary tract disease.* • Dystocia.*

Neoplasia

- General incidence and specifically mammary neoplasia and transitional cell carcinoma.*

Other

- Heat intolerance/heat stroke.*
- Increased anesthetic risk.*
- Decreased lifespan.*

*Conditions where obesity is proven or implicated in causing or exacerbating disease.

**Conditions implicated in causing obesity. Where unspecified, obesity association is likely to be both cause and effect or is unknown.

AGE-RELATED FACTORS

Obesity is most common in middle-aged dogs and middle-aged to old cats.

ZOONOTIC POTENTIAL

N/A

**PREGNANCY/FERTILITY/BREEDING**

Obesity is associated with reduced fertility and dystocia. Food restriction is contraindicated during pregnancy.

SYNOMYMS

Overweight

SEE ALSO

Diabetes Mellitus.

ABBREVIATIONS

- BCS = body condition score.
- MER = maintenance energy requirement.

INTERNET RESOURCES

- <https://www.wsava.org/nutrition-toolkit>
- <https://petnutritionalliance.org/>

Suggested Reading

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Client Education Handout available online

OLIGURIA AND ANURIA



BASICS

DEFINITION

- Oliguria—production of an abnormally small amount of urine. Several proposed definitions; in hydrated patients with good perfusion, urine output (UOP) $<1.0 \text{ mL/kg/h}$ = absolute oliguria. Acute kidney injury (AKI) is typically polyuric, where UOP $>2 \text{ mL/kg/h}$ is expected.
- Anuria—limited/no urine formation (UOP $<0.08 \text{ mL/kg/h}$).

PATHOPHYSIOLOGY

- Physiologic (prerenal) oliguria—kidneys limit water loss during state of reduced renal perfusion to preserve fluid and electrolyte balance. High plasma osmolality or low circulating fluid volume stimulate antidiuretic hormone (ADH) synthesis and release, which induces formation of small quantity of concentrated urine.
- Pathologic (renal) oliguria—severe renal parenchymal impairment. Factors include: high resistance in afferent glomerular vessels, low glomerular permeability, back leak of filtrate from damaged renal tubules, renal intratubular obstruction, and extensive loss of nephrons resulting in marked reduction of glomerular filtrate produced.
- Anuria—may be renal or postrenal origin. Severe renal disease occasionally causes anuria. Mechanisms are the same as for pathologic oliguria (e.g., urinary tract obstruction (UTO) or excretory pathway rupture).

SYSTEMS AFFECTED

- Renal—inability to adequately eliminate wastes and water; hyperkalemia.
- Urologic—obstruction-induced distension of the collecting system. Increased risk of urinary tract infection (UTI) due to failure to empty bladder.

SIGNALMENT

- Dog and cat.
- Young adult cats—higher incidence of anuria associated with UTO.

SIGNS

- Reduction in quantity of urine voided.
- Enlarged urinary bladder, stranguria, pollakiuria with urethral obstruction.
- Systemic signs of uremia if oliguria/anuria persists.

CAUSES

- Physiologic oliguria—renal hypoperfusion or serum hyperosmolality.
- Pathologic oliguria—AKI or advanced chronic kidney disease (CKD).
- Anuria—complete UTO, urinary tract rupture, or severe primary kidney disease.

RISK FACTORS

- Physiologic oliguria—dehydration, decreased cardiac output, hypotension.
- Pathologic oliguria and anuria—primary kidney disease, nephrotoxin exposure, dehydration, low cardiac output, hypotension, electrolyte imbalance, acidosis, fever, sepsis, liver disease, multiple organ failure, trauma, hypoalbuminemia, hyperviscosity syndrome.
- Anuria—caused by urolithiasis, urinary tract neoplasia, idiopathic feline lower urinary tract disease, functional micturition disorder, trauma, gross hematuria.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Physiologic oliguria—poor tissue perfusion, history of recent fluid loss, signs of uremia are typically absent. Oliguria resolves rapidly when renal hypoperfusion is corrected.
- Pathologic oliguria—caused by CKD have a history of progressive kidney disease (polyuria, polydipsia, poor appetite, weight loss). Patients with CKD are at risk for AKI. Signs of uremia are commonly observed; fluid therapy and other measures to restore adequate renal perfusion often fail to increase urine flow.
- Suspect anuria due to UTO or rupture of the excretory pathway with repeated stranguria and inability to produce urine. Patients may have a history of pollakiuria, dysuria, hematuria, urolithiasis, trauma, instrumentation of the urinary tract. Physical exam may reveal enlarged urinary bladder, painful posterior abdomen, masses or uroliths in the urethra or bladder. Patients with rupture of the urinary tract may have ascites, fluid infiltration in tissues, painful caudal abdomen, masses or uroliths in the bladder or urethra, or evidence of trauma. UTO caused by functional urinary obstruction: suspect in patients with urinary bladder enlargement, increased resistance to manual bladder expression, and neurologic signs affecting the hind limbs and/or tail. Signs of uremia may develop. Restoring urinary flow/correcting rents in the excretory pathway rapidly restores adequate urine flow.

CBC/BIOCHEMISTRY/URINALYSIS

- Serum urea nitrogen, creatinine concentration—elevated unless onset of oliguria or anuria is very recent.
- Hyperkalemia—common with pathologic oliguria and anuria, less common/less severe in animals with physiologic oliguria (except with hypoadrenocorticism).
- Physiologic oliguria—characterized by high urine specific gravity (USG) (dogs >1.030 , cats >1.035). Oliguria associated with lower USG suggests renal parenchymal disease or UTO. Patients with urine concentrating defects due to other diseases or drugs are the exception to this rule.
- Renal parenchymal anuria is typically characterized by USG <1.030 (dogs) or <1.035 (cats). USG varies in patients with post-renal anuria. Adequate urine-concentrating ability often lost after UTO.

IMAGING

- Abdominal radiographs and ultrasound are useful to rule out UTO/excretory pathway rupture.
- Excretory urography, retrograde urethro-cystography, pyelography, or vaginourethro-cystography may provide definitive proof of UTO/excretory pathway rupture.
- Distension of the excretory pathway or detection of uroliths in the ureters, bladder neck, urethra suggest UTO.
- Detection of fluid within the peritoneum supports a diagnosis of excretory pathway rupture. Contrast media leakage confirms a rupture.

DIAGNOSTIC PROCEDURES

- Electrocardiography—to identify significant arrhythmia (see Hyperkalemia).
- Urethroscopy—may provide evidence for UTO/urinary tract rupture.
- Urinary catheterization—may provide information about the integrity of the lower urinary tract. Not recommended as a diagnostic procedure because it may be misleading and may cause additional trauma; iatrogenic UTI.



TREATMENT

- Oliguria and anuria are emergencies. Untreated, may lead to death within hours to days from uremia, hyperkalemia, acidosis, sepsis.
- Persistent hypovolemia may lead to ischemic renal injury.
- Correct renal hypoperfusion rapidly by intravenous administration of balanced isotonic crystalloid.
- Therapy for primary renal oliguria/anuria is limited to symptomatic, supportive care while awaiting spontaneous renal function recovery. Elimination of causative factors may slow or stop further renal injury (e.g., terminating aminoglycoside therapy, correcting hypercalcemia, or restoring adequate renal perfusion); however, once pathologic oliguria/anuria has developed, few kidney diseases will be amenable to specific treatment (exception = leptospirosis).
- Correct postrenal causes for anuria by nonsurgical/surgical methods including retrograde hydropropulsion of uroliths/urethral plugs; placement of transurethral catheters to restore low-pressure urinary flow; removal of uroliths, polyps, neoplastic tissue; or surgical repair of rents, strictures, malposition of kidneys, ureters, bladder, urethra.

OLIGURIA AND ANURIA

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

- Diuretics—indicated after establishing euvoolemia in patients with renal oliguria. Diuretic-induced UOP facilitates fluid and electrolyte therapy and may imply less severe kidney injury.
- Administration of diuretics before restoring adequate renal perfusion is counterproductive and may promote renal injury.
- Avoid diuretic-induced dehydration.
- Furosemide 2–4 mg/kg IV—often used first in patients with renal oliguria. Urinary flow should increase within 1 hour; if not, repeat at the same or double dosage. If diuresis ensues, administer to sustain diuresis (0.25–1 mg/kg/h or 2–4 mg/kg IV q8h). Reduction in glomerular filtration rate (GFR) may be seen with therapy.
- Mannitol 0.25–1 g/kg IV can be given as a 10% or 20% solution over 15–20 minutes. Urinary flow should increase within 1 hour. Do not repeat if diuresis does not ensue; may cause excessive volume expansion. If diuresis ensues, mannitol may be continued as continuous infusion (1–2 mg/kg/h) or intermittent IV doses (0.25–0.5 g/kg every 4–6 hours) to sustain diuresis. Avoid mannitol when overhydration, pulmonary edema, or congestive heart failure present.
- Fenoldopam 0.1–0.8 µg/kg/min, a selective dopamine A1 receptor antagonist, promotes diuresis in healthy animals and increases GFR in dogs. Evidence of efficacy in animals with renal disease is lacking.

CONTRAINDICATIONS

Nephrotoxic drugs.

PRECAUTIONS

- Administer fluids carefully to patients that are persistently oligoanuric to avoid overhydration. Do not continue to administer fluids to oligoanuric patients after their fluid volume deficit has been restored in the absence of a plan to prevent development of

overhydration. In patients with unresponsive renal oliguria, peritoneal dialysis/hemodialysis may be required to correct iatrogenic fluid-induced volume overexpansion.

- Failure to correct fluid deficits before initiating diuretic administration may cause further renal hypoperfusion and ischemic renal injury.
- Use drugs requiring renal excretion with caution.
- Avoid electrolyte solutions containing >4 mEq of potassium/L. Some hypokalemic patients may require cautious administration of higher doses of potassium.
- Dopamine can cause arrhythmias, particularly in animals with hyperkalemia. Its use is no longer recommended.

POSSIBLE INTERACTIONS

Furosemide may promote the nephrotoxicity associated with aminoglycoside antibiotics.



FOLLOW-UP

PATIENT MONITORING

- UOP—determine early during the course of management. When unclear, consider transurethral catheterization to accurately determine UOP. Place catheters using aseptic technique. Short indwelling time lowers the risk of UTI. Properly placed/managed indwelling catheters are usually safe for at least 48 hours. Use a closed, sterile drainage system.
- Creatinine, serum urea nitrogen, and potassium concentrations should be reevaluated q12–24 hours; patients with severe hyperkalemia need more frequent monitoring.
- ECG should be performed at appropriate intervals to assess cardiac effects of drugs and hyperkalemia and to monitor response to therapy.

PREVENTION/AVOIDANCE

- Avoid nephrotoxic drugs.
- Avoid dehydration and hypoperfusion.

POSSIBLE COMPLICATIONS

- Hyperkalemia and arrhythmia.
- Uremia.
- Dehydration.
- Overhydration.

EXPECTED COURSE AND PROGNOSIS

- Oliguria and anuria are poor prognostic signs in AKI or CKD; unless urine outflow can be corrected, survival is not expected.
- Anuria associated with UTO is often reversible if urethral patency is restored.



MISCELLANEOUS

SEE ALSO

- Acute Kidney Injury.
- Azotemia and Uremia.
- Chronic Kidney Disease.
- Hyperkalemia.
- Nephrotoxicity, Drug-Induced.
- Urinary Tract Obstruction.

ABBREVIATIONS

- ADH = antidiuretic hormone.
- AKI = acute kidney injury.
- CKD = chronic kidney disease.
- GFR = glomerular filtration rate.
- UOP = urine output.
- USG = urine specific gravity.
- UTI = urinary tract infection.
- UTO = urinary tract obstruction.

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OTITIS EXTERNA AND MEDIA



BASICS

DEFINITION

- Otitis externa—*inflammation of the external ear canal; includes anatomic structures of the pinna, horizontal and vertical canals, and the external layer of the tympanic membrane.*
- Otitis media—*inflammation of the middle ear; includes anatomic structures of the tympanic membrane, bulla (tympanic cavity), auditory ossicles, and auditory tube.*

PATHOPHYSIOLOGY

- Otitis externa—*chronic inflammation results in alterations in the environment of the canal; with inflammation, cerumen glands enlarge and produce excessive wax; the epidermis and dermis thicken and become fibrotic; thickened canal folds reduce canal width; calcification/ossification of auricular cartilage is the end-stage result.*
- Otitis media—*often an extension of otitis externa through the tympanic membrane (dogs); a result of infection ascending through the auditory tube to the middle ear (cats). Chronic viral upper respiratory infection early in life may change the ability of the auditory tube to protect the bulla from infection. Otitis media can occur from polyps or neoplasia within the middle ear or auditory tube.*

SYSTEMS AFFECTED

- Skin/exocrine.
- Nervous.

GEOGRAPHIC DISTRIBUTION

Environmental humidity may predispose to infection.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

- Pendulous-eared dogs—especially spaniel and retriever.
- Dogs with hirsute external canals—terrier and poodle.
- Stenosis of the external ear canal—pug and bulldog; stenosis of the external orifice of ear canal—shar pei.
- Primary secretory otitis media—cavalier King Charles spaniel.

SIGNS

Historical Findings

- Pain—shying from touching of the head, refusing to open the mouth, dropping food.
- Head shaking.
- Scratching at the pinnae.
- Malodor from canals.
- Peripheral vestibular deficits or facial paralysis or paresis.

Physical Examination Findings

Otitis Externa

- Inflammation, pain, pruritus, and erythema of the pinnae and external canals.
- Stenosis of external orifices and/or ear canals.
- Deafness from obstruction.
- Purulent and malodorous exudates.
- Aural hematoma.
- Palpable scarring and calcification of the auricular cartilage.
- Holding of the pinna down and/or head tilt toward the affected side (if unilateral).

Otitis Media

- Vestibular signs—ipsilateral facial nerve paralysis and/or Horner's syndrome; uncommon in the cat, more common in the dog.
- Intact tympanic membrane—bulging pars flaccida.
- Evidence of fluid and/or gas behind the pars tensa; membrane may be opaque; fluid may be purulent or hemorrhagic.
- Ruptured tympanic membrane—discharge into canal or bullae filled with debris.
- Deafness (otitis media progressing to otitis interna).
- Pain on palpation or opening of the mouth.
- Xeromycteria (uni- or bilateral nasal planum hyperkeratosis—lack of nasal secretion due to parasympathetic nerve dysfunction).

CAUSES

- Predisposing factors—present prior to the development of ear disease:
 - Conformation (see Breeds).
 - Excessive moisture (high humidity, swimming).
 - Obstructive ear disease (neoplasia, polyp).
 - Primary otitis media.
- Perpetuating factors—changes in anatomy or physiology in response to otitis externa:
 - Altered wax migration, excessive production of debris.
 - Proliferative changes, stenosis.
 - Calcification.
- Primary causes—directly initiate or cause inflammation within the ear canal:
 - Parasites—*Otodectes cynotis*, *Demodex* spp., *Otobius megnini*, chiggers.
 - Hypersensitivities—atopy, food, contact; recurrent otitis externa may be the only clinical sign of hypersensitivity.
 - Foreign bodies—plant awns.
 - Keratinization disorders and increased cerumen production.
 - Endocrinopathy—immune-mediated; drug reaction (topical or systemic).
- Secondary causes—create disease in an abnormal ear:
 - Bacterial or yeast infection.
 - Excessive moisture and maceration (overcleaning, trauma).
 - Topical irritants.



DIAGNOSIS

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

- Strict diet trial to diagnosis cutaneous adverse reaction to food.

IMAGING

- Bullae radiographs—may be normal; bullae may appear cloudy if filled with exudate; thickening of bulla and petrous temporal bone with chronic disease; presence of bone lysis with osteomyelitis or neoplastic disease.
- CT or MRI—detailed evidence of fluid or tissue density in the bulla, adjacent tissues, or auditory tube.

DIAGNOSTIC PROCEDURES

- Otoscopy or video-otoscopy—visualization of the external canal, tympanic membrane, and portions of the bulla (if tympanum ruptured).
- Cytologic examination of exudate—most important diagnostic tool after complete examination of the ear canal; otic discharge sample should be taken before cleaning or treatment are initiated; examine exudates from each ear canal:
 - Morphologically describe and quantitate bacteria, yeast, inflammatory cells (0 to 4+ scale) for treatment monitoring.
 - Type(s) of bacteria or yeast—assist in the choice of therapy .
- Infections within the canal can change with prolonged or recurrent therapy; repeat cytology is required in chronic cases.
- Myringotomy—spinal needle or sterile catheter is inserted through the tympanic membrane to sample fluid within the bulla for cytologic examination and culture.
- Culture of otic exudate—recommended in cases of otitis media and/or persistent infection.
- Parasites—*Otodectes*, *Otobius*, and chiggers are visualized on otoscopy; *Demodex* can be diagnosed on ear cytology.



TREATMENT

CLIENT EDUCATION

Demonstrate proper method for cleaning and medicating ears (e.g., volume of medication to instill).

SURGICAL CONSIDERATIONS

- Lateral ear resection—disease affects primarily the vertical canal.
- Total ear ablation—entire canal is severely stenotic and oral glucocorticoids have failed to decrease stenosis or proliferative changes; tympanic bulla is diseased; or neoplasia affects the canal.

OTITIS EXTERNA AND MEDIA

(CONTINUED)



MEDICATIONS

DRUG(S) OF CHOICE

Cleansing Solutions

- Tympanum integrity should be assessed prior to introduction of solutions and/or medications into the external ear canal.
- At home cleaning:
 - Cleanser/dryer 2–3 times a week for mild to moderate amounts of wax. Combination cleanser/drying products—contain ceruminolytics (e.g., docusate sodium or dioctyl sodium sulfocuccinate, propylene glycol), drying agents (e.g., dimethicone), germicidals (e.g., acetic acid, boric acid)—contraindicated in cases of perforated tympanic membrane.
 - Acetic acid 5% (white vinegar) diluted 1:2 in water—good activity against bacteria including *Pseudomonas*, and yeast. Safe in middle/inner ear.
 - Tris-EDTA—antibacterial activity; enhances susceptibility of bacteria to various antibiotics. Low ototoxic potential; safe in middle ear.
 - Chlorhexidine—antiseptic, concentrations of less than 0.2% are safe within the middle ear.
 - N-Acetylcysteine—antimicrobial and mucolytic properties, and ability to disrupt bacterial biofilm.
- “In clinic” cleaning on awake animals:
 - Bulb syringe or trimmed French red rubber catheter used to flush in solution and remove debris.
 - Deep ear cleaning with general anesthesia when needed.

Systemic Antibiotics (Indications)

- Severe otitis and neutrophils are seen on cytology suggesting a deeper infection.
- Otitis media.
- Best chosen by culture and sensitivity test—empiric choices include cephalexin 30 mg/kg q12h, amoxicillin+clavulanic acid 13.75 mg/kg q12h, clindamycin 11 mg/kg q12h when cocci are seen cytologically; marbofloxacin 2.75 mg/kg q24h if rods are seen cytologically.

Systemic Antifungals (Indications)

- Refractory *Malassezia* infection or when owners are unable to apply topical treatment.

- Otitis media caused by *Malassezia* or other fungal organism.
- Dogs—ketoconazole 5–10 mg/kg q24h, terbinafine 20–30 mg/kg q24h.
- Cats—itraconazole 5 mg/kg q24h.

Systemic Glucocorticoids (Indications)

- Reduce inflammation and cerumen production associated with otitis externa.
- Reduce proliferative changes secondary to inflammation in ear canals.
- Starting dosages—prednisolone 1 mg/kg/day, dexamethasone 0.1 mg/kg/day, triamcinolone 0.1 mg/kg/day; higher dosages can be used for more severe inflammatory changes.
- Antiparasitic therapy against mites— avermectins, isoxazolines.
- *Otobius* (ear tick) should be removed from inside the ear canal.

Topical

- Continue cleanings until symptoms resolve and then routinely to maintain control.
- Apply appropriate topical medications in sufficient quantity to completely treat the entire canal: Amount used is determined by the size of ear—instilled once or twice daily.
- Antibiotic—based on cytologic evaluation and/or empiric choice. Gentamicin, neomycin—cocci infection; enrofloxacin and silver sulfadiazine—rods; amikacin—resistant *Pseudomonas*.
- Antifungal (anti-*Malassezia*)—clotrimazole, ketoconazole, miconazole, thiabendazole, nystatin, terbinafine; posaconazole—refractory *Malassezia* cases.
- Anti-inflammatory (glucocorticoid)—dexamethasone, flucinolone, betamethasone, triamcinolone, hydrocortisone aceponate, and mometasone.
- Antiparasitic—ivermectin and thiabendazole.

CONTRAINDICATIONS

- Ruptured tympanum—use caution with topical cleaners other than sterile saline or dilute acetic acid; potential for ototoxicity; controversial.
- Ivermectin—non-FDA approved for use systemically; herding (dog) breeds have increased sensitivity (*MDRI/ABCB1* gene mutation).

PRECAUTIONS

- Use caution when cleaning the external ear canals of all animals with severe and chronic otitis externa; the tympanum can easily rupture.
- Post-flushing vestibular complications are more common in cats, although usually

temporary; warn clients of possible complications and residual effects.

POSSIBLE INTERACTIONS

Topical medications infrequently induce contact irritation or allergic response; reevaluate all worsening cases.



FOLLOW-UP

PATIENT MONITORING

Cytology of ear canals should be repeated at each clinic visit.

PREVENTION/AVOIDANCE

- Routine ear cleaning at home.
- Control of underlying diseases.

POSSIBLE COMPLICATIONS

Deafness, vestibular disease, cellulitis, facial nerve paralysis, progression to otitis interna, and rarely meningoencephalitis.

EXPECTED COURSE AND PROGNOSIS

- Otitis externa—with proper therapy, most mild initial cases resolve in 3–4 weeks; failure to correct underlying primary cause results in recurrence.
- Otitis media—requires at least 6 weeks of systemic antibiotics until all signs resolve.
- Osteomyelitis of petrous temporal bone and bulla—may require 6–8 weeks of antibiotics.
- Vestibular signs may improve within 2–6 weeks; some animals may have residual symptoms.



MISCELLANEOUS

Suggested Reading

Harvey RG, Haar G. Ear, Nose and Throat Diseases of the Dog and Cat. Boca Raton, FL: CRC Press, 2017, pp. 1–223.

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Consulting Editor Alexander H. Werner Resnick

Acknowledgment The author acknowledges the prior contribution of Alexander H. Werner Resnick.



Client Education Handout
available online

OTITIS MEDIA AND INTERNA



BASICS

DEFINITION

Inflammation of the middle (otitis media) and inner (otitis interna) ears, commonly caused by bacterial infection.

PATHOPHYSIOLOGY

- Media—from extension of infection of the external ear through the tympanic membrane; may extend from the oral and nasopharyngeal cavities via the eustachian tube.
- Interna—may also result from hematogenous spread of a systemic infection.

SYSTEMS AFFECTED

Nervous

- Impaired balance due to damage to the vestibular apparatus in the inner ear or to the vestibular portion of vestibulocochlear nerve.
- Nausea from dizziness due to impaired balance.
- Hearing loss due to damage to hair cells in the cochlea or to the cochlear portion of vestibulocochlear nerve.
- CNS signs when spread of infection intracranially (otogenic intracranial infection).

Ophthalmic

- Keratoconjunctivitis sicca (KCS; dry eye)—from damage to parasympathetic branch of the facial nerve supplying the lacrimal gland.
- Corneal ulcer—as a consequence of inability to blink due to damage to facial nerve or from KCS.
- Horner's syndrome—from damage to sympathetic nerve as they course through the middle ear.

SIGNALMENT

Breed Predilections

- Dogs more often affected than cats.
- Cocker spaniels and other long-ear breeds.
- Poodles with chronic otitis or pharyngitis from dental disease.
- Primary secretory otitis media in cavalier King Charles spaniels.

SIGNS

Historical Findings

- Pain when opening the mouth; reluctance to chew; shaking the head; pawing at the affected ear.
- Vestibular deficits, which may be persistent, transient, or episodic.
- Unilateral involvement causes head tilt, leaning, veering, or rolling.
- Bilateral involvement causes wide head excursions, truncal ataxia; ± deafness.
- Vomiting and nausea may occur during the acute phase.
- Saliva and food dropping from corner of the mouth; inability to blink; ocular discharge.
- Anisocoria (smaller pupil on affected side), protrusion of the third eyelid, enophthalmos and ptosis (Horner's syndrome) may be noted.

Physical Examination Findings

- The presence of aural erythema, discharge, and thickened and stenotic external canals support otitis externa.
- Pain upon opening of the mouth or on bulla palpation.
- Gray, dull, opaque, and bulging tympanic membrane on otoscopic examination indicates middle ear exudate.
- Dental tartar, gingivitis, tonsillitis, or pharyngitis may be present and have a role in the pathogenesis.
- With severe infections, the ipsilateral mandibular lymph nodes may be enlarged.
- Corneal ulcer from inability to blink or KCS.

Neurologic Examination Findings

- Unilateral damage to vestibular portion of cranial nerve VIII—ipsilateral head tilt, leaning, veering, falling, or rolling.
- Nystagmus—resting or positional; rotary or horizontal; fast phase characteristically opposite the affected side, and does not change in direction with a change in head position.
- Vestibular strabismus—ipsilateral ventral deviation of eyeball with neck extension.
- Bilateral damage of vestibular portion of cranial nerve VIII—patient reluctant to move, may stay in a crouched posture, wide head excursions; physiologic nystagmus poor to absent.
- Facial nerve damage—ipsilateral paresis/paralysis of the ear, eyelids, lips, and nares; reduced tear production (indicated by Schirmer tear test).
- Chronic facial paralysis—contracture of the affected face caused by fibrosis of denervated muscles.
- Sympathetic nerve damage—ipsilateral Horner's syndrome; always miosis; may also note protrusion of third eyelid, ptosis, and enophthalmos.

CAUSES

- Bacteria—*Staphylococcus* spp., *Streptococcus* spp., *Proteus* spp., *Pseudomonas* spp., *Pasteurella* spp., and *E. coli* and obligate anaerobes.
- Fungi—yeast (*Malassezia* spp., *Candida* spp.) and *Aspergillus*.
- Ear mites predispose to secondary bacterial infections.
- Foreign bodies (e.g., grass awns, foxtail awns, or spear grass in endemic areas), trauma, polyps, tumors (e.g., fibromas, squamous cell carcinoma, ceruminous gland carcinoma, primary bone tumors).
- Iatrogenic damage during cleaning or flushing or in investigation of otitis externa.

RISK FACTORS

- Recurrent otitis externa.
- Nasopharyngeal polyps and inner, middle, or outer ear neoplasia may predispose to bacterial infection.
- Ear-cleaning solutions (e.g., chlorhexidine) may be irritating to middle/inner ear or be ototoxic. These should be avoided if tympanum is ruptured.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Congenital vestibular anomalies—signs present from birth.
- Hypothyroidism may be associated with cranial nerve VII and VIII deficits. Abnormal thyroid profile supports diagnosis.
- Neoplasia and nasopharyngeal polyps are common causes of refractory and relapsing otitis media and interna. Diagnosed by oral and otic exam and imaging of the head.
- Idiopathic vestibular disease (old dogs and young to middle-aged cats), idiopathic facial paralysis, and idiopathic Horner's syndrome are diagnoses made by exclusion.
- Cryptococcus* is reported to be associated with peripheral vestibular disease in cats.
- Traumatic causes may have physical external evidence of injury, and history supporting occurrence of a traumatic event.
- Thiamine deficiency occurs in cats with a history of an all-fish diet or persistent anorexia; causes bilateral central vestibular signs.
- Metronidazole used for an extended duration and/or at a high dose damages the vestibular portion of the cerebellum. Signs of bilateral cerebellar disease and history of metronidazole use.
- Central vestibular disease may cause lethargy, somnolence, vertical nystagmus, and other brainstem signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis with left-shift may be noted.
- Globulins may be high if chronic infection.

OTHER LABORATORY TESTS

- Blood, urine cultures may show growth if hematogenous source of infection.
- Low thyroxine (T_4), free T_4 with normal or high thyroid-stimulating hormone (TSH) level with hypothyroidism.

IMAGING

- Video-otoscopy—enables detailed examination of external ear canal and tympanic membrane. With middle ear exudate, the membrane may appear cloudy. Helpful in evaluating the integrity of the tympanic membrane, obtaining samples for cytology and culture/sensitivity, and performing therapeutic lavages of the ear canal and middle ear cavity.
- Bullae radiographs—not sensitive. May show thickening of the bullae and petrous temporal bone with chronic disease, bony lysis with severe cases of osteomyelitis, evidence of neoplasia, or may be normal.
- CT or MRI—necessary to demonstrate fluid and soft tissue density within the middle ear and extent of involvement of adjacent structures. CT is better at revealing associated bony changes, MRI for evaluating soft tissue structures including brainstem and cerebellum.

OTITIS MEDIA AND INTERNA

(CONTINUED)

DIAGNOSTIC PROCEDURES

- Myringotomy—insert a spinal needle (20-gauge; 2.5- to 3.5-inches) through the otoscope and tympanic membrane to aspirate middle ear fluid for cytologic examination and culture and sensitivity. Examine for bacterial and fungal causes of infection.
- Brainstem auditory evoked response (BAER)—tests the peripheral and central auditory pathways, detects hearing loss.
- CSF analysis—if evidence of intracranial extension, perform culture and sensitivity.

PATHOLOGIC FINDINGS

Purulent exudate within the middle ear cavity surrounded by a thickened bullae and microscopic evidence of degenerate neutrophils with intracellular bacteria or other microorganisms; other causes such as polyps or neoplasia.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient care is recommended with severe debilitating infection or if significantly compromising neurologic signs are present.
- Outpatient care is appropriate if the patient is stable, pending further diagnostics, if indicated.

DIET

- If vomiting, withhold food and water for 12–24 hours.
- If unable to stand or severely disoriented, hand-feed and water small amounts frequently. Ensure that the patient is sternal during feeding to decrease risk of aspiration pneumonia.

CLIENT EDUCATION

- Inform client that most bacterial infections resolve without recurrence when treated early with an aggressive course of long-term, broad-spectrum antibiotics.
- Warn client that relapsing signs may occur, that the patient may improve but may never be neurologically normal.
- Warn client that the condition may require surgical intervention.

SURGICAL CONSIDERATIONS

- Severity of neurologic signs is not directly related to degree of pathology, and should not be used to make decisions regarding need for surgical intervention.
- Surgical treatment is indicated for patients with evidence of middle ear exudate, osteomyelitis refractory to medical management, nasopharyngeal polyps, or neoplasia.
- Bullae osteotomy allows drainage of the middle ear cavity.
- Total ablation of ear canal is indicated when otitis media is associated with recurrent otitis externa or neoplasia.
- Perform cytologic examination and culture of middle ear

effusion and histopathology of abnormal tissue sampled at the time of surgery.



MEDICATIONS

DRUG(S) OF CHOICE

- Topical sterile water, saline, or TrizEDTA-based otic antimicrobial preparations if tympanum is ruptured.
- Treat mites if present.
- Long-term (6–8 weeks) topical and systemic antibiotics selected on basis of culture and sensitivity, if available.
 - Amoxicillin/clavulanic acid (12.5–22 mg/kg q12h PO) is a good first-choice antibiotic.
 - Fluoroquinolone or third-generation cephalosporins are good second alternatives or can be used in combination, if culture and sensitivity unavailable; enrofloxacin (Baytril) 5–10 mg/kg q24h (dogs), 5 mg/kg q24h (cats), or marbofloxacin (Zeniquin 5 mg/kg q24h), or cefpodoxime (Simplicef 10 mg/kg q12h); clindamycin (Cleocin 5–30 mg/kg q12h), if anaerobes are suspected.
 - In cats, where oral dosing is too challenging, consider using ceftiofur (Convenia) 8 mg/kg SC every 2 weeks. This can also be used in combination with a fluoroquinolone.
 - Antiemetics to treat or prevent nausea, vomiting, and dizziness. Meclizine (Antivert, Antrizine, Bonine, Dramamine Less Drowsy Formula) 12.5 mg PO q24h (dogs <10 kg and cats), 25 mg PO q24h (dogs >10 kg); or maropitant citrate (Cerenia) 1 mg/kg SC or 2 mg/kg PO q24h (dogs), 1 mg/kg SC or 1 mg/kg PO q24h (cats); or dolasetron mesylate (Anzemet) 0.6 mg/kg IV q24h (dogs, cats).

CONTRAINdications

- If ruptured tympanum or associated neurologic deficits, avoid oil-based or irritating external ear preparations (e.g., chlorhexidine) and aminoglycosides, which are toxic to inner ear structures.
- Use topical and systemic corticosteroids judiciously in treatment of otitis media or interna. May exacerbate infection. Reserve for cases in which flushing of the ear canal is prevented by inflammation, or to treat edema associated with intracranial spread of infection.

PRECAUTIONS

Avoid vigorous external ear flush.



FOLLOW-UP

PATIENT MONITORING

Evaluate for resolution of signs after 10–14 days or sooner if the patient is deteriorating.

POSSIBLE COMPLICATIONS

- Signs associated with vestibular (head tilt) and facial nerve damage or Horner's syndrome may not resolve.
- Severe middle/inner ear infections may spread to brainstem or sometimes forebrain. Clinical signs indicate central vestibular lesion, typically preceded by peripheral vestibular or middle/inner ear signs. Aggressive surgical debridement and antibiotic therapy are required.
- Osteomyelitis of the petrous temporal bone and middle ear effusion are common sequelae to severe, chronic otitis externa.
- Complications following bulla osteotomy include Horner's syndrome, facial paralysis, onset or exacerbation of vestibular dysfunction, and deafness.

EXPECTED COURSE AND PROGNOSIS

- Otitis media-interna is usually responsive to medical management. To decrease likelihood of relapse, a 2- to 4-month course of antibiotic is recommended.
- When medical management of otitis externa is ineffective, consider lateral ear resection.
- Vestibular signs typically improve in 2–6 weeks.



MISCELLANEOUS

AGE-RELATED FACTORS

Ear mites more common in kittens and puppies.

SEE ALSO

- Facial Nerve Paresis and Paralysis.
- Head Tilt.
- Horner's Syndrome.
- Otitis Externa and Media.

ABBREVIATIONS

- BAER = brainstem auditory evoked response.
- KCS = keratoconjunctivitis sicca.
- T₄ = thyroxine.
- TSH = thyroid-stimulating hormone.

Suggested Reading

Negrin A, Cherubini GB, Lamb C, et al. Clinical signs, magnetic resonance imaging findings and outcome in 77 cats with vestibular disease: a retrospective study. J Feline Med Surg 2010, 12:291–299.

Sturges BK, Dickinson PJ, Kortz GD, et al. Clinical signs, magnetic resonance imaging features, and outcome after surgical and medical treatment of otogenic intracranial infection in 11 cats and 4 dogs. J Vet Intern Med 2006, 20:648–656.

Authors Richard J. Joseph and Anne E. Buglione



Client Education Handout
available online

PANCREATITIS—CATS



BASICS

DEFINITION

- Inflammation of the pancreas most often of unknown cause(s). • Acute pancreatitis— inflammation of the pancreas that occurs abruptly with little or no permanent pathologic change. • Chronic pancreatitis— continuing inflammatory disease that is accompanied by irreversible morphologic change such as fibrosis.

PATHOPHYSIOLOGY

- Host defense mechanisms normally prevent pancreatic autodigestion by pancreatic enzymes, but under select circumstances these natural defenses fail; autodigestion occurs when these digestive enzymes are activated within acinar cells. • Local and systemic tissue injury is due to the activity of released pancreatic enzymes and a variety of inflammatory mediators such as kinins, free radicals, and complement factors that are released by infiltrating neutrophils and macrophages. The most common pathologies involving the feline pancreas include acute necrotizing pancreatitis (ANP), acute suppurative pancreatitis, and chronic nonsuppurative pancreatitis.

SYSTEMS AFFECTED

- Gastrointestinal (GI)—altered GI motility (ileus) due to regional chemical peritonitis; local or generalized peritonitis due to enhanced vascular permeability; concurrent inflammatory bowel disease (IBD) may be seen in some cats. • Hepatobiliary—lesions due to shock, pancreatic enzyme injury, inflammatory cellular infiltrates, hepatic lipidosis, and intra/extrahepatic cholestasis. Feline GI inflammatory disease (concurrent cholangitis ± IBD) may be seen in some cats.
- Respiratory—pulmonary edema or pleural effusion. • Cardiovascular—cardiac arrhythmias may result from release of myocardial depressant factor.
- Hematologic—activation of the coagulation cascade and systemic consumptive coagulopathy (disseminated intravascular coagulation [DIC]) may occur.

GENETICS

No genetic basis for disease pathogenesis in cats has been identified.

INCIDENCE/PREVALENCE

- True prevalence is unknown but this is a relatively common clinical disorder in cats.
- Necropsy surveys suggest an increased prevalence in cats with cholangitis, and IBD. The unique feline pancreaticobiliary anatomy and intestinal microbiota likely contribute to multiorgan inflammatory disease in this species.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cat

Breed Predilections

Siamese cats.

Mean Age and Range

Mean age for acute pancreatitis is 7.3 years; any age may be affected.

Predominant Sex

None

SIGNS

Historical Findings

- Vague, nonspecific, and nonlocalizing signs.
- Anorexia, lethargy, and vomiting are reported most frequently. • Weakness.
- Abdominal pain. • Diarrhea—small bowel and large bowel diarrhea and fever are less common in cats than in dogs.

Physical Examination Findings

- Severe lethargy. • Inappetance.
- Dehydration—common; due to GI losses.
- Abdominal pain—recognized much less frequently in cats than dogs. • Mass lesions may be palpable. • Fever—observed in 25% of cats.

CAUSES

- Etiology is most often unknown; possibilities include:
- Hepatobiliary disease—both inflammatory and degenerative (hepatic lipidosis).
 - Pancreatic trauma/ischemia.
 - Duodenal reflux.
 - Drugs/toxins (organophosphates).
 - Pancreatic duct obstruction.
 - Hypercalcemia.
 - Inflammatory GI disease.
 - Nutrition—excessively lean body mass is associated with ANP.

RISK FACTORS

- Breed? • Obesity? • Organophosphate poisoning. • Concurrent hepatic/intestinal inflammatory disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- GI disease (obstruction, foreign body, perforation, infectious gastroenteritis, ulcer disease)—exclude with CBC/biochemistry/urinalysis, diagnostic imaging, and paracentesis.
- GI or hepatic neoplasia—exclude with tissue biopsy.
- Urogenital disease (pyelonephritis, prostatitis or abscessation, pyometra, urinary tract rupture or obstruction, acute renal failure)—exclude with CBC/biochemistry/urinalysis, urine culture/sensitivity, and imaging.
- Hepatobiliary disease (cholangitis and extrahepatic biliary obstruction [EHBO])—exclude with CBC/biochemistry/urinalysis, bile acids, imaging, and liver biopsy.
- Abdominal neoplasia—exclude with imaging and cytology or biopsy.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—often reveals nonregenerative anemia (40%), leukocytosis (38%), and/or leukopenia (15%). • Serum biochemistries—often show prerenal azotemia; liver enzyme activities (alanine aminotransferase, alkaline phosphatase) are often elevated because of hepatic ischemia or exposure to pancreatic enzymes; hyperbilirubinemia with intra/extrahepatic biliary obstruction; hyperglycemia with necrotizing pancreatitis due to hyperglucagonemia; hypoalbuminemia, hypercholesterolemia, and hypertriglyceridemia are common. Hypocalcemia is more common in cats than dogs, and a low ionized calcium concentration is a negative prognostic indicator in cats.
- Urinalysis—increased urine specific gravity associated with dehydration or can be unremarkable.

OTHER LABORATORY TESTS

- Serum amylase and lipase activities are unreliable serologic markers—may be elevated, but are nonspecific; can also increase with hepatic, renal, or neoplastic disease in the absence of pancreatitis.
- Serum pancreatic lipase immunoreactivity (fPL) is a highly sensitive and specific serologic marker of acute pancreatic inflammation. A cage-side fPL assay (SNAP fPL) has been developed as a useful screening tool. Elevation in SNAP fPL should be followed up by laboratory measurement of serum Spec fPL to quantitate the degree of elevation.

IMAGING

- Abdominal radiographs—may include increased soft tissue opacity in the right cranial abdominal compartment; loss of visceral detail (“ground glass appearance”) due to abdominal effusion; static gas pattern in the proximal duodenum.
- Abdominal ultrasound—nonhomogeneous solid or cystic mass lesions suggest pancreatic abscess; may be a pancreatic mass or altered echogenicity (hypoechoic) in the area of the pancreas; pancreas is usually enlarged with irregular borders, surrounding mesentery may be hyperechoic due to focal peritonitis, may see peritoneal effusion and extrahepatic biliary obstruction.
- fPL assay and pancreatic ultrasound in combination have the highest specificity for an antemortem diagnosis of acute pancreatitis.

DIAGNOSTIC PROCEDURES

- Ultrasound-guided needle aspiration may confirm inflammation (cytology), abscess, or cyst.
- Laparoscopy with pancreatic forceps biopsy for histologic diagnosis.
- Histopathologic evaluation may miss focal or segmental pancreatic inflammation and results should be interpreted with caution.

PATHOLOGIC FINDINGS

- Gross findings (acute pancreatitis)—mild swelling with edematous pancreatitis.
- Gross findings (chronic pancreatitis)—pancreas is reduced in size, firm, gray, and irregular; may contain extensive adhesions to surrounding

PANCREATITIS—CATS

(CONTINUED)

- viscera. • Microscopic changes (acute pancreatitis)—include edema, parenchymal necrosis, hemorrhage, and neutrophilic cellular infiltrate with acute lesions.
- Microscopic changes (chronic pancreatitis)—pancreatic fibrosis around ducts, ductal epithelial hyperplasia, atrophy, and mononuclear cellular infiltrate.



TREATMENT

APPROPRIATE HEALTH CARE

- Eliminate the inciting cause (if possible).
- Supportive care is most important.

NURSING CARE

- Aggressive IV fluid therapy. Fluid therapy goals—correct hypovolemia and maintain pancreatic microcirculation. • An isotonic crystalloid such as lactated Ringer's solution or Normosol-R® is the first-choice rehydration fluid. • Correct initial dehydration ($mL = \frac{\%}{2} \text{ dehydration} \times \text{weight in kg} \times 1000$) and give over 4–6 hours. • May need colloids to improve pancreatic circulatory needs and prevent ischemia. • Following replacement of deficits, give additional fluids to match maintenance requirements ($2.5 \times \text{weight in kg} = mL/kg/h$) and ongoing losses (estimated). • Potassium chloride (KCl) supplementation usually needed because of potassium loss in the vomitus; base potassium supplementation on measured serum levels (use 20 mEq of KCl/L of IV fluid if serum potassium levels are not known; do not administer faster than 0.5 mEq/kg/h).

ACTIVITY

Restrict

DIET

- Continue to feed orally unless vomiting is intractable; feeding maintains intestinal epithelial integrity and minimizes bacterial translocation. • Initiate enteral feeding via esophagostomy, gastrostomy enteral feeding device, or nasoesophageal tube placement.
- NPO in animals with persistent vomiting for the shortest time possible; when there has been no vomiting for 12 hours, offer small volumes of water; if tolerated, begin small, frequent feedings of a diet that does not contain excessive amounts of dietary fat. Most nutritionists agree that excessive dietary fat restriction is not necessary in cats with pancreatitis.

CLIENT EDUCATION

- Discuss the need for extended hospitalization.
- Discuss the expense of diagnosis and treatment. • Discuss possible short-term and long-term complications (see Associated Conditions).

SURGICAL CONSIDERATIONS

- May need surgery to remove pseudocysts, abscesses, or devitalized tissue seen with

necrotizing pancreatitis. • May need laparotomy and pancreatic biopsy to confirm pancreatitis and/or rule out other, nonpancreatic diseases such as cholangitis, lipidosis, and/or IBD. • EHBO from pancreatitis may require ductal decompression with surgical correction.



MEDICATIONS

DRUG(S) OF CHOICE

- Animals with intermittent vomiting should be treated with antiemetics. Maropitant 1 mg/kg SQ or PO q24h or ondansetron 0.1–0.5 mg/kg slow IV q8–12h are good first-choice options. • Analgesics to relieve abdominal pain, e.g., butorphanol 0.1–0.4 mg/kg SQ q6h, buprenorphine 0.005–0.015 mg/kg IM or IV q6–12h or fentanyl CRI 2–4 µg/kg/h as needed. • Antibiotics only if evidence of sepsis from bacterial translocation and to prevent pancreatic infection.

CONTRAINdications

Drugs reported to cause or exacerbate pancreatitis:

- Anticholinergics (e.g., atropine).

- Azathioprine. • Chlorothiazide. • Estrogens. • Furosemide. • Tetracycline. • L-Asparaginase.

PRECAUTIONS

Only use antibiotics if a clear clinical condition exists, such as infection.



FOLLOW-UP

PATIENT MONITORING

- Evaluate hydration status closely during first 24 hours of therapy; twice daily check physical examination, body weight, hematocrit, total plasma protein, BUN, and urine output. Evaluate the effectiveness of fluid therapy after 24 hours and adjust flow rates and fluid composition accordingly; repeat biochemistries to assess electrolyte/acid-base status. • Watch closely for systemic complications involving a variety of organ systems; perform appropriate diagnostic tests as needed (see Associated Conditions).
- Gradually taper fluids down to maintenance requirements if possible. Maintain oral alimentation or enteral nutrition as described above, being careful to feed diets that do not contain excessive amounts of dietary fat.
- Monitor for clinical evidence of IBD and treat accordingly. • Monitor for progression to diabetes mellitus, exocrine pancreatic insufficiency (EPI), and/or hepatic lipidosis in cats with ANP.

PREVENTION/AVOIDANCE

- Weight reduction if obese. • Avoid high-fat diets.

POSSIBLE COMPLICATIONS

- Failed response to supportive therapy.
- Associated conditions such as EPI, diabetes mellitus, and hepatic lipidosis. • Progression of acute pancreatitis to chronic pancreatitis.

EXPECTED COURSE AND PROGNOSIS

- Guarded for most patients with ANP; cats with multiorgan inflammation may be less responsive to treatment. • More guarded to poor for patients with severe necrotizing pancreatitis, decreased ionized calcium fraction, hyperkalemia, fPL >20 µg/L, and systemic conditions.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Life-Threatening

- Pulmonary edema (e.g., adult respiratory distress syndrome). • Cardiac arrhythmias. • Peritonitis. • DIC.

Non-Life-Threatening

- Diabetes mellitus. • EPI. • Chronic pancreatitis. • Cholangitis and hepatic lipidosis. • IBD.

SEE ALSO

- Acute Abdomen. • Cholangitis/Cholangiohepatitis Syndrome. • Exocrine Pancreatic Insufficiency. • Inflammatory Bowel Disease.

ABBREVIATIONS

- ANP = acute necrotizing pancreatitis.
- DIC = disseminated intravascular coagulation. • EHBO = extrahepatic biliary obstruction. • EPI = exocrine pancreatic insufficiency. • fPL = feline pancreatic lipase immunoreactivity. • GI = gastrointestinal.
- IBD = inflammatory bowel disease.

INTERNET RESOURCES

Veterinary Information Network: <http://www.vin.com/VIN.plx>

Suggested Reading

Simpson KS. Pancreatitis and triaditis in cats: causes and treatment. J Small Anim Pract 2015, 56(1):40–49.

Stockhaus C, Teske E, Schellenberger K, et al. Serial serum feline pancreatic lipase immunoreactivity concentrations and prognostic variables in 33 cats with pancreatitis. J Am Vet Med Assoc 2013, 243:1713–1718.

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Client Education Handout
available online

PANCREATITIS—DOGS



BASICS

DEFINITION

Inflammation of the pancreas, which may occur abruptly with little or no permanent pathologic change (acute pancreatitis) or occur continuously or intermittently with irreversible morphologic change such as fibrosis and atrophy (chronic pancreatitis).

PATHOPHYSIOLOGY

- Premature intrapancreatic activation of zymogens results in local inflammation, edema, and necrosis of the pancreas and peripancreatic fat.
- Pancreatic enzymes and inflammatory cytokines result in local (abdominal pain, vomiting) and possibly systemic effects (pyrexia, systemic inflammatory response syndrome [SIRS], multiple organ dysfunction syndrome [MODS], and acute kidney injury [AKI]).
- An autoimmune mechanism is suspected in English cocker spaniels, but remains unproven.

SYSTEMS AFFECTED

- Gastrointestinal (GI)—altered GI motility (ileus) due to regional chemical peritonitis; local or generalized peritonitis due to enhanced vascular permeability.
- Cardiovascular—cardiac arrhythmias may result from release of myocardial depressant factor.
- Hemic/lymphatic/immune—circulating proinflammatory cytokines and altered endothelial cell function can result in complications such as SIRS and/or disseminated intravascular coagulation (DIC).
- Hepatobiliary—hepatocellular damage can occur secondary to regional inflammation. Inflammation of the pancreas can also result in extrahepatic bile duct obstruction.
- Renal/urologic—AKI can occur as a consequence of MODS.
- Respiratory—regional vasculitis can cause pulmonary edema and/or pleural effusion. In severe cases, life-threatening acute respiratory distress syndrome can develop.

GENETICS

A possible genetic basis has been reported in miniature schnauzers where mutations in the *SPINK1* gene may confer increased susceptibility.

INCIDENCE/PREVALENCE

- Unknown, but it is a relatively common clinical disorder.
- Up to 1% of normal dogs may have histologic evidence of pancreatitis.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog

Breed Predilections

- Acute—miniature schnauzer, Yorkshire terrier, other terriers.
- Chronic—cocker spaniel and cavalier King Charles spaniel.

Mean Age and Range

Acute pancreatitis is most common in middle-aged and older (>7 years) dogs.

Predominant Sex

Females overrepresented in some reports.

SIGNS

Historical Findings

- Duration and severity of clinical signs can be variable, depending on the form of disease (acute vs. chronic).
- Lethargy/anorexia.
- Vomiting.
- Weakness.
- Abdominal pain (may be absent in chronic disease).
- Diarrhea—small or large bowel type.

Physical Examination Findings

- Lethargy.
- Dehydration—common; due to GI losses.
- Abdominal pain—may adopt a “prayer position.”
- Mass lesions may be palpable.
- Fever—common with more severe acute pancreatitis.
- Less common—respiratory distress, bleeding, and cardiac arrhythmias.

CAUSES

Etiology is most often unknown; possibilities include:

- Nutritional factors (e.g., dietary indiscretion, hyperlipoproteinemia).
- Pancreatic trauma/ischemia.
- Duodenal reflux.
- Drugs/toxins.
- Pancreatic duct obstruction.
- Hypercalcemia.
- Infectious agents—babesiosis.

RISK FACTORS

- Breed—miniature schnauzers, terriers.
- Obesity.
- Prior GI disease.
- Endocrine disease.
- Dietary indiscretion—access to garbage or fatty foods.
- Hypertriglyceridemia—while an association exists between hypertriglyceridemia and pancreatitis, a causative link remains unclear.
- Infectious—vector-borne diseases (babesiosis, ehrlichiosis, and leishmaniasis) have been identified in some cases of acute pancreatitis.
- Drugs/toxins—idiosyncratic reactions to certain drugs (L-asparaginase, azathioprine, chlorpromazine, clomipramine, potassium bromide) have been described. Zinc toxicosis, mainly from ingestion of pennies minted after 1982, may cause pancreatitis.
- Hypercalcemia—not specifically documented in dogs, but shown in multiple species.
- Surgery—possible; secondary to hypoperfusion or traumatic manipulation of the pancreas.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- GI (obstruction, septic peritonitis, ulcer, neoplasia)—differentiate via abdominal imaging.
- Hepatobiliary (cholangiohepatitis, copper hepatopathy, mucocele, neoplasia, toxicity)—abdominal imaging showing significant gallbladder pathology, liver histopathology, hepatic copper quantification.

- Genitourinary (AKI, pyelonephritis, leptospirosis, uroabdomen, pyometra, prostatitis)—azotemia, hyperphosphatemia, hyperkalemia, isosthenuric urine, active urinary sediment; positive urine culture; leptospiral microscopic agglutination titers. Abdominal imaging showing uterine, prostatic or urinary bladder pathology.
- Other:

- Hypoadrenocorticism—concurrent hyponatremia and hyperkalemia, lack of a stress leukogram, post adrenocorticotropic hormone stimulation cortisol of <1 µg/dL.
- Splenic torsion—splenomegaly with abnormal splenic positioning on abdominal imaging.

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—hemoconcentration; inflammatory leukogram; thrombocytopenia.
- Biochemistry—azotemia; increased liver enzyme activities; hyperbilirubinemia; electrolyte abnormalities associated with vomiting; hyperglycemia; hypoalbuminemia; hypercholesterolemia and hypertriglyceridemia.
- Urinalysis—may show evidence of proteinuria or may be unremarkable.

OTHER LABORATORY TESTS

- Serum amylase and lipase activities are unreliable serologic markers.
- Serum pancreatic lipase immunoreactivity (cPL) is a sensitive and specific marker of acute pancreatic inflammation, although is less sensitive for detecting chronic pancreatic inflammation. A cage-side cPL assay (SNAP cPL) is a useful screening tool. Elevation in SNAP cPL should be followed up by measurement of serum Spec cPL to obtain a quantitative value.

IMAGING

- Abdominal radiographs—increased soft tissue opacity in the right cranial abdomen; loss of visceral detail (“ground glass” appearance) due to abdominal effusion; static gas pattern in the proximal duodenum; widened pyloroduodenal angle.
- Abdominal radiographs are insensitive for pancreatitis and are of greater value for ruling out other causes of vomiting such as gastric or intestinal foreign bodies.
- Thoracic radiographs—may be normal, reveal pleural effusion or pulmonary edema.
- Abdominal ultrasound—imaging modality of choice; nonhomogeneous mass lesions suggest pancreatic abscess; pancreas is usually enlarged and irregular; may be a pancreatic mass or hypoechogenicity in the area of the pancreas due to edema; surrounding mesentery is typically hyperechoic due to peritonitis; may see peritoneal effusion and extrahepatic biliary obstruction.
- cPL assay and ultrasound in combination have the highest sensitivity for an antemortem diagnosis of acute pancreatitis.

DIAGNOSTIC PROCEDURES

- Ultrasound-guided needle-aspiration cytology may confirm inflammation, abscess, or cyst.
- Laparoscopy with pancreatic biopsy for histologic diagnosis.
- Histopathologic

PANCREATITIS—DOGS

(CONTINUED)

evaluation may miss focal or segmental pancreatic inflammation and must be interpreted with caution.

PATHOLOGIC FINDINGS

- Gross findings (acute)—mild swelling with edema; gray-yellow areas of necrosis with varying amounts of hemorrhage with necrotizing pancreatitis.
- Gross findings (chronic)—pancreas is reduced in size, firm, gray, and irregular; may contain extensive adhesions to surrounding viscera.
- Microscopic changes (acute)—edema, parenchymal necrosis, hemorrhage, and neutrophilic cellular infiltrate.
- Microscopic changes (chronic)—fibrosis around ducts, ductal epithelial hyperplasia, atrophy, and mononuclear cellular infiltrate.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient management typically required.
- Identify and remove any predisposing causes.

P

NURSING CARE

- Patients are at increased risk of aspiration pneumonia because of the concurrent presence of vomiting and lethargy. Therefore, aggressive nursing care (maintain in sternal recumbency with elevated head) and management of vomiting (antiemetics and promotility drugs, suction of gastric contents with nasogastric tube) should be instituted.
- Aggressive IV fluid resuscitation with isotonic crystalloids should be administered to correct dehydration and encourage perfusion of the pancreas.
- In cases where hypoalbuminemia is present, colloid support with synthetic colloids may be needed (10–20 mL/kg/day).
- Hypokalemia is common, so IV potassium supplementation (not to exceed 0.5 mEq/kg/h) is often required.

ACTIVITY

Clinical status will determine.

DIET

- Food should be withheld if patient has uncontrolled vomiting.
- Enteral feeding should be encouraged as it supports enterocyte health, decreases bacterial translocation, and decreases incidence of vomiting episodes.
- Feeding cranial to the duodenum (prepyloric) is safe. Therefore, if the patient is not eating voluntarily, nasoesophageal, nasogastric, or esophageal feeding tubes should be used to deliver low-fat diets.

CLIENT EDUCATION

Discuss possible complications, variable clinical severity, and risk of recurrence associated with pancreatitis.

SURGICAL CONSIDERATIONS

- Surgery should be avoided if possible; minimally invasive techniques (laparoscopy) or alternatives to surgery (ultrasound-guided percutaneous drainage) should be used.

- Surgical intervention may be indicated if there is suspicion of an infected necrotic area of the pancreas, pancreatic abscess, or pancreatic enlargement causing extrahepatic biliary obstruction.



MEDICATIONS

DRUG(S) OF CHOICE (EMPHASIS ON ACUTE PANCREATITIS)

- Analgesic—fentanyl 2–5 µg/kg/h IV CRI; buprenorphine 0.01–0.02 mg/kg q6–8h IV or IM.
- Antiemetics—maropitant 1 mg/kg SQ q24h; ondansetron 0.5–1.0 mg/kg IV or SQ q8h; metoclopramide 2 mg/kg/day IV CRI.
- Antibiotics—usually not indicated. If bacterial translocation from the GI tract is suspected, broad-spectrum antibiotic therapy is recommended (e.g., ampicillin/sulbactam 30 mg/kg IV q8h).
- Fresh frozen plasma—no clinical benefit has been shown.
- Glucocorticoids—limited evidence to support benefit. Dogs with chronic autoimmune pancreatitis (English cocker spaniels are predisposed) may be treated with prednisone 2 mg/kg PO as induction therapy and then tapered as based on cPL levels and clinical signs.

CONTRAINdications

- Anticholinergics.
- Azathioprine.
- Chlorothiazide.
- L-Asparaginase.
- Meglumine antimonite.
- Potassium bromide.

PRECAUTIONS

Use antimicrobials only if indicated.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- The patient's hydration status as well as electrolyte levels should be monitored frequently. Special attention should be paid to development of systemic signs suggestive of SIRS or MODS (increased respiratory rate, decreased urine production, bleeding).
- The patient's need for more or less aggressive pain control should be frequently reassessed.
- Since ultrasound findings can lag behind clinical improvement and circulating cPL levels can remain increased for extended periods, the decision of when a patient is ready to be discharged from veterinary care should be based on the overall clinical disease activity.

PREVENTION/AVOIDANCE

Patients with a history of pancreatitis should be fed a low-fat diet and medications known to be triggers for pancreatitis should be avoided.

POSSIBLE COMPLICATIONS

- Acute complications—extrahepatic biliary tract obstruction, aspiration pneumonia, SIRS, MODS.
- Chronic complications—exocrine pancreatic insufficiency, diabetes mellitus.

EXPECTED COURSE AND PROGNOSIS

Prognosis is generally good for mild cases. Severe cases with development of SIRS/MODS have a more guarded prognosis. Negative prognostic factors—increases in blood urea/creatinine, thrombocytopenia, and marked increases in Spec cPL have been associated with increased mortality. Increased alanine aminotransferase has been associated with extended hospitalization in dogs with acute pancreatitis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Endocrinopathy.
- Epilepsy.
- Prior GI disease.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

N/A

SEE ALSO

- Acute Vomiting.
- Vomiting, Chronic

ABBREVIATIONS

- AKI = acute kidney injury.
- cPL = canine pancreatic lipase immunoreactivity.
- DIC = disseminated intravascular coagulation.
- GI = gastrointestinal.
- MODS = multiple organ dysfunction syndrome.
- PLI = pancreatic lipase immunoreactivity.
- SIRS = systemic inflammatory response syndrome.

INTERNET RESOURCES

Veterinary Information Network: <http://www.vin.com/VIN.plx>

Suggested Reading

- Mansfield C. Pathophysiology of acute pancreatitis: potential applications from experimental models and human medicine to dogs. J Vet Intern Med 2012, 26:875–887.
- Watson P. Chronic pancreatitis in dogs. Top Companion Anim Med 2012, 27:133–139.
- Xenoulis PG, Steiner JM. Pancreas: necrosis and inflammation: canine. In: Washabau RJ, Day MJ, eds., Canine and Feline Gastroenterology. St. Louis, MO: Elsevier, 2013, pp. 812–821.

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Client Education Handout
available online

PERIODONTAL DISEASE



BASICS

DEFINITION

Inflammation and destruction of the periodontium (i.e., gingiva, cementum, periodontal ligament, and alveolar bone) secondary to the subgingival biofilm of bacteria.

PATHOPHYSIOLOGY

A pellicle of salivary glycoproteins adheres to the clean tooth and first colonizing Gram-positive aerobic bacteria attach; the plaque biofilm is created. The supragingival plaque biofilm matures and influences the development of the subgingival biofilm. The constituents of the biofilm progress to Gram-negative anaerobic, motile, and spirochete bacteria. Bacterial byproducts and proteolytic enzymes with the host inflammatory response cause destruction of the periodontium, resulting in the loss of attachment for the tooth. The biofilm forms within days. Calculus is the mineralization of plaque. It is rough, acts a surface area for more plaque development, and can be mechanically irritating to the tissues.

SYSTEMS AFFECTED

Gastrointestinal—oral cavity/dentition (primary); systemic inflammation/distant organ changes.

GENETICS

N/A

INCIDENCE/PREVALENCE

Common—estimated to be around 85%.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Toy, brachycephalic, sighthounds, long-facial haired, and purebred cats.

Mean Age and Range

Begins as juvenile and progresses through life.

Predominant Sex

None

SIGNS

Historical Findings

Hidden/no clinical signs to halitosis, head shyness, oral bleeding, dropping food, reluctance to chew, pawing at the mouth, exaggerated jaw movements, face rubbing, maxillofacial swellings, ptalism, sneezing, and nasal discharge.

Physical Examination Findings

- Conscious examination—inflammation of the gingiva, plaque and/or calculus, root exposure, furcation exposure, mobile teeth, parulides, disproportionate plaque and

calculus distribution, oral discharge, maxillofacial swellings, and mandibular lymphadenopathy. The conscious examination significantly underestimates the presence and severity of PD and therefore an anesthetized examination with periodontal probing and intraoral radiographs is required for complete assessment. • Anesthetized examination—the degree of severity of periodontal disease relates to a single tooth.

- American Veterinary Dental College (AVDC) nomenclature:
 - Normal (PD 0)—clinically normal; no gingival inflammation or periodontitis clinically evident.
 - Stage 1 (PD 1)—gingivitis only without attachment loss. The height and architecture of the alveolar margin are normal.
 - Stage 2 (PD 2)—early periodontitis; less than 25% of attachment loss,* or at most, there is a Stage 1 furcation involvement in multirooted teeth.
 - Stage 3 (PD 3)—moderate periodontitis; 25–50% of attachment loss*, and/or there is a Stage 2 furcation involvement in multirooted teeth.
 - Stage 4 (PD 4)—advanced periodontitis; more than 50% of attachment loss* or there is a Stage 3 furcation involvement in multirooted teeth. Furcation indices subjectively measure when the periodontal probe extends less than half way between the roots (F1), extends greater than half way (F2), or through and through from one side of the furcation and out the other under the crown (F3).

*Periodontal attachment loss is measured by probing of the clinical attachment level and radiographic determination of the distance of the alveolar margin from the tooth's cementoenamel junction relative to the length of the root.

CAUSES

Bacterial plaque biofilm and associated host inflammatory response.

RISK FACTORS

Lack of daily preventive home care and professional veterinary dental care, signalment, systemic health (e.g., immunosuppression from pharmaceuticals or metabolic disease), inappropriate chewing behavior, malocclusions, crowding of dentition, oral foreign bodies.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Oral neoplasia, drug-associated gingival enlargement (e.g., cyclosporine, amlodipine), oral autoimmune inflammatory conditions, viral ulcerative gingivitis/mucositis (e.g., calicivirus), oral trauma and foreign bodies, rare fungal. Clinical history, imaging (i.e., intraoral radiographs and/or advanced imaging), and histopathology for differentiation.

CBC/BIOCHEMISTRY/URINALYSIS

Overall systemic/metabolic health status and for preparation for anesthesia.

OTHER LABORATORY TESTS

N/A

IMAGING

- Intraoral radiography—required diagnostic instrument to assess attachment loss, to include marginal bone loss, loss of the lamina dura, widening of the periodontal ligament space, horizontal and vertical bone loss, inflammatory resorption of the tooth root surface, furcation bone loss, combined patterns of bone loss. Horizontal bone loss is a pattern where the cortical and alveolar bone surrounding the tooth and adjacent teeth are lost at a similar rate; the periodontal pocket is above the bone (i.e., suprabony pocket). Vertical bone loss is a pattern where there is bone loss around a tooth root where the adjacent supporting bone remains more coronal; the periodontal pocket is within the bone (i.e., infra(intra) bony pocket).
- Osteopermeative patterns mimicking neoplasia can be present in severe cases. Osteitis secondary to the inflammation may result in paradoxical proliferation of bone.
- Cone-beam CT has been reported to be of additional valuable in assessing periodontal attachment loss in brachycephalic breeds.

P

DIAGNOSTIC PROCEDURES

- Periodontal probing—the distance between free gingival margin and apical extent of the sulcus or pocket; probing depths <3 mm in dogs and <1 mm in cats are considered normal gingival sulcus; variations based on the range of breed sizes in dogs.
- Measurement of root exposure, furcation exposures and tooth mobility are recorded.
- Clinical probing information and intraoral radiographic assessment are used to assign periodontal score to each tooth (PD0–PD4).

PATHOLOGIC FINDINGS

Tissues may be edematous, exhibit gingival hyperplasia/enlargement, exocytosis of inflammatory cells such as lymphocytes, plasma cells, and polymorphonuclear leukocytes, abundant colonies of bacterial microorganisms, areas of fibrosis, edema, and hemorrhage; bone may demonstrate infiltration of inflammatory cells, and resorption with both osteoclastic and osteoblastic activity. Osteomyelitis/osteitis can result.



TREATMENT

APPROPRIATE HEALTH CARE

- Prevention of PD with daily home care and annual preventive cleaning, starting in first 1–2 years of life; oral examinations and

PERIODONTAL DISEASE

(CONTINUED)

periodontal treatments before excessive attachment loss. • Daily home care prevention should begin the first year of life. Daily tooth brushing is the best daily home care prevention. • Annual or semi-annual evaluations and periodontal cleanings/“prophylaxis” and treatment based on the patient signalment and progressive PD stage status. • Client communication and education throughout all patient life stages.

NURSING CARE

Acute-on-chronic periodontal abscessation—nonsteroidal anti-inflammatory medications, if not contraindicated; analgesia and appropriate antibiotic selection pending scheduling for anesthesia, assessment, and treatment.

ACTIVITY

No restrictions.

DIET

Dental diets with fiber arrangements and/or added dental products added for patients without other dietary restrictions, or needs, and who have teeth remaining to chew.

CLIENT EDUCATION

Daily home care, the necessity of general anesthesia, and the lifelong prevention, management, and treatment of PD.

SURGICAL CONSIDERATIONS

- Remove the plaque biofilm and calculus, eliminate periodontal pocket(s), prevent further attachment loss, extract hopelessly compromised teeth, address contributing dental factors, and treat oral/dental pain. Individualized general anesthetic management.
- Periodontal surgery including, but not limited to, gingivectomy/gingivoplasty, periceutical treatment, closed root planing, open root planing, periodontal flaps, osseous resective surgery, osseous additive surgery including bone augmentation and guided tissue regeneration. Plans are based on PD stage, tooth/teeth involved, overall systemic health of the patient, ability for home care, ability to have further follow-up treatments and anesthetic procedures, and overall financial aspects for the client with the goal to have a pain- and infection-free oral cavity.



MEDICATIONS

DRUG(S) OF CHOICE

Systemic use of antimicrobials is *not* indicated in the treatment of PD without surgical attention to the underlying cause. Clindamycin, amoxicillin/clavulanic acid, and doxycycline may be chosen to augment periodontal surgical treatment. Metronidazole may be selected based on clinical findings and patient history.

CONTRAINDICATIONS

- Immunosuppressive drugs in untreated PD can cause acute-on-chronic exacerbations.
- Chronic use of bisphosphonates should be avoided unless the oral cavity and dentition have all active infection and inflammation treated.

PRECAUTIONS

Prolonged/increased dosages of immunosuppressive medications may contribute to acute on chronic exacerbations.

POSSIBLE INTERACTIONS

Oral chlorhexidine and oral fluoride inactivate with simultaneous use.

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

The diagnosed PD stage guides the recheck interval; evaluation every 3–12 months.

PREVENTION/AVOIDANCE

Daily tooth brushing with pet toothpaste mechanically removes the supragingival plaque biofilm. Oral 0.1–0.12% chlorhexidine products target oral bacteria involved in the plaque biofilm. Dental diets, dental chews, barriers sealants, dental wipes, dental enzyme systems, dental gels, and water additives can be a part of a dental home care program based on individual patient and client needs. The Veterinary Oral Health Council can help guide selection of pet dental products.

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Due to the multifactorial aspect of PD and individual patient response, the expected course and prognosis can be variable, but predictable with appropriate treatment.



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

Progresses with age; Adult-onset periodontitis is most common; juvenile and aggressive forms of periodontitis occur.

ZOONOTIC POTENTIAL

Capnocytophaga spp. may cause serious opportunistic infections in immunosuppressed humans; *Pasteurella multocida* may cause severe infections in humans following cat bites. Scientific developments in the study of oral microbiomes suggest transmission/sharing of oral bacteria can occur between species.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

N/A

ABBREVIATIONS

- AVDC = American Veterinary Dental College.
- PD = periodontal disease.

INTERNET RESOURCES

- <https://avdc.org/avdc-nomenclature/>
- <http://www.vohc.org>

Suggested Reading

Lobprise H, Stepaniuk K. Oral surgery—periodontal surgery. In: Lobprise H, Dodd JR, eds., ‘Wiggs’ Veterinary Dentistry—Principles and Practice, 2nd ed. Hoboken, NJ: Wiley-Blackwell, 2019, pp. 193–228.

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Client Education Handout
available online



BASICS

DEFINITION

Inflammatory process involving the serous membrane of the abdominal cavity.

PATHOPHYSIOLOGY

- Insult to the peritoneal cavity (localized or generalized) leads to inflammation characterized by vasodilation, cellular infiltration, pain, and development of adhesions. Fluid production is eventually favored over absorption, and progresses from transudate to exudate.
- Extent and severity depend on type and severity of insult.
- Response to bacterial peritonitis associated with lipopolysaccharide (LPS; Gram-negative bacteria) or peptidoglycans (Gram-positive bacteria), causing inflammatory cytokine and nitric oxide (NO) production. NO causes vasodilation, can lead to hypotension.
- Inflammation causes vasodilation and increased vascular permeability. Cytokine release from leukocytes results in chemotaxis and activation of complement. Activation of complement results in coagulation, fibrin production and decreased fibrinolysis, resulting in adhesion formation.
- Result of significant abdominal inflammation can be systemic inflammatory response syndrome (SIRS) and sepsis. SIRS can progress to multiple organ dysfunction (MODS) and affect respiratory system (acute respiratory distress syndrome or pulmonary thromboembolism), or cause renal dysfunction, reduced cardiac function, and neurologic dysfunction.

SYSTEMS AFFECTED

- Cardiovascular.
- Gastrointestinal (GI).
- Hemic/lymphatic/immune.
- Renal/urologic hepatobiliary.

GENETICS

N/A

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat.

Breed Predilections

None

Mean Age and Range

None

Predominant Sex

None

SIGNS

General Comments

Signs may be vague and nonspecific and depend on timeline of evaluation in relation to inflammation and systemic response.

Historical Findings

Lethargy, depression, anorexia, vomiting (common), diarrhea, collapse.

Physical Examination Findings

- Abdominal discomfort or pain—localized or generalized.
- Shock:
 - Compensatory—tachycardia, tachypnea, injected mucus membranes, rapid capillary refill time (CRT).
 - Early decompensatory—tachycardia, poor pulse quality, depressed mentation, pallor, prolonged CRT. Cats may show a normal to decreased heart rate (<140/min).
 - Decompensatory—bradycardia, weak or absent pulses, severely depressed mentation, pallor or cyanosis, prolonged CRT.
 - Arrhythmias/pulse deficits may be detected.
- Fever.
- Weight loss—reported in 1/3 of dogs and cats with secondary peritonitis.
- SIRS—tachycardia (dog >140/min, cat >240/min) or bradycardia (cat <130/min); tachypnea (dog >30/min, cat >40/min), hyperthermia (dog >102.5°F [39.1°C], cat >104.5°F [40.3°C]) or hypothermia (dog or cat <100°F [37.7°C]), leukocytosis (dog >19,000/µL, cat >18,000/µL), or leukopenia (dog <6000/µL, cat <5000/µL).

CAUSES

Primary Peritonitis

- Uncommon, no identifiable intraperitoneal source. More common in cats (14%).
- May be monomicrobial, Gram-positive in 80% of dogs, 60% of cats.
- Results from hematogenous or lymphatic spread or translocation from GI tract; may spread from oviduct.
- Feline infectious peritonitis (FIP) in cats.

Secondary Peritonitis

- Most common.
- Contamination of peritoneal cavity from abdominal organ:
 - GI source (up to 75%) from perforation (ulcerations, neoplasia, ischemia), leakage following GI surgery, penetrating trauma, biliary tract rupture (obstruction, trauma, mucocele), or pancreatitis.
 - Abscessation (liver, pancreas, kidney, prostate, lymph nodes, spleen).
 - Urogenital source (pyometra, urine leakage).
 - Uroabdomen and bile peritonitis may or may not be septic; regardless, chemical peritonitis is present.

RISK FACTORS

- Trauma.
- Foreign body ingestion.
- Biliary mucocele.
- GI surgery.
- Nonsteroidal anti-inflammatory drug (NSAID) use associated with GI perforation.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other causes of abdominal pain or distention, sepsis, and shock.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis common; possible left shift; degenerative left shift, or development of neutropenia may portend worsening prognosis.
- Hemoconcentration or anemia.
- Hypoproteinemia.
- Hypo- or hyperkalemia; hyponatremia (fluid loss into peritoneum).
- Azotemia—prerenal, renal, or post renal.
- Metabolic acidosis.
- Hypoglycemia—may indicate sepsis; hyperglycemia may be present in cats.
- Liver enzyme activity elevations—hepatic causes of peritonitis or MODS.
- Hyperlactatemia—poor tissue oxygen delivery.

OTHER LABORATORY TESTS

Coagulation testing—disseminated intravascular coagulation (DIC): prolonged activated partial thromboplastin time (aPTT) and thrombocytopenia initially, progress to prolonged prothrombin time (PT), aPTT, elevated D-dimers (>1,000 ng/mL).

IMAGING

Radiography

- Findings depend on cause; make right and left lateral projections of abdomen.
- Loss of serosal detail (ground-glass appearance suggests fluid in abdominal cavity)—rule out lack of intra-abdominal fat (cachexia, neonates).
- Generalized ileus.
- Pneumoperitoneum—gas in abdomen may be slight, closely evaluate region near diaphragm; consider making lateral beam images with patient in a sternal or lateral recumbency.
- Can be diagnostic for gastric dilatation/volvulus, GI foreign bodies, mass lesions, organs enlargement (neoplasia, abscess).
- Contrast procedures—rarely warranted; may complicate management if contrast material enters abdominal cavity; avoid barium if GI perforation suspected.

Ultrasound

Identify (and aspirate) small volumes of peritoneal effusion, abscesses, gallbladder rupture or mucocele, tumors, obstructions, or mass lesions.

DIAGNOSTIC PROCEDURES

- Abdominocentesis and diagnostic peritoneal lavage—perform as soon as possible:
 - Cytology—collect aliquot of sample into EDTA tube; note color and clarity and presence of fibrin.
 - Place second aliquot into red-top tube for biochemical testing if needed, based on suspected etiology.
- Chemical

PERITONITIS

(CONTINUED)

peritonitis—analyze abdominal fluid for creatinine (for uroabdomen), specific pancreatic lipase (for pancreatitis), and bilirubin (for bile leakage). • Culture and sensitivity—next, aseptically place an aliquot of sample in a sterile-white top (no additive) tube. • Suspect FIP—submit abdominal fluid for protein electrophoresis and globulin determination.

PATHOLOGIC FINDINGS

- Intracellular bacteria, degenerative neutrophils, and plant material are diagnostic of septic peritonitis. • Normal peritoneal fluid contains <2,500 cells/ μ L. • Glucose concentration in abdominal fluid more than 20 mg/dL less than peripheral blood glucose concentration suggests septic peritonitis.
- Peritoneal lactate >4.2 mmol/L suggests peritonitis in dogs. • Recent surgery results in <10,000 cells/mL; primary peritonitis usually results in 7,000 cells/ μ L in dogs and 3,000 cells/ μ L in cats. • Fluid bilirubin or creatinine levels at least two times higher than that of peripheral blood indicate bile peritonitis or uroabdomen, respectively. Acellular homogenous, laminated, basophilic material on cytology may be mucoid material associated with bile peritonitis.



TREATMENT

APPROPRIATE HEALTH CARE

• Inpatient—intensive monitoring and supportive care are required. • Goals—blood pressure >90 mmHg (measured by Doppler), heart rate 80–140/min (dogs) and 160–225/min (cats), CRT 1.5–2 seconds, urine output >1–2 mL/kg/h, blood lactate <2.5 mmol/L. Blood lactate concentration should improve with resuscitation; inability to do so suggests poorer prognosis.

IV Fluid Therapy

- Critical for correction of hemodynamic disturbances, electrolyte and acid–base abnormalities prior to surgery. • Balanced isotonic replacement crystalloid solution—evaluate response to therapy frequently:
 - Rate—may initially require multiple boluses of 10–30 mL/kg (depending on other patient parameters); reevaluate patient frequently, adjust fluid rate or repeat boluses as patient status changes. • Potassium and glucose supplementation as necessary:
 - Rate of potassium supplementation should not exceed 0.5 mEq/kg/h of potassium.
 - Synthetic colloids sometimes utilized (up to 20 mL/kg/d); concerns for acute kidney injury have decreased usage, especially in patients with sepsis. • Canine albumin transfusion indicated for severe hypoalbuminemia (<1.2 mg/dL).
 - Whole blood or packed red blood cells—as required

for anemia. • Inadequate response to therapy may prompt vasopressor administration (norepinephrine, vasopressin, dopamine). Norepinephrine is recommended for animals with sepsis. • DIC—remove inciting cause, support coagulation with fresh frozen plasma transfusion.

NURSING CARE

- Significant; dependent upon severity of systemic signs.
- IV fluid therapy and maintenance of tissue oxygen delivery.

ACTIVITY

Decreased; depends on inciting cause and clinical signs.

DIET

- Dictated by cause and concurrent conditions (e.g., heart disease). • Feeding tube placement should be considered and placed at time of surgery for early nutritional support (e.g., esophagostomy, gastrostomy, jejunostomy). Nasogastric tube for feeding and gastric decompression if necessary.
- Adequate nutrition—essential to optimize outcome, attenuate hypermetabolic state, preserve hepatic antioxidant defenses, prevent protein-calorie malnutrition, maintain GI barrier function.

CLIENT EDUCATION

- Advise client of high rate of morbidity and (especially septic peritonitis) mortality.
- Extensive monitoring and intensive care may be costly, with prolonged hospitalization.

SURGICAL CONSIDERATIONS

- Decision to treat medically or surgically—dictated by etiology, patient's response to initial treatment, and owner's financial constraints. • Known bacterial contamination or suspected chemical peritonitis—surgical intervention necessary. • Perform surgery as soon as patient is stable. Prompt source control allows deescalation of antibiotic, which may only be required for 4–8 days.
- Exploratory laparotomy—prepare for incision extending from xiphoid to pubis; goals of surgery are to remove source of contamination, debride and lavage abdomen, collect fluid or tissue for Gram stain and aerobic and anaerobic culture, and provide access for nutritional support; use monofilament absorbable or nonabsorbable suture within abdomen; before closing, thoroughly lavage abdomen with 200–300 mL/kg warm sterile saline. Do not add antimicrobials or other products to lavage solution; remove all lavage solution from abdomen. • Surgeon must assess organ viability and perform resections if necessary. Anastomosis of GI tract should utilize healthy tissue; consider serosal patching, perform omental patching if serosal patching not done. Stapled anastomoses may have a decreased risk of dehiscence in septic

peritonitis. • Consider omentectomy of pancreatic abscesses, perform omentectomy for prostatic abscessation. Remove affected organ or part in other cases of abscessation (liver lobectomy, nephrectomy). • Consider abdominal drainage—based on degree of contamination, ability to debride abdomen, severity of illness, and anticipation of septic complications:

- Allows continued removal of fluid, bacteria, and toxins.
- Forms include closed suction drains, vacuum-assisted peritoneal drainage (VAPD), and closure of caudal abdomen with partial closure of cranial abdomen. Sterile bandaging is required in each form; less external materials for VAPD, but regulate suction and specialized foam and connections to suction required.
- Requires anesthesia for abdominal closure unless closed suction drains are used. Severe peritonitis may require repeated exploration, debridement, and lavage prior to closure.



MEDICATIONS

DRUG(S) OF CHOICE

- Antimicrobials—early and aggressive broad-spectrum therapy for suspected septic peritonitis; final therapy based on culture and susceptibility testing.
- Initial therapy—Gram-negative (enrofloxacin, cefotaxime, amikacin); Gram-positive (ampicillin, clindamycin); anaerobes (metronidazole):
 - Ampicillin 22 mg/kg IV q6–8h.
 - Ampicillin/sulbactam 25–30 mg/kg IV q6–8h. • Clindamycin 12 mg/kg IV q12h.
 - Cefotaxime 20–80 mg/kg IV q8h.
 - Enrofloxacin 10–20 mg/kg IV q24h (dogs); 5 mg/kg IV q24h (cats).
 - Amikacin 15 mg/kg IV q24h.
 - Metronidazole 10 mg/kg IV q12h.
 - Analgesia—depends on pain severity; may be intermittent or via CRI; opioids recommended:
 - Multimodal IV combinations for pain; dogs, morphine 0.05–0.2 mg/kg/h or fentanyl 2–5 μ g/kg/h, ketamine 0.2–0.5 mg/kg/h, lidocaine 2–4 mg/kg/h; cats, fentanyl 2–5 μ g/kg/h, ketamine 0.05–0.2 mg/kg/h. Lidocaine may improve outcome following surgery in dogs.
- GI protectants—if GI ulceration:
 - Famotidine 0.5–1.0 mg/kg IV q12h.
 - Pantoprazole 1 mg/kg IV q12–24h (more effective acid reduction).
 - Sucralfate: dogs, 0.5–1.0 mg PO q8h; cats, 0.25–0.5 mg PO q8h.

CONTRAINdications

- Glucocorticoids—physiologic dose (0.5 mg/kg prednisone equivalent) may be indicated for hypotension unresponsive to fluids and pressors.
- NSAIDs are not recommended due to risk of acute kidney injury and GI ulceration in poorly perfused patients.

(CONTINUED)

PERITONITIS**PRECAUTIONS**

- Aminoglycosides—use with caution if hypotensive, dehydrated, impaired renal function.
- Adequate hydration—essential to enhance safety of these drugs.

POSSIBLE INTERACTIONS

Sucralfate works best at low pH; administration should be staggered with GI acid reducers, if both used. Avoid giving oral medications at same time as sucralfate.

ALTERNATIVE DRUG(S)

Fluoroquinolone—enrofloxacin or orbifloxacin; substitute for an aminoglycoside, especially with impaired renal function.

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

- Fluid balance, electrolyte balance, acid–base status, blood lactate—as necessary depending on severity of condition.
- Frequency of monitoring—varies with condition and response to treatment; generally q2h.
- Urine output—target 1–2 mL/kg/h.
- Quantify and replace fluid losses (vomiting, diarrhea).
- Change recumbency q4–6h.
- Enteral nutrition as soon as possible via oral or tube feeding: promotes enterocyte health and decreases bacterial translocation. Does not increase risk of complications.
- Repeat ultrasound and abdominal fluid cytologic evaluation depending on index of suspicion for leakage of intestinal surgery sites.
- CBC, chemistry profile, urinalysis—every 1–2 days during periods of intensive monitoring, even in patients that are responding.
- Coagulation testing q24–48h.

PREVENTION/AVOIDANCE

Prevention—difficult except with specific risk factors (e.g., pyometra, prostatic abscess can be avoided with sterilization).

POSSIBLE COMPLICATIONS

- If underlying cause is not identified and managed, patient is at risk for complications.
- Open peritoneal drainage—increased cost and required intensive care, repeated sedation

or anesthesia for aseptic bandage changes, nosocomial infection, hypoproteinemia, electrolyte imbalances, enterocutaneous fistulation, and abdominal hernia formation.

- Adhesions, granuloma formation with barium peritonitis.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—depends on rapid identification and successful management of underlying cause and appropriate follow-up care.
- Septic peritonitis—mortality of 30–68%. Prognosis worse in animals with preexisting septic peritonitis, uncorrectable hypotension, low serum albumin and total protein concentrations, respiratory dysfunction, DIC, low concentrations of protein C, or antithrombin, MODS; better survival in patients with lower preoperative alanine aminotransferase, gamma-glutamyltransferase, packed cell volume, total solids, and albumin concentration. Open peritoneal drainage may improve survival.
- Septic bile peritonitis—27% survival compared to 100% with nonseptic bile peritonitis.
- Antibiotic treatment within first hour in cases of suspected septic peritonitis may significantly reduce mortality.
- Blood lactate >2.5 mmol/L or inability to normalize plasma lactate—poorer survival.
- Feeding tube complications depend on site of placement—esophagostomy (localized infection or abscessation); gastrostomy and jejunostomy (leakage or premature dislodgement associated peritonitis): nasoesophageal or nasogastric (sneezing, epistaxis). Refeeding syndrome—decreased magnesium, phosphorus, potassium; relatively rare but warrants close monitoring.
- Bradycardia and hypothermia in cats with primary septic peritonitis associated with mortality.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Sepsis and Bacteremia.

ABBREVIATIONS

- aPTT = activated partial thromboplastin time.
- CRT = capillary refill time.
- FIP = feline infectious peritonitis.
- LPS = lipopolysaccharide.
- MODS = multiple organ dysfunction.
- NO = nitric oxide.
- NSAID = nonsteroidal anti-inflammatory drug.
- PT = prothrombin time.
- SIRS = systemic inflammatory response syndrome.
- VAPD = vacuum-assisted peritoneal drainage.

Suggested Reading

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Client Education Handout
available online

PLEURAL EFFUSION



BASICS

DEFINITION

Abnormal accumulation of fluid within the pleural cavity.

PATHOPHYSIOLOGY

- More than normal production or less than normal resorption of fluid.
- Alterations in hydrostatic and oncotic pressures or vascular permeability and lymphatic function may contribute to fluid accumulation.

SYSTEMS AFFECTED

- Cardiovascular.
- Respiratory.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Varies with underlying cause.

Mean Age and Range

- Young animals—more commonly infection.
- Old animals—more commonly cardiac or neoplastic.

Predominant Sex

Varies with underlying cause.

SIGNS

General Comments

Depend on the fluid volume, rapidity of fluid accumulation, and the underlying cause.

Historical Findings

- Dyspnea.
- Tachypnea.
- Orthopnea.
- Open-mouth breathing.
- Cyanosis.
- Exercise intolerance.
- Lethargy.
- Inappetence.
- Cough.

Physical Examination Findings

- Dyspnea—respirations often shallow and rapid.
- Muffled or inaudible heart and lung sounds ventrally.
- Preservation of breath sounds dorsally.
- Dullness ventrally on thoracic percussion.

CAUSES

High Hydrostatic Pressure

- Congestive heart failure (CHF).
- Overhydration.
- Intrathoracic neoplasia.

Low Oncotic Pressure

Hypoalbuminemia—occurs in protein-losing enteropathy, protein-losing nephropathy, and liver disease.

Vascular or Lymphatic Abnormality

- Infectious—bacterial, viral, or fungal.
- Neoplasia (e.g., mediastinal lymphoma, thymoma, mesothelioma, primary lung tumor, and metastatic disease).
- Chylothorax (e.g., from lymphangiectasia, CHF, cranial vena caval obstruction [sometimes associated with transvenous pacemaker implantation], neoplasia, fungal infections, heartworms, diaphragmatic hernia, lung lobe torsion,

trauma).

- Diaphragmatic hernia.
- Hemothorax (e.g., from trauma, neoplasia, coagulopathy, *Angiostrongylus vasorum*).
- Lung lobe torsion.
- Pulmonary thromboembolism.
- Pancreatitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Historical or physical evidence of external trauma—consider hemothorax or diaphragmatic hernia.
- Fever suggests an inflammatory, infectious, or neoplastic cause.
- Murmurs, gallops, or arrhythmias combined with jugular venous distension or pulsation suggest an underlying cardiac cause.
- Concurrent ascites suggests feline infectious peritonitis (FIP), CHF (mainly dogs), severe hypoalbuminemia, diaphragmatic hernia, disseminated neoplasia, or pancreatitis.
- In cats, decreased compressibility of the cranial thorax suggests a cranial mediastinal mass.
- Concurrent ocular changes (e.g., chorioretinitis and uveitis) suggest FIP or fungal disease.
- Hypothermia often associated with cardiac cause.

CBC/BIOCHEMISTRY/URINALYSIS

- Hemogram results may be abnormal in patients with pyothorax, FIP, neoplasia, or lung lobe torsion.
- Severe hypoalbuminemia (generally <1 g/dL to cause effusion) suggests protein-losing enteropathy, protein-losing nephropathy, or liver disease.
- Hyperglobulinemia (polyclonal) suggests FIP.

OTHER LABORATORY TESTS

- Fluid analysis should include physical characteristics (i.e., color, clarity, odor, clots), pH, glucose, total protein, total nucleated cell count, and cytologic examination; Table 1 provides characteristics of various pleural fluid types and their disease associations.
- In cats the lactate dehydrogenase concentration in transudates is <200 IU/L and in exudates it is >200 IU/L.
- Pleural fluid pH <6.9 suggests pyothorax in cats.
- Glucose concentration in pleural fluid usually parallels levels in serum. In cats, pyothorax and malignancy lower pleural fluid glucose concentration relative to serum glucose concentration; thus, pleural fluid with a normal pH and low glucose concentration suggests malignancy in cats.
- Serologic tests for feline leukemia virus (if patient has mediastinal lymphoma), feline immunodeficiency virus (if patient has pyothorax), and coronavirus (if FIP is suspected) are available.
- Cardiac disease suspected—consider a heartworm test in dogs and cats; NT-proBNP and thyroid evaluation in cats.
- Infection suspected—obtain aerobic and anaerobic bacterial culture and sensitivity

tests and consider special stains (e.g., Gram and acid-fast stains) of the fluid.

- FIP suspected—consider protein electrophoresis of the fluid; gamma-globulin level >32% of total protein strongly suggests a diagnosis of FIP.
- Chyle suspected—do an ether clearance test or Sudan stain of the pleural fluid, and triglyceride and cholesterol evaluations of the fluid and serum.

IMAGING

Radiographic Findings

- Used to confirm pleural effusion; should not be performed until after thoracocentesis in dyspneic patients with evidence of pleural effusion on physical examination.
- Evidence of pleural effusion includes separation of lung borders away from the thoracic wall and sternum by fluid density in the pleural space, fluid-filled interlobar fissure lines, loss or blurring of the cardiac and diaphragmatic borders, blunting of the lung margins at the costophrenic angles (ventrodorsal view), and widening of the mediastinum (ventrodorsal view).
- Rounding of the caudal lung lobe borders (lateral view)—most common in patients with fibrosing pleuritis caused by chylothorax, pyothorax, or FIP.
- Unilateral effusion—most common in patients with chylothorax and pyothorax; hemothorax, pulmonary neoplasia, diaphragmatic hernia, and lung lobe torsion.
- Evaluate post-thoracocentesis radiographs carefully for cardiomegaly, intrapulmonary lesions, mediastinal masses, diaphragmatic hernia, lung lobe torsion, and evidence of trauma (e.g., rib fractures).
- Can diagnose a diaphragmatic hernia with positive-contrast peritoneography.
- Can evaluate the thoracic duct by positive-contrast lymphangiography.
- CT imaging may help differentiate malignant from inflammatory effusions.

Echocardiographic Findings

- Ultrasonographic evaluation of the thorax is recommended whenever cardiac disease, diaphragmatic hernia, or cranial mediastinal mass is suspected.
- Echocardiography is easiest to perform before thoracocentesis, provided the patient is stable.

DIAGNOSTIC PROCEDURES

- Thoracocentesis—allows characterization of the fluid type and determination of potential underlying cause.
- Exploratory thoracotomy or thoracoscopy—to obtain biopsy specimens of lung, lymph nodes, or pleura, if indicated.



TREATMENT

- First, thoracocentesis to relieve respiratory distress; if the patient is stable after thoracocentesis, outpatient treatment may be possible for some diseases. Most patients are

(CONTINUED)

PLEURAL EFFUSION

Table 1

| | Characterization of pleural fluid. | | | | | |
|--------------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| | <i>Transudate</i> | <i>Modified Transudate</i> | <i>Nonseptic Exudate</i> | <i>Septic Exudate</i> | <i>Chyle</i> | <i>Hemorrhage</i> |
| Color | Colorless to pale yellow | Yellow or pink | Yellow or pink | Yellow to red-brown | Milky white | Red |
| Turbidity | Clear | Clear to cloudy | Clear to cloudy; fibrin | Cloudy to opaque; fibrin | Opaque | Opaque |
| Protein (g/dL) | <1.5 | 2.5–5.0 | 3.0–8.0 | 3.0–7.0 | 2.5–6.0 | 3.0 |
| Nucleated cells/ μ L | <1,000 | 1,000–7,000 (LSA up to 100,000) | 5,000–20,000 (LSA up to 100,000) | 5,000–300,000 | 1,000–20,000 | Similar to peripheral blood |
| Cytology | Mostly mesothelial cells and macrophages | Mostly macrophages and mesothelial cells; few nondegenerate PMNs; neoplastic cells in some cases | Mostly nondegenerate PMNs and macrophages; neoplastic cells in some cases | Mostly degenerate PMNs; also macrophages; bacteria | Small lymphocytes, PMNs, and macrophages | Mostly RBCs; with erythrophagocytosis |
| Disease associations | Hypoalbuminemia (protein-losing nephropathy, protein-losing enteropathy, or liver disease); early CHF | CHF; neoplasia; diaphragmatic hernia; pancreatitis | FIP; neoplasia; diaphragmatic hernia; lung lobe torsion | Pyothorax | Lymphangiectasia, CHF, cranial vena cava obstruction, neoplasia, fungal, dirofilariasis, diaphragmatic hernia, lung lobe torsion, trauma | Trauma, coagulopathy, neoplasia, lung lobe torsion |

Source: Modified from Sherding RG. Diseases of the pleural cavity. In: Sherding RG, ed., The Cat: Diseases and Clinical Management, 2nd ed. New York: Churchill Livingstone, 1994, p. 1061.

hospitalized because they require intensive management such as indwelling chest tubes (e.g., patients with pyothorax) or thoracic surgery. • Preventing fluid reaccumulation requires treatment based on a definitive diagnosis. • Surgery is indicated for management of some neoplasias, diaphragmatic hernia repair, lymphangiectasia (i.e., thoracic duct ligation), foreign body removal, and lung lobe torsion (i.e., lung lobectomy). • Pleuroperitoneal shunts may relieve clinical signs in animals with intractable pleural effusion. • Vascular access ports attached to intrathoracic Jackson–Pratt drains can be tried for chronic effusions that are not responsive to the therapy of the underlying disorder.

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

- Treatment varies with specific disease.
- Diuretics generally reserved for patients with diseases causing fluid retention and volume overload (e.g., CHF).

PRECAUTIONS

- Avoid drugs that depress respiration or decrease blood pressure. • Inappropriate use of diuretics predisposes the patient to

dehydration and electrolyte disturbances without eliminating the effusion.

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

Radiographic evaluation is key to assessment of treatment in most patients.

POSSIBLE COMPLICATIONS

- Death due to respiratory compromise.
- Reexpansion pulmonary edema may develop after pleural effusion is manually removed.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying cause, but usually guarded to poor. In a study of 81 cases of pleural effusion in dogs, 25% recovered completely and 33% died during or were euthanized immediately after completing diagnostic evaluation.

**MISCELLANEOUS****SYNOMYMS**

- Hydrothorax = transudates and modified transudates. • Pyothorax = empyema, septic pleuritis.

ABBREVIATIONS

- CHF = congestive heart failure. • FIP = feline infectious peritonitis. • LSA = lymphoma. • PMN = polymorphonuclear cell. • RBC = red blood cell.

Suggested Reading

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Client Education Handout available online

PNEUMONIA, ASPIRATION



BASICS

OVERVIEW

- Inflammation of the lungs caused by inhalation of oral ingesta, regurgitated material, and vomitus with subsequent pulmonary dysfunction; develops when laryngeal reflexes function improperly or are overwhelmed.
- Pulmonary dysfunction—caused by (1) direct obstruction of small airways and indirect obstruction from bronchospasm and production of mucus and exudate; (2) aspiration of gastric acid—damages respiratory epithelium; can cause bronchospasm and acute lung injury/acute respiratory distress syndrome (ALI/ARDS); (3) bacterial pneumonia—bacteria in aspirated material can initiate an immediate infection; or later infections occur secondary to lung damage.

SIGNALMENT

Dogs; less commonly cats.

SIGNS

- Peracute, acute, or chronic.
- Cough, tachypnea, nasal discharge, or exercise intolerance.
- Respiratory distress or cyanosis when severe.
- Depending on underlying cause—regurgitation; vomiting; dysphagia; altered consciousness; stertor or stridor.

CAUSES & RISK FACTORS

- Pharyngeal abnormalities—local paralysis; generalized neuromuscular disease; cricopharyngeal motor dysfunction; anatomic malformations.
- Esophageal abnormalities—megaesophagus; reflux esophagitis; esophageal dysmotility; esophageal obstruction; broncho-esophageal fistula.
- Laryngeal paralysis, webbing, or obstruction; post-laryngeal surgery.
- Altered consciousness—sedation, anesthesia; post-ictus; forebrain disease; metabolic disturbance.
- Iatrogenic—force feeding; tube feeding, mineral oil administration.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial pneumonia.
- Lung abscess.

CBC/BIOCHEMISTRY/URINALYSIS

Neutrophilic leukocytosis, left shift, although white blood cells may be normal.

OTHER LABORATORY TESTS

- Arterial blood gas analysis—hypoxemia; Paco_2 generally low.
- Consider tests for predisposing problems—acetylcholine receptor antibodies, resting cortisol or adrenocorticotropic hormone stimulation, creatine kinase.

IMAGING

- Thoracic radiography—bronchoalveolar pattern usually most severe in the gravity-dependent lobes (right cranial and middle, left cranial); can take up to 24 hours for pattern to develop after aspiration; scrutinize for evidence of esophageal or mediastinal disease.
- Videofluoroscopic swallowing study—provides evidence of swallowing or esophageal dysfunction that can predispose to aspiration. Caution: could result in aspiration of contrast medium.

DIAGNOSTIC PROCEDURES

- Tracheal wash—for bacterial culture and sensitivity testing before administering antibiotics; infection often caused by multiple organisms with unpredictable susceptibility.
- Bronchoscopy—rarely indicated.
- Laryngeal function examination—always perform if patient anesthetized for other purposes; otherwise, after resolution of pneumonia if supportive clinical signs.



TREATMENT

- Oxygen and cage rest—respiratory distress.
- Ventilatory support—if not oxygen responsive.
- IV fluids—avoid overhydration, which can exacerbate secondary edema.
- Oral intake— withhold until primary problem identified and managed.
- Do not allow patient to remain laterally recumbent on one side for more than 2 hours.
- Mild exercise and saline nebulization with coupage can facilitate airway clearance.
- Airway suction—only if performed immediately following aspiration (such as during recovery from anesthesia).
- Airway lavage—contraindicated.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotic therapy—if signs of sepsis or severe compromise, ampicillin with sulbactam (20 mg/kg IV q8h) plus a fluoroquinolone IV. Adjust antibiotic selection based on results of airway cytology, culture and sensitivity, and clinical response; continue for 10 days after resolution of clinical and radiographic signs; if no signs of sepsis, ampicillin with sulbactam pending results of culture.
- Beta-agonist bronchodilators—sometimes cause dramatic improvement but have the potential to worsen ventilation:perfusion mismatch; most often helpful in acute aspiration or with auscultable wheezes.
- Short-acting corticosteroids—consider for up to 48 hours to combat inflammation associated with life-threatening aspiration.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

- Diuretics—generally contraindicated; drying of airways reduces mucociliary clearance.
- Corticosteroids—contraindicated beyond initial stabilization; predispose patient to infection.
- Fluoroquinolones and chloramphenicol—can prolong clearance of theophylline-derivative bronchodilators; decrease theophylline dosage by 30–50% or prolong dosing interval.



FOLLOW-UP

PATIENT MONITORING

- Radiographs—evaluate every 2–7 days initially to determine appropriateness of treatment; then every 1–2 weeks.
- If signs do not resolve or suddenly worsen—possible recurrence of aspiration or a secondary infection; repeat diagnostic evaluation, including tracheal wash or bronchoscopy.

PREVENTION/AVOIDANCE

- Predisposed patients undergoing anesthesia—cisapride (slow infusion, 1 mL/kg over 30 minutes) 1–2 hours pre-induction may decrease esophageal reflux.
- Suction esophagus prior to extubation.
- Antacids could decrease acid-related lung injury in predisposed patients; may also increase risk of infection.

POSSIBLE COMPLICATIONS

- Secondary infection common.
- ALI/ARDS.
- Abscessation or granuloma formation rare.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—depends on severity of signs and ability to correct underlying disease.
- Severe aspiration—can be fatal.
- Recurrence—likely if underlying cause not addressed.



MISCELLANEOUS

SEE ALSO

- Acute Respiratory Distress Syndrome.
- Megaesophagus.
- Bacterial Pneumonia.

ABBREVIATIONS

- ALI/ARDS = acute lung injury/acute respiratory distress syndrome.

Suggested Reading

Lappin MR, Blondeau J, Boothe D, et al. Antimicrobial use guidelines for the treatment of respiratory tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. J Vet Intern Med 2017; 31:279–294.

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PNEUMONIA, BACTERIAL



BASICS

DEFINITION

Acquired inflammatory response to bacteria in lung parenchyma characterized by exudation of cells and fluid into conducting airways and alveolar spaces.

PATHOPHYSIOLOGY

- Bacteria—enter the lower respiratory tract primarily by inhalation or aspiration; less commonly by the hematogenous route. Infection incites an inflammatory reaction.
- Tracheobronchial tree and carina—normally not sterile.
- Oropharyngeal bacteria—frequently aspirated; may be present for an unknown time period in the normal tracheobronchial tree and lung; can cause or complicate respiratory infection; presence complicates interpretation of airway and lung cultures.
- Respiratory infection—development depends on the complex interplay of many factors: inoculation site, number of organisms and their virulence, and age and resistance of the host.
- Bacteria produce extracellular proteins called invasins that impair host defenses and assist in the spread of bacteria.
- Viral infections—alter bacterial colonization patterns; increase bacterial adherence to respiratory epithelium; reduce mucociliary clearance and phagocytosis; allow resident bacteria to invade the lower respiratory tract.
- Foreign body—inoculates bacteria into a focal lung region and leads to obstructive pneumonia.
- Exudative phase—increased vascular permeability; extravasation of high-protein fluid into interstitial and alveolar spaces.
- Leukocytic migration phase—leukocytes infiltrate the airways and alveoli; consolidation, ischemia, tissue necrosis, and atelectasis owing to bronchial occlusion, obstructive bronchiolitis, and impaired collateral ventilation.

SYSTEMS AFFECTED

Respiratory—primary or secondary infection.

GENETICS

Heritable rhinitis/bronchopneumonia syndrome of Irish wolfhounds, unknown pathogenesis.

INCIDENCE/PREVALENCE

Common in both young and old dogs, less common in cats.

GEOGRAPHIC DISTRIBUTION

Widespread

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Dogs—sporting breeds, hounds, working breeds, and mixed breeds >12 kg.

Mean Age and Range

Dogs—range, 1 month–15 years.

Predominant Sex

Dogs—60% males.

SIGNS

Historical Findings

- Cough.
- Labored breathing.
- Recent vomiting/regurgitation (aspiration).
- Anorexia.
- Lethargy.
- Nasal discharge.

Physical Examination Findings

- Cough.
- Fever.
- Difficult or rapid breathing.
- Abnormal breath sounds on auscultation—increased intensity, crackles, and wheezes.
- Nasal discharge.
- Lethargy.
- Dehydration.

CAUSES

Dogs

- Most common primary pathogens—*Bordetella bronchiseptica* and *Mycoplasma* spp.
- Most common Gram-positive bacteria—*Staphylococcus*, *Streptococcus*, and *Enterococcus* spp.
- Most common Gram-negative bacteria—*Escherichia coli*, *Klebsiella* spp., *Pseudomonas* spp., *Pasteurella* spp.
- Anaerobic bacteria—found in pulmonary abscesses and various types of pneumonia (particularly with aspiration or foreign bodies); reported in ~20% of cases.

Cats

- Bacterial pathogens—poorly documented; *B. bronchiseptica*, *Pasteurella* spp., and *Moraxella* spp. most frequently reported.
- Mycoplasma* spp. may be a primary pathogen in the lower respiratory tract.
- Carrier state—may exist; periods of shedding *B. bronchiseptica* after stress; infected queens may not shed organism prepartum but begin shedding post partum, serving as a source of infection for kittens.

RISK FACTORS

- Prior viral infection.
- Regurgitation, dysphagia, or vomiting.
- Functional or anatomic defects—laryngeal paralysis, brachycephalic breed, megaesophagus, cleft palate, primary ciliary dyskinesia.
- Reduced level of consciousness—stupor, coma, and anesthesia.
- Bronchial foreign body.
- Bronchiectasis.
- Immunosuppressive therapy—chemotherapy, glucocorticoids.
- Severe metabolic disorders—uremia, diabetes mellitus, hyperadrenocorticism.
- Sepsis.
- Age—very young more susceptible to fatal infections.
- Immunization status.
- Environment—housing, sanitation, ventilation.
- Phagocyte dysfunction—feline leukemia virus and diabetes mellitus.
- Complement deficiency—rare.
- Selective IgA deficiency—rare.
- Combined T-cell and B-cell dysfunction—rare.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Viral pneumonia (canine distemper virus, adenovirus, influenza virus, herpesvirus).

• Protozoal pneumonia (*Toxoplasma*).

- Parasitic pneumonia (capillariasis, filarioidiasis, lungworm).
- Fungal pneumonia (*Histoplasma*, *Blastomycetes*, *Coccidioides*, *Cryptococcus*).
- Eosinophilic pneumonia.
- Feline bronchial disease (asthma).
- Pulmonary abscess.
- Pleural infection (pyothorax).
- Bronchial foreign body.

CBC/BIOCHEMISTRY/URINALYSIS

Inflammatory leukogram—neutrophilic leukocytosis with or without a left shift; absence does not rule out the diagnosis.

OTHER LABORATORY TESTS

- Arterial blood gas analysis—values correlate well with the degree of physiologic disruption; sensitive monitor of progress during treatment; $\text{PaO}_2 < 80 \text{ mmHg}$ on room air = mild or moderate hypoxemia; $\text{PaO}_2 < 60 \text{ mmHg}$ on room air = severe hypoxemia.
- Consider viral serology.
- Molecular diagnostics also available for viral and bacterial presence.

IMAGING

Thoracic Radiography

- Variable—diffuse, bronchointerstitial pattern, partial or complete alveolar infiltrates, consolidation.
- Most common—alveolar pattern characterized by increased pulmonary densities (margins indistinct; air bronchograms or lobar consolidation).
- More variable lung patterns in cats such as multifocal, patchy interstitial and alveolar changes and/or a diffuse nodular pattern.

DIAGNOSTIC PROCEDURES

- Microbiologic (aerobic, anaerobic, and *Mycoplasma* culture) and cytology for definitive diagnosis.
- Samples—transtracheal or endotracheal washing, bronchoscopy, bronchoalveolar lavage (with or without bronchoscope), or fine-needle lung aspiration.
- Degenerate neutrophils with septic inflammation (intracellular bacteria) predominating.
- Recent antibiotic administration—nonspecific inflammation likely.
- Bacteria—not always obvious microscopically; always culture specimens even if no bacteria are seen on cytology.

PATHOLOGIC FINDINGS

- Irregular consolidation in cranoventral regions.
- Consolidated lung—varies from dark red to gray-pink to more gray, depending on age of patient and nature of the process.
- Palpable firmness of the tissue.
- Nidus of inflammation—bronchiolar-alveolar junction.
- Early—bronchioles and adjacent alveoli filled with neutrophils and an admixture of cell debris, fibrin, and macrophages; necrotic to hyperplastic epithelium.
- Later—neutrophilic, fibrinous, hemorrhagic, or necrotizing inflammation depending on virulence of bacteria and host response.

(CONTINUED)



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient—recommended with multisystemic signs (e.g., anorexia, fever) or in patients with respiratory compromise in the absence of multisystemic signs.

NURSING CARE

- Maintain normal systemic hydration—important to aid mucociliary clearance and secretion mobilization; use a balanced electrolyte solution.
- Saline nebulization—results in more rapid resolution if used with physical therapy and systemic antimicrobials.
- Physical therapy—chest wall coupage, tracheal manipulation to stimulate mild cough and postural drainage; may enhance clearance of secretions; always do immediately after nebulization; avoid allowing the patient to lie in one position for a prolonged time.
- Oxygen therapy—as warranted for patients with hypoxemia, signs of respiratory distress.

ACTIVITY

Restrict during treatment (inpatient or outpatient), except as part of physical therapy after aerosolization.

DIET

- Ensure normal intake with food high in protein and energy density.
- Enteral or parenteral nutritional support—indicated in severely ill patients.
- Use caution in feeding animals with megaesophagus, laryngeal dysfunction or surgery, pharyngeal disease, or recumbent patients.

CLIENT EDUCATION

Warn client that high morbidity and mortality are associated with severe hypoxemia and sepsis.

SURGICAL CONSIDERATIONS

Lung lobectomy may be required with pulmonary abscessation or bronchopulmonary foreign body with secondary pneumonia; may be indicated if patient is unresponsive to conventional treatment and disease is limited to one or two lobes.



MEDICATIONS

DRUG(S) OF CHOICE

Antimicrobials

- Antimicrobials are best selected based on results of culture and susceptibility testing from tracheal wash or other pulmonary specimens.
- Empiric antimicrobial therapy is justified when there is significant risk in obtaining adequate samples or if the time required to culture causes a life-threatening delay in treatment.
- Recently administered antimicrobials should be avoided.
- Reasonable initial antimicrobial choices pending culture results include amoxicillin-clavulanic acid 15 mg/kg PO q12h or cephalexin 22–30 mg/kg PO q12h with enrofloxacin (dogs,

10–20 mg/kg q24h; cats, maximum 5 mg/kg q24h), or trimethoprim-sulfonamide 15 mg/kg PO q12h. • Gram-positive cocci—ampicillin 20–40 mg/kg IV q6–8h, ampicillin-sulbactam 22–30 mg/kg IV q6–8h; amoxicillin 22 mg/kg PO q12h; amoxicillin-clavulanic acid; azithromycin; chloramphenicol, erythromycin; trimethoprim-sulfonamide; first-generation cephalosporins. • Gram-negative rods—enrofloxacin or marbofloxacin; cefpodoxime; chloramphenicol; trimethoprim-sulfonamide; amikacin. • *Bordetella*—doxycycline 5 mg/kg PO q12h; chloramphenicol; enrofloxacin; azithromycin. • *Mycoplasma*—doxycycline, enrofloxacin, marbofloxacin, chloramphenicol.

• Anaerobes—amoxicillin-clavulanic acid; chloramphenicol; metronidazole; clindamycin; ticarcillin-clavulanic acid. • Antimicrobial nebulization for *Bordetella*—gentamicin nebulization 5 mg/kg q24h for 5–7 days, typically adjunctive with systemic antimicrobials.

Duration of Treatment

- Authors have traditionally recommended continued treatment for at least 10 days beyond clinical resolution and/or 1–2 weeks following radiographic resolution.
- Total of ≤14 days of therapy is not associated with worse outcomes when compared to >14 days of therapy in dogs.

CONTRAINdications

- Anticholinergics and antihistamines—may thicken secretions and inhibit mucokinesis and exudate removal from airways.
- Antitussives—potent, centrally acting agents inhibit mucokinesis and exudate removal from airways; can potentiate pulmonary infection and inflammation.

POSSIBLE INTERACTIONS

Avoid use of theophylline and fluoroquinolones concurrently.

ALTERNATIVE DRUG(S)

- Expectorants—recommended by some clinicians; no objective evidence that they increase mucokinesis or mobilization of secretions.
- Bronchodilators—recommended by some clinicians to alleviate bronchospasm.



FOLLOW-UP

PATIENT MONITORING

- Monitor respiratory rate and effort.
- Complete blood count will normalize.
- Arterial blood gases—sensitive monitor of progress, pulse oximetry can be helpful.
- Frequent thoracic auscultation.
- Thoracic radiographs—improve more slowly than the clinical appearance.

PREVENTION/AVOIDANCE

- Vaccination—against upper respiratory viruses and *Bordetella* if a dog is boarded or exposed to large numbers of other animals.
- Catteries—environmental strategies to lower population density and improve hygiene help control outbreaks of bordetellosis.

PNEUMONIA, BACTERIAL

POSSIBLE COMPLICATIONS

- Sepsis can develop.
- Severe respiratory compromise may require intubation/mechanical ventilation.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—good with aggressive antibacterial and supportive therapy; more guarded in young animals, patients with immunodeficiency, and patients that are debilitated or have severe underlying disease.
- Prolonged infection—potential for chronic bronchitis or bronchiectasis in any patient.
- Mortality—associated with severe hypoxemia and sepsis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Frequently develops secondary to underlying functional or anatomic abnormalities—cleft palate; tracheal hypoplasia; primary ciliary dyskinesia; laryngeal paralysis; megaesophagus or other esophageal dysmotility disorder.
- Bronchiectasis—both predisposing factor and potential complication.

P

AGE-RELATED FACTORS

- Young puppies and kittens—may have a poorer prognosis.
- Underlying functional and anatomic problems and immunodeficiencies—suspect in young patients.

PREGNANCY/FERTILITY/BREEDING

Bitches or queens infected with *B. bronchiseptica*—may transmit infection to neonates.

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Melissa A. Herrera.



Client Education Handout
available online

POLYPHAGIA



BASICS

DEFINITION

Increased food intake.

PATHOPHYSIOLOGY

- Failure to assimilate or loss of nutrients (e.g., maldigestion/malabsorption syndromes such as exocrine pancreatic insufficiency).
- Inability to use nutrients (e.g., diabetes mellitus, poor-quality diets, gastrointestinal parasites).
- Hypoglycemia (e.g., insulinoma, insulin overdose).
- Increased metabolic rate or demand (e.g., hyperthyroidism, cold environments, pregnancy, lactation).
- Psychologic or learned behaviors (e.g., palatable diets, competition with other household pets).
- Iatrogenic (e.g., drugs such as anticonvulsants or glucocorticoids).
- Genetic (e.g., Labrador and flat-coated retrievers).

SYSTEMS AFFECTED

- Cardiovascular—obesity can worsen clinical cardiac disease.
- CNS—tumors of the brain, especially of the hypothalamus, can cause polyphagia.
- Integument—obese animals, especially cats, are susceptible to dermatitis.
- Musculoskeletal—overweight patients are susceptible to arthritis and other orthopedic problems.
- Respiratory—obesity exacerbates dyspnea in patients with respiratory disease.

SIGNALMENT

- Dogs and cats.
- Some dog breeds are prone to obesity: beagle, Rottweiler, cocker spaniel, dachshund, Shetland sheepdog, dalmatian, and the retrievers.

SIGNS

Historical Findings

- Eating more frequently and/or a greater quantity than normal.
- Excessive food-seeking and food-stealing behaviors.
- Weight loss may occur with certain disease states (e.g., exocrine pancreatic insufficiency, diabetes mellitus, hyperthyroidism).
- Polyuria/polydipsia (PU/PD) occurs in some patients (diabetes mellitus, hyperthyroidism, hyperadrenocorticism).

Physical Examination Findings

Patients may have excessive body fat, but those with an underlying medical problem (e.g., exocrine pancreatic insufficiency, diabetes mellitus, hyperthyroidism) may be thin.

CAUSES

Physiologic

- Pregnancy.
- Lactation.
- Growth.
- Response to a cold environment.
- Increased exercise.
- Genetic predispositions:
 - 14-bp deletion in the pro-opiomelanocortin (*POMC*) gene of Labrador and flat-coated retrievers leading to increases in obesity, adiposity, and food motivation.
 - Polymorphism in the melanocortin 4 receptor gene (*MC4R*: c.92C>T) predisposing obese cats to development of diabetes mellitus.

Pathologic

- Diabetes mellitus.
- Hyperthyroidism—cats.
- Hyperadrenocorticism—dogs.
- Exocrine pancreatic insufficiency.
- Gastrointestinal parasites.
- Insulinoma.
- Insulin overdose.
- Lymphangiectasia.
- Growth hormone-secreting pituitary tumor.
- Megaesophagus.
- Lymphocytic plasmacytic enteritis in cats—uncommon.
- Neoplasms of the brain—rare.
- Gastrointestinal neoplasms—rare.
- Compulsive polyphagia—rare.

Iatrogenic

- Corticosteroids.
- Progestins.
- Benzodiazepines.
- Anticonvulsants.
- Palatable food.
- Free feeding/overfeeding.
- Poor diet.
- Competition for food.

RISK FACTORS

Environmental

- Lower income owners.
- Older age of the patient.
- Older age of the owner.
- Female spayed > male neutered > intact both sexes.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

PU/PD (excessive trips to food/water area)—differentiate by observation.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia, monocytosis, lymphopenia, and eosinopenia with hyperadrenocorticism, and in patients receiving corticosteroids.
- Hyperglycemia with diabetes mellitus, growth hormone-secreting pituitary tumors

(cats, insulin-resistant diabetes mellitus), and hyperadrenocorticism (mild).

- Hypercholesterolemia with recent food intake, hyperadrenocorticism, and diabetes mellitus, and in patients receiving corticosteroids.
- High alkaline phosphatase and alanine aminotransferase activity with hyperadrenocorticism (dogs), hyperthyroidism (cats), and diabetes mellitus, and in patients receiving corticosteroids.
- Hypoproteinemia with protein-losing enteropathies (e.g., lymphangiectasia, inflammatory bowel disease).
- Hypoglycemia in patients with insulinoma or insulin overdose.
- Low urine specific gravity with diabetes mellitus, diabetes insipidus, hyperthyroidism, and hyperadrenocorticism, and in patients receiving corticosteroids.
- Glucosuria, possibly ketonuria, with diabetes mellitus.

OTHER LABORATORY TESTS

- Fecal examination to rule out gastrointestinal parasites.
- Serum trypsin-like immunoreactivity to diagnose exocrine pancreatic insufficiency.
- Total serum T_4 to rule out hyperthyroidism (cats); T_3 suppression testing if hyperthyroidism is suspected but serum total T_4 is normal.
- Low-dose dexamethasone suppression or adrenocorticotropic hormone (ACTH) stimulation test to diagnose hyperadrenocorticism; plasma ACTH level or high-dose dexamethasone suppression testing to differentiate pituitary-dependent hyperadrenocorticism from adrenal tumor if hyperadrenocorticism is confirmed with the low-dose dexamethasone suppression test or ACTH stimulation test.
- Serum insulin levels in hypoglycemic patients to rule out insulinoma.

IMAGING

- Abdominal radiology may demonstrate hepatomegaly associated with hyperadrenocorticism, diabetes mellitus, and corticosteroid administration.
- Abdominal ultrasonography may demonstrate an adrenal mass or bilateral adrenomegaly (hyperadrenocorticism), hepatomegaly (hyperadrenocorticism, diabetes mellitus, and corticosteroid administration), bowel wall thickening or bowel wall layering disruption (inflammatory bowel disease, lymphoma, lymphangiectasia), and pancreatic masses (insulinoma).
- MRI could be used to visualize a neoplasm of the hypothalamus.

DIAGNOSTIC PROCEDURES

Endoscopy with biopsy of the upper gastrointestinal tract to rule out gastrointestinal diseases.

POLYPHAGIA



TREATMENT

- Usually outpatient medical management.
- Polyphagia without weight gain or with weight loss is more likely due to a medical problem; evaluate the animal prior to food restriction or manipulation.
- Once pathologic causes of polyphagia have been excluded, limit the amount of food available, feed a reduced-calorie diet, and/or increase exercise if obesity or weight gain is present:
 - Owners must measure food to accurately assess intake.
 - Gram scale measuring provides best accuracy.
 - Some dogs may benefit by the addition of low-calorie bulky foods such as canned or frozen green beans.
 - Feeding smaller meals 2–3 times daily may be beneficial for some patients, provided the total food provided remains the same as required by life stage and activity to promote weight loss or prevent weight gain.
 - Removing the pet during human meal preparation and consumption to reduce begging behavior and the pet obtaining additional food.
 - Slowing down the rate of eating may be beneficial in some dogs, using food-dispensing toys that require manipulation to obtain daily ration.
 - If social issues within the home influence intake these must be addressed:
 - Feed all dogs in separate locations, preferably without visual contact.
 - Have multiple feeding stations available in a multiple-cat home.
 - The average animal's daily caloric need can be estimated by the formula $30 \times \text{weight (kg)} + 70$:
 - Alternatively, using the website <https://petnutritionalliance.org/> can provide clinicians with the ability to quickly calculate necessary weight loss and feeding amounts based on specific diet being fed.
 - Chew toys can be used as a substitute for food and desires for mastication.

P



MEDICATIONS

DRUG(S) OF CHOICE

- See specific diseases for detailed therapy.
- Drug-induced—attempt to taper or discontinue drug.
- If a compulsive eating disorder is suspected in dogs, clomipramine 1–3 mg/kg PO q12h or fluoxetine 1–2 mg/kg q24h may be used or in cats clomipramine 0.25–1.0 mg/kg q24h or fluoxetine 0.5–1.0 mg/kg q24h.



FOLLOW-UP

PATIENT MONITORING

- Monitor body weight in patients with nonpathologic causes of polyphagia.
- Assess compliance with feeding regime and food measurement to decrease intake and promote weight loss.

POSSIBLE COMPLICATIONS

- Obesity in nonpathologic polyphagia.
- Owner compliance:
 - Owner responds to begging behavior and caloric intake is not decreased.
 - Owner does not factor treats or additives into daily caloric count.
- Weight loss/emaciation in pathologic causes of polyphagia.
- Worsening of respiratory or cardiovascular disease processes in obese patient.
- Difficulty achieving level of appropriate exercise due to respiratory, cardiovascular, or musculoskeletal diseases.
- Decreased metabolic rate after spaying/neutering.
- Increased resource guarding behaviors.

- Dietary options:
 - High fiber, high protein diets provide greater satiety and reduce begging behavior (e.g., Royal Canin Veterinary Diet® Canine and Feline Satiety® Support).
 - Metabolism-increasing diets naturally increase metabolic rate (e.g., Hill's® Prescription Diet® Metabolic Canine and Feline).

- Increased irritability and aggression.
- Anesthetic complications associated with obesity and adiposity.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Obesity

PREGNANCY/FERTILITY/BREEDING

A normal physiologic response to pregnancy.

SYNONYMS

- Eating disorder.
- Hyperphagia.

SEE ALSO

- Compulsive Disorders—Cats.
- Compulsive Disorders—Dogs.
- Coprophagia and Pica.
- Obesity.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- PU/PD = polyuria/polydipsia.
- T_3 = triiodothyronine.
- T_4 = thyroxine.

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Acknowledgment The authors and editors acknowledge the prior contribution of Katherine A. Houpt.

(CONTINUED)

POLYURIA AND POLYDIPSIA



BASICS

DEFINITION

- Polyuria (PU)—increased urine production (dogs, >45 mL/kg/day; cats, >40 mL/kg/day).
- Polydipsia (PD)—increased water consumption (dogs, >90 mL/kg/day; cats, >45 mL/kg/day).

PATHOPHYSIOLOGY

- The volumes of urine produced and water consumed are controlled by interactions between the kidneys, pituitary gland, and hypothalamus through monitoring of plasma osmolality. Volume receptors within the atria and aortic arch also influence thirst and urine production. PU may occur when the quantity of functional antidiuretic hormone (ADH) synthesized in the hypothalamus or released from the posterior pituitary is limited, or when the kidneys fail to respond normally to ADH. PD occurs when the thirst center in the anterior hypothalamus is stimulated.
- In most PU patients, plasma becomes relatively hypertonic and activates thirst mechanisms; the PD maintains hydration as a compensatory response. Occasionally PD is the primary process and PU is compensatory. In this case, the patient's plasma becomes relatively hypotonic because of excessive water intake, ADH secretion is reduced, resulting in PU.

SYSTEMS AFFECTED

- Urologic—full bladder.
- Cardiovascular—circulating volume.
- Endocrine/metabolic—pituitary gland, hypothalamus play a role in compensation to PU or PD.

SIGNALMENT

- Dog and cat.
- Congenital diseases in many breeds (e.g., central diabetes insipidus [CDI], nephrogenic diabetes insipidus [NDI], portavascular anomaly, kidney disease).
- Kidney disease, hyperadrenocorticism (HAC), hyperthyroidism, neoplasia affecting the pituitary or hypothalamus predominantly affect middle-aged and older animals.

CAUSES

- Primary PU due to impaired kidney response to ADH—kidney disease, HAC, hyperthyroidism, pyelonephritis, leptospirosis, pyometra, hepatic failure, hypercalcemia, hypokalemia, kidney medullary solute washout, dietary protein restriction, drugs, congenital NDI.
- Primary PU caused by osmotic diuresis—diabetes mellitus (DM), primary kidney glucosuria, postobstructive diuresis, some diuretics (e.g., mannitol and furosemide), ingestion or administration of large quantities of solute (e.g., sodium chloride or glucose), and hypersomatotropism.

- Primary PU due to ADH deficiency—idiopathic, traumatic, neoplastic, or congenital CDI; some drugs (e.g., alcohol and phenytoin).

- Primary PD—behavioral, pyrexia, pain, organic disease of the anterior hypothalamic thirst center of neoplastic, traumatic, or inflammatory origin.

RISK FACTORS

- Kidney, liver and/or endocrine disease.
- Administration of diuretics, corticosteroids, anticonvulsants.
- Low-protein diets.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiating Similar Signs

- Differentiate PU from pollakiuria. Pollakiuria: often associated with dysuria, stranguria, hematuria. Patients with PU void large quantities of urine; patients with pollakiuria frequently void small quantities of urine. Confirm PU/PD by measuring 24-hour water intake and urine output (3- to 5-day collection period preferred).
- Urine specific gravity (USG) measurement may provide evidence of hypersthenuria (dogs, >1.030; cats, >1.035), ruling out persistent PU/PD.

Differentiating Causes

- Kidney disease, HAC, DM, hyperthyroidism.
- Progressive weight loss—consider chronic kidney disease, DM, hyperthyroidism, hepatic failure, pyometra, pyelonephritis, hyperadrenocorticism, malignancy-induced hypercalcemia.
- Decreased appetite—consider kidney disease, pyelonephritis, malignancy-induced hypercalcemia, hepatic disease, hyperadrenocorticism.
- Polyphtagia—consider DM, hyperthyroidism, HAC, acromegaly.
- Bilateral alopecia or other cutaneous problems—consider HAC, endocrinologic disorders
- Uremic breath and stomatitis—consider advanced kidney disease.
- Vomiting—consider kidney disease, hyperadrenocorticism, pyelonephritis, hepatic failure, hypercalcemia, hypokalemia, hyperthyroidism, DM.
- Malaise and/or weakness—kidney disease, hyperadrenocorticism, pyometra, hypercalcemia, DM, hepatic disease, hypokalemia, HAC.
- Palpable thyroid nodule—consider hyperthyroidism.
- Hypertensive retinopathy—consider chronic kidney disease (CKD), hyperthyroidism, DM, HAC.

- Recent estrus (previous 2 months) in a middle-aged intact female—consider pyometra.

- Abdominal distention—consider hepatic failure, HAC, pyometra, nephrotic syndrome.

- Lymphadenopathy, anal sac mass or other neoplastic process—consider hypercalcemia of malignancy.

- Behavioral or neurologic disorder—consider hepatic failure, primary PD, CDI.

- Marked PD (patients almost continuously seek and consume water)—consider primary PD, CDI, NDI.

- Consider drug-induced (steroids, diuretics, anticonvulsants) PU/PD.

- Consequence of urolith prevention/dissolution or high salt diet.

Key point: PU/PD may be the first symptom of many diseases.

CBC/BIOCHEMISTRY/URINALYSIS

- Urinalysis is useful to confirm PU, discriminate water diuresis from solute diuresis, and identify urinary tract infection (UTI).
- Serum sodium concentration or osmolality may help differentiate primary PU from PD. Measuring serum osmolality is preferred; calculated serum osmolality is not an acceptable alternative.
- Relative hypernatremia or high serum osmolarity suggests primary PU.
- Hyponatremia or low serum osmolarity suggests primary PD, except in animals with hypoadrenocorticism, which have hyponatremia and primary PU.
- Azotemia is typical of kidney causes for PU/PD, but may also indicate dehydration resulting from inadequate compensatory PD.
- Unexpectedly low BUN concentrations suggest hepatic failure.
- With high hepatic enzymes, consider HAC, hyperthyroidism, hepatic failure, pyometra, DM, or administration of drugs (e.g., anticonvulsants and corticosteroids).
- Persistent hyperglycemia suggests DM.
- Hyperkalemia, particularly if associated with hyponatremia, suggests hypoadrenocorticism or therapy with potassium-sparing diuretics.
- Hypercalcemia induces PU only when it results from increased ionized calcium (not protein-bound calcium) concentration.
- Hypoalbuminemia supports kidney or hepatic causes of PU/PD.
- Neutrophilia is consistent with pyelonephritis, pyometra, HAC, corticosteroid administration.
- USG values 1.001–1.003 suggest primary PD, CDI, and congenital NDI.
- Glucosuria supports a diagnosis of DM or kidney glucosuria.
- Pyuria, white blood cell casts, and/or bacteriuria should prompt consideration of pyelonephritis.

PROLAPSED GLAND OF THE THIRD EYELID (CHERRY EYE)



BASICS

OVERVIEW

- Definition—prolapsed gland of the third eyelid.
- Pathophysiology—the gland is normally anchored by a fibrous attachment to the periorbita beneath the third eyelid. In cases of prolapse these attachments are weak, resulting in dorsal movement of the gland. Commonly occurs in dogs and rarely in cats; animals may have unilateral or bilateral prolapse.

SIGNALMENT

- Dog and cat.
- Dog—usually in young dogs (6 months to 2 years of age); common breeds: American cocker spaniel, English bulldog, beagle, bloodhound, Lhasa apso, mastiff, shih tzu, other brachycephalic breeds.
- Cat—rare; occurs in Burmese, Persians, and has been reported in domestic shorthair cats.

SIGNS

- Oval, hyperemic mass protruding from behind the leading edge of the third eyelid in the medial canthus.
- May be unilateral or bilateral.
- May see signs of epiphora, hyperemic conjunctiva, keratitis, or blepharospasm.
- Additional swelling and hyperemia of the exposed gland can result from environmental exposure leading to irritation and desiccation.

CAUSES & RISK FACTORS

- Congenital weakness of the attachment of the gland of the third eyelid.
- Inheritance unknown but considered complex and multigenic.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Scrolled or everted cartilage of the third eyelid—seen in Weimaraner, Great Dane, German shorthaired pointer, and other breeds in which the T-shaped cartilage of the third eyelid is rolled away from the surface of the cornea instead of conforming to the surface of the cornea.
- Neoplasia of the third eyelid—usually seen in older animals. Most common third eyelid neoplasms in the dog are adenocarcinoma, adenoma, and squamous cell carcinoma. May also see lymphoma or fibrosarcoma. Most common third eyelid neoplasms in the cat are adenocarcinoma followed by squamous cell carcinoma. A small incisional biopsy is indicated to differentiate.
- Orbital fat prolapse—may dissect anteriorly between the conjunctiva and globe; occasionally occurs in the medial canthus.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

N/A



TREATMENT

- Surgical replacement of the gland (various techniques can be performed)—see Suggested Reading.
- Gland excision contraindicated; gland can produce up to 50% (or more) of the aqueous tear film; puts patient at substantial risk for developing keratoconjunctivitis sicca as the dog ages. Excision may be considered if neoplasia is confirmed, although potential complications and risks should be discussed.
- Elizabethan collar—to prevent self-trauma.



MEDICATIONS

DRUG(S) OF CHOICE

- Topical anti-inflammatory medications, such as corticosteroids (if no corneal ulceration) or nonsteroidal anti-inflammatory medications—may be used before and after surgery.
- Topical lubricating medications (ointments or gels)—may be used to reduce environmental exposure causing irritation and/or desiccation.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

- Recurrence—5–20%, depending on the breed, with large-breed dogs (e.g., mastiff) having the highest recurrence rates; replacement of the gland is encouraged.
- If unilateral, warn client that the other gland may also prolapse and that no preventive procedure or medication exists.



MISCELLANEOUS

SYNONYMS

Cherry eye.

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Brian C. Gilger.

PROTEIN-LOSING ENTEROPATHY



BASICS

DEFINITION

• A disease process characterized by excessive loss of protein into the gastrointestinal (GI) lumen. • Protein-losing enteropathy (PLE) may be associated with primary GI diseases (e.g., inflammatory bowel disease, intestinal lymphoma, or intestinal lymphangiectasia) and systemic disorders (e.g., fungal disease or congestive heart failure [CHF]).

PATHOPHYSIOLOGY

• Under physiologic conditions, two-thirds of normal protein loss in dogs occurs through the small intestine. • Plasma proteins that leak into the GI lumen are rapidly digested into constituent amino acids that can be reabsorbed and used for the synthesis of new proteins. • This normal loss of plasma proteins can be accelerated by GI mucosal disease or by increased leakage of lymph into the GI lumen. • GI protein loss is associated with loss of both albumin and globulin, often resulting in panhypoproteinemia. • In response to increased GI protein loss, the liver increases albumin synthesis. However, the liver cannot increase albumin synthesis to more than twice the normal output. • When protein loss exceeds protein synthesis, hypoproteinemia results. • Hypoproteinemia causes decreased plasma oncotic pressure, which may lead to hemodynamic changes, effusion into body cavities or peripheral edema.

SYSTEMS AFFECTED

• Coagulation—patients with PLE lose antithrombin and other anticoagulants, resulting in a hypercoagulable state which may lead to thromboembolic events such as pulmonary thromboembolism (PTE). • GI—primary GI disease may be associated with diarrhea, vomiting, or weight loss. • Hemodynamic—decreased oncotic pressure leading to cavitary effusion. • Lymphatic—lymphangiectasia. • Respiratory—dyspnea due to pleural effusion or PTE. • Skin—subcutaneous edema.

GENETICS

PLE due to specific underlying causes is suspected to be hereditary based on an increased prevalence in specific dog breeds.

INCIDENCE/PREVALENCE

• Unknown. • Many dogs with subacute or acute gastroenteritis have transient PLE.

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Soft-coated wheaten terrier, Basenji, Yorkshire terrier, and Norwegian lundehund.

Mean Age and Range

Any age.

Predominant Sex

No predilection.

SIGNS

General Comments

Clinical signs are variable.

Historical Findings

• Chronic diarrhea, weight loss, sarcopenia, and lethargy are most frequently reported. However, many dogs with PLE have normal stools. • Vomiting is uncommon. • Dogs can be presented for apparent weight gain or abdominal distension.

Physical Examination Findings

• Ascites, dependent edema, and dyspnea from pleural effusion may be detected in patients with marked hypoproteinemia. • Abdominal palpation may reveal thickened bowel loops, though this is uncommon.

CAUSES

Disorders of Lymphatics

• Intestinal lymphangiectasia. • GI lymphoma. • Granulomatous infiltration of the small bowel. • CHF leading to lymphatic hypertension.

Diseases Associated with Increased Mucosal Permeability or Mucosal Ulceration

• Viral gastroenteritis—parvovirus and others. • Bacterial gastroenteritis—salmonellosis and others. • Fungal gastroenteritis—histoplasmosis and others (note: serum globulin concentrations can be within the reference interval due to increased production secondary to massive antigenic stimulation). • Parasitic enteritis—hookworms, whipworms, and others. • Inflammatory bowel disease—lymphocytic-plasmacytic, eosinophilic, or granulomatous gastroenteritis. • Adverse food reactions. • Mechanical enteropathies—chronic intussusception, chronic foreign body, and others. • Intestinal neoplasia—lymphoma, adenocarcinoma, and others. • Gastric or intestinal ulcers.

RISK FACTORS

• GI disease. • Lymphatic disease. • Heart disease.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

• Hypoalbuminemia due to hepatic failure—often associated with normal or increased serum globulin concentration. Hepatic enzyme activity may be increased, serum BUN, cholesterol, and glucose may be decreased, and serum pre- and postprandial bile acids concentrations may be increased. • Hypoalbuminemia due to protein-losing nephropathy (PLN)—mild in patients with fever or hyperadrenocorticism, moderate to severe in patients with glomerulonephritis or amyloidosis; commonly associated with a normal or increased serum globulin

concentration; ruled out by a normal urine protein:creatinine ratio. • Hypoalbuminemia due to severe blood loss: excluded by assessment of the CBC and a thorough physical examination; in some cases a test for fecal occult blood may be necessary. • Starvation is a rare cause of hypoalbuminemia.

CBC/BIOCHEMISTRY/URINALYSIS

• Hypoalbuminemia and frequently hypoglobulinemia (panhypoproteinemia). • Normal or increased serum globulin concentration in some cases, if the underlying disease is associated with chronic antigenic stimulation (e.g., immunoproliferative enteropathy of the basenji). • Hypocalcemia. • Hypcholesterolemia. • Lymphopenia may be seen with lymphangiectasia.

OTHER LABORATORY TESTS

• Increased fecal α_1 -protease inhibitor concentration (must be assessed in naturally passed and freshly frozen fecal samples from 3 consecutive days). • Once PLE has been identified as the cause of the hypoalbuminemia, specific tests may be useful to determine the cause of PLE: multiple fecal examinations to rule-out intestinal parasitism as a cause of PLE; serum cobalamin and folate concentrations to diagnose small intestinal dysbiosis or cobalamin deficiency.

IMAGING

• Thoracic radiographs may show evidence for cardiac, mediastinal, or fungal disease. • Abdominal radiographs may show evidence for a mechanical enteropathy (i.e., foreign body, intussusception, or other). • Abdominal ultrasound may show evidence for a mechanical enteropathy or other causes of PLE. • Abdominal ultrasound is helpful for evaluating the pattern of intestinal wall layering that can be associated with a variety of enteropathies. Hyperechoic mucosal striations ("tiger stripe" effect), mucosal speckles, and a hyperechoic line within the mucosa that runs parallel to the submucosa are common findings in dogs with intestinal lymphangiectasia. • Echocardiogram may show evidence for cardiac disease.

DIAGNOSTIC PROCEDURES

• Broad-spectrum anthelmintic agent to treat for potential parasitism. • Elimination diet trial using a novel or hydrolyzed protein source to rule out food sensitivity. One study in a group of soft-coated wheaten terriers suggests a hydrolyzed protein diet may be the best choice in dogs with PLE. • Histoplasma antigen test (serum or urine) and rectal mucosal scraping in geographic regions where histoplasmosis is endemic. • Gastroduodenoscopy and colonoscopy—to visualize the GI mucosa and to collect endoscopic biopsies for histopathologic evaluation. Visualization of white "plaques" (e.g., chylomicron distended lacteals) along the mucosa suggests lymphangiectasia. • Abdominal exploratory laparotomy may show dilated intestinal lymphatics and allows for full-thickness biopsies of intestines and lymph

(CONTINUED)

nodes. • Fecal α_1 -protease inhibitor concentration to document excessive GI protein loss. Assays are species-specific and currently only an assay for measurement of α_1 -protease inhibitor in dogs is available through the GI Laboratory at Texas A&M University. Samples from 3 consecutive defecations need to be collected in special preweighed fecal tubes that can be sourced from the GI Lab.

PATHOLOGIC FINDINGS

- In dogs with PLE due to lymphangiectasia, gross findings may include dilated lymphatics that are visible as a web-like network throughout the mesentery and serosal surface.
- May see small yellow-white nodules and foamy granular deposits adjacent to lymphatics (lipogranulomas). • Lacteal dilatation, villous blunting, and crypt lesions (e.g., dilatation, cysts, abscesses) are the most consistent findings on histopathology in dogs with lymphangiectasia and PLE. • PLE due to other causes may show lesions specific for the disease.



TREATMENT

APPROPRIATE HEALTH CARE

Inpatient or outpatient medical management depending on the severity of clinical signs at the time of diagnosis.

NURSING CARE

- With clinical signs due to edema or effusion from severe hypoalbuminemia, albumin transfusion, or colloids (such as hetastarch) may be considered to increase plasma oncotic pressure. Both human and canine albumin can provide a temporary increase in serum albumin, but human albumin transfusion may be associated with adverse reactions in dogs.
- Abdominocentesis to remove ascites or pleurocentesis to remove pleural effusion is indicated in cases where effusion has led to respiratory compromise. • Consider placement of an esophageal feeding tube in hyporexic patients to meet increased caloric demands.

ACTIVITY

Normal

DIET

- May need to be modified depending on the underlying cause of PLE. • If lymphangiectasia is diagnosed or highly suspected, an ultra-low-fat diet, containing 20 g fat/1,000 kcal or less, is indicated. It should be noted that there are currently no commercial diets lower than 20 g fat/1,000 kcal and one study has suggested that an even lower fat content is beneficial.

CLIENT EDUCATION

Prepare clients for long-term therapy; spontaneous cures are rare.

SURGICAL CONSIDERATIONS

- Hypoalbuminemia increases postoperative morbidity because of slow wound healing.
- Some causes of PLE (e.g., intussusception,

chronic foreign body, and some intestinal neoplasms), however, require surgical intervention.



MEDICATIONS

DRUG(S) OF CHOICE

- There is no pharmacologic therapy for PLE itself. Instead, the underlying cause of PLE must be addressed.
- However, patients with PLE also lose antithrombin and other anticoagulants and can be hypercoagulable. Thus, patients should be treated with a platelet aggregation inhibitor:
 - In dogs or cats—clopidogrel bisulfate (1–4 mg/kg PO q24h in dogs; 18.75 mg/cat PO q24h, which equals one-fourth of a 75 mg tablet).
 - In dogs—low-dose aspirin (0.5 mg/kg PO q12h; use an 81 mg tablet of aspirin and put into the barrel of a 10 mL syringe, add 8.1 mL of water and shake until completely dissolved to make a 10 mg/mL solution; discard unused portion immediately).

CONTRAINDICATIONS

- Aspirin and clopidogrel should not be used concurrently.
- Clopidogrel should not be used with NSAIDs, phenytoin, torsemide, or warfarin.

PRECAUTIONS

Bleeding may be enhanced in patients treated with platelet aggregation inhibitors that have to undergo surgery.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Diuretics such as furosemide (1 mg/kg PO q12h) in combination with spironolactone (1 mg/kg PO q12h) have been used by some clinicians to control edema, pleural effusion, and ascites. However, they do not work consistently in patients with PLE because of decreased plasma oncotic pressure and may be associated with side effects. • There are anecdotal reports about the use of the long-acting somatostatin analogue octreotide in dogs with PLE, but no clinical trials have been completed to date and no specific dosing regimen has been suggested.



FOLLOW-UP

PATIENT MONITORING

Check body weight, serum albumin concentration, and evidence of recurrent clinical signs (i.e., pleural effusion, ascites, and/or edema). Frequency depends on the severity of the condition. Monitor serum cobalamin concentration if patient was hypcobalaminemic and supplemented with cobalamin.

PREVENTION/AVOIDANCE

N/A

PROTEIN-LOSING ENTEROPATHY

POSSIBLE COMPLICATIONS

- Thromboembolic events, especially PTE.
- Respiratory difficulty from pleural effusion or PTE. • Severe protein-calorie malnutrition.
- Intractable diarrhea.

EXPECTED COURSE AND PROGNOSIS

- Prognosis is guarded and depends on the underlying cause. Smaller breed dogs carry a more favorable prognosis because nutritional support is easier to perform. • The primary disease cannot be treated in many cases.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Soft-coated wheaten terriers may have PLN in conjunction with PLE and should be evaluated accordingly.

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Some GI parasites have zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

N/A

SEE ALSO

- Cobalamin Deficiency.
- Diarrhea, Chronic—Cats.
- Diarrhea, Chronic—Dogs.
- Inflammatory Bowel Disease.
- Lymphangiectasia.

ABBREVIATIONS

- CHF = congestive heart failure.
- GI = gastrointestinal.
- NSAID = nonsteroidal anti-inflammatory drug. • PLE = protein-losing enteropathy.
- PLN = protein-losing nephropathy.

INTERNET RESOURCES

<http://vetmed.tamu.edu/gilab/>

Suggested Reading

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Client Education Handout
available online

PROTEINURIA



BASICS

DEFINITION

- Urinary protein detected by dipstick analysis, urinary protein:creatinine ratio (UP:C ≥ 0.4 in cats or ≥ 0.5 in dogs), urinary albumin:creatinine ratio (UA:C $> 30 \text{ mg/g}$), or 24-hour urine protein content ($> 20 \text{ mg/kg}$). UP:C of 0.2–0.4 in cats and 0.2–0.5 in dogs is borderline.
- Microalbuminuria (MA) is the abnormal presence of low concentrations of albumin in the urine (1–30 mg/dL), below the limit of detection of standard urine dipsticks.

PATHOPHYSIOLOGY

- Prerenal—greater than normal delivery of low-molecular-weight plasma proteins to glomeruli.
- Renal, glomerular—excessive loss of larger molecular weight proteins (e.g., albumin) across the glomerular basement membrane (GBM) secondary to altered permselectivity of glomeruli.
- Renal, tubular—reduced tubular reabsorption of proteins.
- Postrenal—exudation of blood or plasma into lower urinary tract.

SYSTEMS AFFECTED

- Renal/urologic—chronic glomerular proteinuria causes progressive tubular damage resulting in chronic kidney disease (CKD).
- Cardiovascular—systemic hypertension.
- Hemic/lymphatic/immune—severe glomerular proteinuria can lead to edema and/or hypercoagulability. Hypercoagulability is brought about by vascular stasis, hyperfibrinogenemia, platelet abnormalities, loss of antithrombinic substances, and an increase in procoagulant factors. The pathogenesis of edema involves both inappropriate renal sodium retention and decreased plasma oncotic pressure.

GENETICS

Familial nephropathies associated with glomerular proteinuria have been described in several breeds of dogs; in only a few has the mode of inheritance been established: Samoyed (X-linked), English cocker spaniel (autosomal recessive), bull terrier (autosomal dominant), Dalmatian (autosomal dominant), Bernese mountain dog (autosomal recessive), Brittany spaniel (autosomal recessive), bullmastiff (autosomal recessive), Newfoundland (autosomal recessive), soft-coated wheaten terrier (complex), Chinese shar-pei (suspect autosomal recessive). Doberman pinscher, Rottweiler, Pembroke Welsh corgi, beagle, English foxhound, and others.

INCIDENCE/PREVALENCE

- In a study of urinalysis data from 500 dogs, the prevalence of proteinuria was approximately 19%.
- The prevalence of MA was 25% in dogs and 25% in cats. Prevalence increased with advancing age.

GEOGRAPHIC DISTRIBUTION

None, however an association may be observed with some infectious diseases that are regional.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Glomerular proteinuria may be the initial manifestation of several familial renal diseases (see Genetics).

Mean Age and Range

Proteinuria can occur at any age. Familial renal diseases tend to occur in younger animals; acquired glomerular proteinuria more likely in middle-aged or older animals

Predominant Sex

Varies with different diseases

SIGNS

- Vary with underlying cause and severity of proteinuria.
- Patients with glomerular proteinuria are frequently asymptomatic or have signs attributable to underlying diseases.

Historical Findings

- Weight loss and lethargy; animals with pulmonary thromboembolism may have acute dyspnea.
- Patients with lower urinary tract (LUT) disorders may have dysuria, pollakiuria, inappropriate urination, and/or hematuria.

Physical Examination Findings

- May have edema or abdominal distention.
- May have oral ulceration (if uremic), edema or cavity effusion, or changes in pulse quality (if thromboembolic).

CAUSES

Prerenal Proteinuria

Overload proteinuria—tubular resorptive capacity exceeded by large amounts of low-molecular-weight plasma proteins in glomerular filtrate (e.g., excessive hemolysis or rhabdomyolysis, neoplastic production of paraproteins or Bence Jones proteins).

Renal Proteinuria

- Functional proteinuria—strenuous exercise, fever, hypothermia, seizures, or venous congestion.
- Glomerulonephritis (e.g., immune complex-mediated, membranous, membranoproliferative, proliferative), minimal change disease, hereditary nephritis, amyloidosis, podocyopathy, focal segmental glomerulosclerosis, glomerulosclerosis.

- All glomerular diseases can be associated with severe proteinuria, subsets of immune complex-mediated (particularly membranoproliferative and membranous) may be associated with higher magnitude proteinuria than others.

- Tubular dysfunction resulting in failure of tubular protein reabsorption is associated with mild-to-moderate proteinuria.

Postrenal Proteinuria

Hemorrhage or inflammation of the urogenital tract.

RISK FACTORS

- Chronic inflammatory (e.g., infectious and immune-mediated) and neoplastic diseases can lead to development of glomerulonephritis or amyloidosis. Examples include dirofilariasis, ehrlichiosis, borrellosis, babesiosis, chronic bacterial infections (e.g., endocarditis, pyoderma), pyometra, bartonellosis, feline immunodeficiency virus, mast cell tumor, lymphosarcoma, hyperadrenocorticism, and systemic lupus erythematosus.
- Systemic hypertension.
- Chronic hyperlipidemia.
- Multiple myeloma can produce Bence Jones proteinuria.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Differentiate prerenal, postrenal, and renal-tubular from glomerular causes.

CBC/BIOCHEMISTRY/URINALYSIS

- Urine dipstick and sulfosalicylic acid (SSA) tests allow qualitative and semiquantitative assessment of urine protein content. Results are affected by urine concentration and must be interpreted in context of urine specific gravity. Low urine protein (trace or 1+) may be normal in a concentrated urine sample.
- The dipstick lacks specificity (dog, 69%; cat, 31%) and sensitivity (dog, 54%; cat, 60%).
- False-positive test results occur when urine is highly alkaline ($\text{pH} > 8-9$) or when the dipstick is immersed in the urine for a prolonged time.
- Low concentrations of Bence Jones proteins or gamma globulins may not be detected by urine dipstick.
- SSA turbidometric test results are falsely increased by radiographic contrast media, penicillins, sulfisoxazole, or the urine preservative thymol.
- SSA test results are falsely decreased by very alkaline urine and increased by uncentrifuged urine.
- If proteinuria is detected by these methods, the urine sediment should be evaluated for hematuria, pyuria, and/or bacteriuria. Hematuria alone typically does not increase urine albumin content above the negligible range (i.e., $> 1 \text{ mg/dL}$) or the UP:C above 0.4

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PROTEINURIA

until there is a color change in the urine. 81% of dogs with pyuria had normal UP:C.

- To determine persistence, repeat the urine protein screening test in proteinuric patients that initially have a normal urine sediment or have been treated for urinary tract inflammation or hemorrhage. If proteinuria is transient and the urine sediment is normal, consider functional proteinuria or false-positive test results.
- Although not all animals with glomerular disease are hypoalbuminemic, glomerular proteinuria should be suspected when proteinuria and hypoalbuminemia are concurrent. As disease progresses, clinicopathologic changes consistent with glomerular disease may develop.

OTHER LABORATORY TESTS

- Urine protein should be quantified in dogs and cats that have hypoalbuminemia and/or repeatedly positive urine dipstick or SSA tests in absence of LUT hemorrhage or inflammation. The UP:C is the preferred because more is known about use of this test and it is technically easier to perform than 24-hour urine collections.
- MA is detected in dogs using a point-of-care immunoassay or quantitation using an immunoassay. MA is an early predictor of proteinuria. If repeatedly positive, and if the concentration is increasing, the patient may be at risk for glomerular disease.
- Thoroughly evaluate an animal for an underlying disease when persistent proteinuria is believed to be of glomerular origin.
- Urine and serum protein electrophoresis may identify pre-glomerular proteinuria in patients with monoclonal gammopathies or urinary immunoglobulin light chains (Bence Jones proteins).

IMAGING

Ultrasound and radiographs may reveal an underlying infectious, inflammatory, or neoplastic disease process or evidence of LUT disease. Ultrasound may show structural changes suggesting primary renal disease (e.g., loss of corticomedullary distinction, hyper-echogenicity, and irregular surface margin) or evidence in support of LUT disease.

DIAGNOSTIC PROCEDURES

- Blood pressure should be monitored in patients with persistent renal proteinuria.
- Renal biopsy is needed to specifically diagnose the glomerular disease when an underlying disease cannot be identified or proteinuria has persisted following treatment of an underlying disease.

PATHOLOGIC FINDINGS

- Vary with cause of proteinuria.
- Biopsy from an animal with glomerular proteinuria may reveal any of the following: glomerulonephritis (e.g., immune complex-mediated, membranous, membranoproliferative, proliferative), minimal change disease, hereditary

nephritis, amyloidosis, podocyopathy, focal segmental glomerulosclerosis, glomerulosclerosis.

- Animals with tubular proteinuria most often have a degree of tubulointerstitial nephritis.
- Postrenal proteinuria would be expected to have inflammatory, neoplastic, or polypoid lesions.

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

Most can be managed as outpatients. Inpatient care may be required during select diagnostic evaluation (renal biopsy) or when there are complications associated with uremia, thromboembolism or edema in patients with glomerular proteinuria.

NURSING CARE

Physical therapy and exercise may limit formation of edema in patients with glomerular proteinuria and hypoalbuminemia.

ACTIVITY

Activity should not be restricted in animals with proteinuria.

DIET

If glomerular disease is suspected, feed a diet formulated for kidney disease.

CLIENT EDUCATION

It is important to determine the cause of persistent proteinuria, which may indicate the presence of kidney disease. Renal proteinuria is a risk factor for progressive kidney disease, thromboembolism, and edema.

SURGICAL CONSIDERATIONS

Animals with severe hypoalbuminemia (i.e., <2 g/dL) present unique challenges to anesthesia. Consideration should be given to referral of these patients to a secondary or tertiary care facility if anesthesia and/or surgery are indicated.

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

An angiotensin receptor blocker (ARB) or angiotensin-converting enzyme (ACE) inhibitor should be administered. Preliminary evidence suggests telmisartan (ARB) may be more efficacious in reducing proteinuria than ACE inhibitors. Combined use of an ARB and an ACE inhibitor should be done with caution as this is associated with a greater risk of death in people. Use of aldosterone antagonists in management of proteinuria needs further investigation but may be indicated for patients that have increased aldosterone concentrations following

treatment with an ACE inhibitor or ARB. Animals with hypertension may be controlled with telmisartan alone, however some may require addition of a calcium channel blocker (e.g., amlodipine) to control both hypertension and proteinuria. Supplementation with *n*-3 polyunsaturated fatty acid (PUFA) should be considered in dogs, and possibly cats, with glomerular proteinuria when the diet being fed does not have a reduced *n*-6/*n*-3 PUFA ratio that approximates 5:1. Dogs with glomerular disease should also be given low-dose aspirin or clopidogrel as thromboprophylaxis.

CONTRAINdications

There are no known contraindications in animals with proteinuria.

PRECAUTIONS

Drugs highly bound to albumin may have an altered effect if hypoalbuminemia is present. The use of warfarin as an anticoagulant should be avoided. With hypoalbuminemia or azotemia, higher doses of furosemide may be required to mobilize edema effectively; however, it should be used with extreme caution.

POSSIBLE INTERACTIONS

There are no known important drug interactions in dogs with proteinuria other than the previously mentioned concern with highly protein-bound drugs.

ALTERNATIVE DRUG(S)

ARB and ACE inhibitor are alternatives to each other.

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

- UP:C, urinalysis, systemic arterial blood pressure and serum albumin, creatinine and potassium concentrations should be monitored at least quarterly.
- Use the UP:C to assess progression of disease. Response to treatment should be evaluated for several months after resolution of any underlying disease. Reduction of UP:C to <0.5 (dog) or <0.2 (cat) without inappropriate worsening of renal function is considered a therapeutic success. However, this target is often not achieved and a reduction in UP:C of >50% is the recommended alternate target.
- Monitor serum creatinine—reduced proteinuria or reduced albuminuria that is concurrent to a rising serum creatinine may reflect deteriorating renal function.
- Because UP:Cs may vary, 2–5 serial assessments may be needed to evaluate response to treatment or progression in patients with glomerular proteinuria. Alternatively, the UP:C can be measured in a

PROTEINURIA

sample that has been pooled by adding equal aliquots of 2–3 samples that have been collected and refrigerated over a 48-hour time period.

- When given an ACE inhibitor or an ARB, dogs with stage 1 or 2 CKD can have an increase in serum creatinine of up to 30% without warranting a change in treatment. Worsening of renal function in dogs with stage 3 or 4 CKD should be avoided. During therapy the serum potassium concentration should not be >6 mmol/L and the systolic blood pressure should not be <120 mmHg.

PREVENTION/AVOIDANCE

Annual urinalyses and UP:C are recommended. Repeat in 2–4 weeks if proteinuria is detected. Patients with persistent proteinuria or MA of glomerular origin should be evaluated more thoroughly for underlying causes of glomerular injury. Potential underlying causes should be eliminated or managed. If proteinuria persists, potential underlying causes have been managed appropriately or underlying causes were not identified, consider renal biopsy.

POSSIBLE COMPLICATIONS

- Edema.
- Thromboembolism.
- Systemic hypertension.
- Progressive kidney disease.
- Poor wound healing.

EXPECTED COURSE AND PROGNOSIS

- Vary with the cause of proteinuria.
- Postrenal and prerenal proteinuria should resolve following resolution of inciting causes.
- Most diseases associated with renal tubular proteinuria are progressive.
- The rate of progression varies and spontaneous remissions have been reported. Animals with persistent glomerular

proteinuria may develop renal tubular damage resulting in advanced CKD and eventual uremia and death. Some dogs die shortly after the initial detection of proteinuria, while others remain alive for years. Dogs with nephrotic syndrome and/or azotemia may have a shorter survival.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Hypoalbuminemia, hypoglobulinemia (rare), hypercholesterolemia, low antithrombin III, thrombocytosis, hyperfibrinogenemia, edema, thromboembolism, and systemic hypertension.

AGE-RELATED FACTORS

Familial glomerular diseases should be considered in young animals with glomerular range proteinuria.

ZOONOTIC POTENTIAL

Proteinuria does not have a zoonotic potential. However, glomerular proteinuria can occur with a variety of infectious diseases, some of which could have a zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

Some drugs used in the treatment of diseases associated with proteinuria may be contraindicated in pregnancy.

SYNONYMS

None

SEE ALSO

- Amyloidosis.
- Azotemia and Uremia.
- Glomerulonephritis.
- Hematuria.
- Hypoalbuminemia.
- Nephrotic Syndrome.

- Pyuria.

ABBREVIATIONS

- ACE = angiotensin-converting enzyme.
- ARB = angiotensin receptor blocker.
- CKD = chronic kidney disease.
- GBM = glomerular basement membrane.
- LUT = lower urinary tract.
- MA = microalbuminuria.
- PUFA = polyunsaturated fatty acid.
- SSA = sulfosalicylic acid.
- UA:C = urinary albumin:creatinine ratio.
- UP:C = urine protein:creatinine ratio.

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**Client Education Handout
available online**

PRURITUS



BASICS

DEFINITION

Pruritus (itch) is an unpleasant sensation that causes the clinical symptom of scratching, rubbing, hair pulling, and/or licking.

PATHOPHYSIOLOGY

Keratinocytes, mast cells, eosinophils and lymphocytes interact with neuronal cells via the release of cytokines, neurotrophins, and neuropeptides. The sensation of itch is conducted via the peripheral nervous system to the sensory cortex. Other factors can modify the perception of pruritus at this level. Pruritus is an adaptive protective mechanism, however excessive itch can lead to cutaneous damage. Identification and treatment or removal of the causative agent(s) is the most important aspect of long-term control. Avoidance or reduction of long-term medical therapy should be pursued when possible. Chronic cases may be best handled by a dermatologist.

P

SYSTEMS AFFECTED

- Skin/exocrine/neuronal.
- Behavioral.

SIGNS

- Scratching, licking, biting, rubbing, hair pull, or chewing.
- Variable evidence of self-trauma and cutaneous inflammation.
- Non-well-demarcated alopecia with or without excoriations, and without obvious gross inflammation may be the only sign.

CAUSES

- Parasitic—fleas, *Sarcoptes* spp., *Demodex* spp., *Otodectes* spp., *Notoedres* spp., *Cheyletiella* spp., *Trombicula* spp., lice, *Pelodera* spp., endoparasite migration.
- Allergic—flea allergy, atopic dermatitis, food allergy, contact allergy, drug allergy, bacterial hypersensitivity, malassezia hypersensitivity.
- Bacterial/fungal—*Staphylococcus* spp. and *Malassezia pachydermatis*; rarely dermatophyte (*Trichophyton* is more pruritic than other dermatophytes).
- Miscellaneous—primary and secondary seborrhea, calcinosis cutis, cutaneous neoplasia, immune-mediated dermatoses, and endocrinopathies are variably pruritic; psychogenic diseases may also be associated with pruritus (especially in cats).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pruritus often causes alopecia.
- Alopecia without pruritus may accompany endocrine diseases. Some animals excessively lick themselves without the owner's

knowledge.

- Demodicosis, dermatophytosis, superficial pyoderma (bacteria), *Malassezia* dermatitis, immune-mediated dermatoses, seborrhea, some cutaneous neoplasms, and unusual diseases such as leishmaniasis may cause alopecia with varying degrees of inflammation and pruritus.
- History is paramount for determining the diagnostic workup.
- Severe pruritus that keeps the patient and owner awake may suggest scabies, allergies (flea allergy/infestation, food allergy, atopic diseases) or *Malassezia* dermatitis. All but the latter typically have an acute onset.
- Uncomplicated atopic diseases (dermatitis, rhinitis, conjunctivitis, asthma) are steroid-responsive and may manifest seasonally, but may progress to nonseasonal pruritus of the face, feet, ears, forelimbs, axillae, and caudal body.
- Flea-allergic and food-allergic animals may be predisposed to atopic diseases and may show similar signs. Food allergy is the least common of these three differentials.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

DIAGNOSTIC PROCEDURES

Miscellaneous Procedures

- Identification and treatment of the underlying cause of pruritus is of paramount importance. It is common for multiple causes to be present concurrently and this can significantly complicate the workup and management of pruritus.
- Skin scrapes, epidermal cytology, and dermatophyte cultures
- A skin biopsy is useful when the lesions associated with pruritus are unusual, an immune-mediated dermatosis is suspected, or the history and physical findings do not correlate.

Allergy Testing

- Allergy testing does not diagnose atopic disease: The presence of positive test results does not diagnose that allergy is the cause or even a contributory cause of pruritus. Results must be carefully correlated with the patient's history and physical examination.
- Two methods for allergy testing—intradermal and serum:
 - Intradermal testing remains the gold standard and the preferred method for allergy testing.
 - Serum tests for allergy measure serum IgE and do not measure localized IgE found in the skin. Patients with symptoms of atopic disease but negative on testing are diagnosed as having "atopic-like disease."
- Positive reactions identified on testing are correlated with the history, in order to formulate allergen-specific immunotherapy solution (ASIT). The choice of allergens is based on the patient's history, test results, local allergen exposure, and the veterinarian's

experience in treating allergies; not just the highest reactive allergens in the testing panel should be selected. Administration of immunotherapy may be via either subcutaneous or sublingual routes.

Trial Courses of Treatment as a Diagnostic Tool

- A trial course of therapy for scabies may be appropriate in some animals; canine scabies can be difficult to diagnose and skin scrapes are often negative.
- Laboratory tests (serum, hair, saliva) cannot be used for the diagnosis of food allergy; a properly performed strict dietary trial must be conducted. Novel protein diets based on the patient's history or hydrolysate diets should be fed during the testing period. Careful client counseling to avoid all treats, supplements, chews, and flavored medications is necessary for a diet trial to succeed. Diet trials should be continued until the patient improves or for a duration of 8–10 weeks. Challenge with the original diet is a critical part of the test, and demonstrates that improvement was not due to concurrent therapy (e.g., relief of parasites, resolution of infection).



TREATMENT

- More than one disease can contribute to itching.
- Secondary infections are common and may result in self-perpetuation of pruritus.



MEDICATIONS

DRUG(S) OF CHOICE

Topical Therapy

- Topical therapy is helpful for pruritic patients.
- Colloidal oatmeal—duration of effect is usually less than 2 days.
- Topical antihistamines have not demonstrated efficacy.
- Topical anesthetics may offer only a very short duration of effect.
- Topical corticosteroids—can be effective. But if used excessively, can cause localized and systemic side effects.
- Antimicrobial shampoos help control bacterial and/or yeast infections that cause itching; they can be excessively drying, necessitating use of moisturizers.
- Lime sulfur is mildly antipruritic as well as being antiparasitic, antibacterial, and antifungal.

Systemic Therapy

- Therapy is complex and depends on the etiology.

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PRURITUS

- Parasite prevention/treatment—fleas, scabies, demodicosis.
- ASIT—atopic disease.
- Chronic medical therapy with corticosteroids, cyclosporine, lokivetmab, or oclacitinib without evaluation by a dermatologist should be avoided.
- Corticosteroids affect many biological responses associated with pruritus. For acute relief, oral prednisone/prednisolone results in significant benefit for 2–5 days but rarely causes significant side effects.
- Cyclosporine 5 mg/kg/day initially; every other day maintenance—very useful in the treatment of atopic dermatitis. Adverse effects include gastrointestinal upset, oral papilloma, gingival hyperplasia, and hirsutism. Not useful for quick relief due to its long lag phase (4–6 weeks).
- Oclacitinib 0.4–0.6 mg/kg twice daily for 14 days, then 0.4–0.6 mg/kg q24h—fast acting without the common side effects of prednisone. Useful for temporary control of pruritus. Not for use in dogs less than 12 months of age; may cause a mild, dose-dependent reduction in hemoglobin, hematocrit, and reticulocyte counts as well as decreases in leukocytes. Potential for immune suppression, demodicosis, recurrent pyoderma, exacerbation of neoplastic conditions and pneumonia. Agitation with use reported. Avoid use at higher than recommended dosage.
- Lokivetmab 2 mg/kg—caninized monoclonal antibody against interleukin 31; for dogs only. Rapid onset (within 3 days from administration) and duration of effect between 2 and 8 weeks; effective in 60–70% of dogs with pruritus. Few side effects reported, including anaphylaxis, transient lethargy, and behavioral changes. Efficacy may be diminished by development of an immune response to this biologic medication and/or secondary infection.
- Fatty acids—block formation of inflammatory mediators; require 6–8 weeks of administration for maximum effect.

CONTRAINDICATIONS

- Some topicals will exacerbate pruritus: monitor treatment response.
- Corticosteroids should be avoided in cases of pruritus caused by an infectious etiology.

PRECAUTIONS

- Client frustration is common.
- Scabies is curable.
- Food allergy is manageable without medications if a proper food trial is conducted.
- Atopic dermatitis disease is a progressive common cause of pruritus and ASIT is the only therapy that can safely manage the disease alone or in combination with other medications.
- Corticosteroids—potentially significant long-term side effects.
- Cyclosporine—serum drug levels should be measured at least once initially in cats and in dogs if the maintenance dosage required to control symptoms is above the standard recommendation.
- Oclacitinib—long-term use associated with potential immunosuppression.

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

- Patient monitoring as well as client communication are imperative.
- Many different unrelated diseases may contribute to pruritus and the control of one disease does not mean that other causes cannot remain.
- Multiple etiologies such as *Malassezia* dermatitis, flea bite allergy, atopic dermatitis, and pyoderma are commonly present in a single patient. Elimination of these may not be enough to significantly reduce the pruritus. Animals with both food allergy and atopic disease may do well during the winter season with a hypoallergenic diet only to become pruritic during the warmer months in association with atopic dermatitis.

- Patients receiving chronic medication should be evaluated every 3–12 months for potential side effects as well as the occurrence of new contributing factors.

POSSIBLE COMPLICATIONS

- Skin scrapes and other tests that may have been negative or normal during the original workup should be repeated if symptoms return.
- Complications and/or gradual loss of efficacy are not uncommon with chronic medical therapy.

**MISCELLANEOUS****ABBREVIATIONS**

- ASIT = allergen-specific immunotherapy solution.

Suggested Reading

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Authors W. Dunbar Gram and Domenico Santoro

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(CONTINUED)

PYODERMA

deep pyoderma; more likely false-negative results with superficial pyoderma.

- Freshly expressed exudate from a draining tract or from beneath a crust—may yield the pathogen or a contaminant if the lesion is not intact.

PATHOLOGIC FINDINGS

- Subcorneal pustules.
- Intraepidermal neutrophilic microabscesses.
- Perifolliculitis.
- Folliculitis.
- Furunculosis.
- Nodular to diffuse dermatitis.
- Panniculitis.
- Inflammatory reaction—suppurative or pyogranulomatous.
- Tissue grains within pyogranulomas—observed most often with *Actinomyces*, *Actinobacillus*, and *Nocardia*.
- Special stains—used to identify Gram-negative bacteria or acid-fast organisms.

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

Usually outpatient, except for severe, generalized deep pyoderma.

NURSING CARE

- Severe, generalized, deep pyoderma—may require IV fluids, parenteral antibiotics, and/or daily whirlpool baths.
- Benzoyl peroxide or chlorhexidine shampoos—remove surface debris.
- Frequent topical therapy can help reduce the severity and frequency of recurrence.
- Whirlpool baths—deep pyoderma; remove crusted exudate; encourage drainage; decrease inflammation and improve tissue oxygenation.

DIET

Novel protein or hydrolysate diet if secondary to cutaneous adverse reaction to food.

SURGICAL CONSIDERATIONS

Fold pyoderma may require surgical correction to prevent recurrence.

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

- S. pseudintermedius* isolates—usually susceptible to cephalosporins, amoxicillin-clavulanate, erythromycin, clindamycin, and trimethoprim-sulfamethoxazole; somewhat less responsive to lincomycin; frequently resistant to amoxicillin, ampicillin, penicillin.

- Amoxicillin-clavulanate—most isolates of *Staphylococcus* and *P. multocida* susceptible; generally effective for skin infections in cats.
- Superficial pyoderma—initially treated empirically with one of the antibiotics listed above.
- Recurrent, resistant, or deep infections—choose antibiotic therapy based upon culture and susceptibility testing (e.g., chloramphenicol).
- Multiple organisms with different antibiotic susceptibilities—select antibiotic on basis of the staphylococcal susceptibility.

CONTRAINdications

Corticosteroids—mask inflammation causing therapy to be discontinued prematurely and resulting in selection for resistant organisms; if used concurrently, therapy should be extended and the patient should be reevaluated before discontinuing antibiotic therapy.

PRECAUTIONS

- Cephalosporins, erythromycin, lincomycin, and clindamycin—vomiting; administer with food.
- Aminoglycosides—renal toxicity usually precludes prolonged systemic use.
- Trimethoprim-sulfamethoxazole—keratoconjunctivitis sicca, fever, hepatotoxicity, polyarthritis, and hematologic abnormalities, especially neutropenia; not recommended for use in Doberman pinschers.
- Chloramphenicol—use with caution in cats; mild, reversible anemia in dogs (uncommon); associated with aplastic anemia in humans; rear temporary limb muscle weakness is a possible side effect.

POSSIBLE INTERACTIONS

Trimethoprim-sulfamethoxazole—falsely decreased thyroid hormone test results.

ALTERNATIVE DRUG(S)

Bacterin (Staphage Lysate, Delmont Laboratories), staphoid AB, or autogenous injections—may improve antibiotic efficacy and decrease infection recurrence.

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

Administer oral antibiotics for a minimum of 7–10 days beyond clinical cure; approximately 3–4 weeks for superficial pyoderma; 6–10 weeks for deep pyoderma.

PREVENTION/AVOIDANCE

- Routine bathing with benzoyl peroxide or chlorhexidine shampoos—may help prevent recurrences.

- Padded bedding—may ease pressure point pyoderma; also consider causes for poor wound healing including hypothyroidism.

- Topical benzoyl peroxide gel or mupirocin 2% ointment may be helpful adjunct therapies—chin acne, fold pyoderma, respectively.

- Identification and management of the underlying cause is crucial to prevent recurrence.

POSSIBLE COMPLICATIONS

Bacteremia and septicemia.

EXPECTED COURSE AND PROGNOSIS

Likely to be recurrent or nonresponsive if underlying cause is not identified and effectively managed.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

P

AGE-RELATED FACTORS

- Impetigo—affects young dogs before puberty; can be associated with poor husbandry; often requires only topical therapy.
- Superficial pustular dermatitis—occurs in kittens; associated with overzealous “mouthing” by the queen.
- Pyoderma secondary to atopic dermatitis—usually begins between 1 and 3 years of age.
- Pyoderma secondary to endocrine disorders—usually begins in middle adulthood.

ZOONOTIC POTENTIAL

- Cutaneous tuberculosis—rare.
- Feline leprosy—unknown.

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Acne—Cats.
- Acne—Dogs.
- Perianal Fistula.
- Pododermatitis.

Suggested Reading

Helton Rhodes KA, Werner A.

Blackwell's Five-Minute Veterinary Consult: Clinical Companion: Small Animal Dermatology, 3rd ed. Hoboken, NJ: Wiley-Blackwell, 2018.

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BASICS

DEFINITION

Pyometra is a bacterial suppurative inflammation of the endometrium leading to intraluminal accumulation of purulent exudate within the uterus.

PATHOPHYSIOLOGY

- Incompletely understood and multifactorial.
- Classic theory—repeated exposure of endometrium to high concentrations of estrogen during proestrus and estrus followed by high concentrations of progesterone during diestrus without pregnancy leads to development of cystic endometrial hyperplasia (CEH), which predisposes uterus to ascending bacterial infections.
- Strains of *Escherichia coli* with uropathogenic virulence factors that allow adhesion to the endometrium and establishment of an infection without CEH enter uterus during proestrus and estrus and act as a mucosal irritant stimulating development of CEH under the influence of progesterone. Uterine secretions may act as a growth medium for ascending bacteria.
- Regardless of underlying cause, pyometra does not occur in absence of progesterone (endogenous or exogenous).

SYSTEMS AFFECTED

- Reproductive.
- Hemic/lymphatic/immune.

GENETICS

- Genetic predisposition suspected in some related bitches.
- Suggested breed predisposition in Bernese mountain dog, Rottweiler, rough-coated collie, oriental cat breeds.

INCIDENCE/PREVALENCE

Accurate assessment difficult because most dogs and cats in the United States undergo elective ovariohysterectomy (OHE). A recent Swedish study reported overall incidence of pyometra in bitches as 199 per 10,000 dogs at risk and in queens as 17 per 10,000 cats at risk. Lower incidence in queens because they are induced ovulators.

SIGNALMENT

Species

Dog and cat.

Mean Age and Range

Usually >6 years old; range 4 months to 16 years; mean 7.25 years.

Predominant Sex

- Female—ovary intact.
- Spayed bitches and queens with ovarian remnant syndrome may develop a stump pyometra.

SIGNS

Historical Findings

- Dogs—usually within 12 weeks of last estrus.
- Cats—usually within 4 weeks of last estrus.
- History of treatment with estrogens and/or progestogens.

Physical Examination Findings

- Uterus—may be enlarged on abdominal palpation.
- Systemic illness—depends on duration and severity.
- Open cervix—bloody, purulent vaginal discharge, may not be noticed in queens.
- Closed cervix—systemically ill from endotoxemia and bacteremia: polyuria, polydipsia, lethargy, inappetence/anorexia, vomiting, abdominal distension, dehydration, shock.
- Pyrexia.

CAUSES

- Dogs—repeated exposure of endometrium to estrogen followed by prolonged exposure to progesterone without pregnancy.
- Cats—may be the result of estrogen at estrus followed by a gestational (pseudo-pregnancy) phase caused by spontaneous ovulation or ovulation induction.

RISK FACTORS

- Middle-aged to older, nulliparous ovary-intact females may be predisposed.
- Pharmacologic use of estrogen (mismate shot) during midestrus to early diestrus.
- No correlation with pseudopregnancy in dogs.
- Long-term and high-dose use of progestagens (for estrus prevention) in both queens and bitches.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Pregnancy.
- Vaginitis.
- Metritis and retained fetal membranes (associated within first days post partum).
- Hydrometra (serous intrauterine discharge); mucometra (mucoïd intrauterine discharge); hematometra (hemorrhagic intrauterine discharge).
- Other causes of polyuria/polydipsia—diabetes mellitus, hyperadrenocorticism, renal disease.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia or neutropenia with left shift ± toxic change; more severe with closed cervix.
- Normocytic, normochromic anemia.
- Hyperglobulinemia, hyperproteinemia, hypoalbuminemia, hypercholesterolemia, elevated C-reactive protein concentration.
- Azotemia.

- Elevated alanine aminotransferase and alkaline phosphatase enzyme activities.
- Electrolyte disturbances.
- Urinalysis—isosthenuria, bacteriuria, glucosuria, and proteinuria possible. Collect sample by catheterization of urinary bladder to avoid risk of uterine puncture with cystocentesis. Midstream urine sample may be contaminated by vaginal discharge.

OTHER LABORATORY TESTS

- Cytologic examination of vulvar discharge—degenerate neutrophils, phagocytized bacteria; may be indistinguishable from purulent discharge associated with vaginal disease (e.g., vaginitis, vaginal mass, foreign object). Vaginoscopy can confirm origin and rule out other causes of discharge.
- Bacterial culture and sensitivity—vulvar discharge sample to be taken directly from the uterus transcervically or cranial vagina with the aid of a vaginal speculum and guarded swab. A free-catch urine sample can also be useful as the causative agent in the pyometra is often located in the bladder.
- Serologic testing for *Brucella canis*—rapid slide agglutination test as a screen; sensitive but not specific. If positive, recheck by an agar gel immunodiffusion test or bacterial culture of whole blood, lymph node aspirate, or vulvar discharge.
- Hormone assay—in most cases, progesterone concentration will be >2 ng/mL; important to measure in animals that present in anestrus, as treatment with a progesterone receptor antagonist will be ineffective.

IMAGING

Radiography

- Enlarged, distended uterus (see Web Figure 1).
- Rule out pregnancy—fetal skeletal ossification occurs 45 days after ovulation.

Ultrasonography

- Uterine horns distended with intraluminal fluid, with or without flocculation. Uterine wall thickened with irregular edges and small hypoechoic areas consistent with cystic change (CEH) (see Web Figure 2), uterine wall can appear thin if severely distended; monitoring of the volume of uterine fluid is necessary during medical therapy; presence of severe CEH and/or ovarian cysts associated with poorer prognosis for medical management and fertility.
- Rule out pregnancy—20–24 days after ovulation.
- Pyometra may rarely occur with pregnancy in dogs.

DIAGNOSTIC PROCEDURES

Vaginoscopy—indicated in dogs with purulent vulvar discharge and no apparent uterine enlargement; allows determination of site of origin of the discharge; not possible in cats.

PYOMETRA

(CONTINUED)

PATHOLOGIC FINDINGS

- Endometrium (dogs and cats)— cobblestone appearance (see Web Figure 3).
- Cystic endometrial surface—covered by malodorous, mucopurulent exudate; thickened by increased endometrial gland size and cystic gland distension.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient; life-threatening condition if the cervix is closed, resulting in endotoxemia, bacteremia, and sepsis. Resuscitation requires immediate IV fluid administration and broad-spectrum antibiotics to stabilize for anesthesia and surgery.
- Open-cervix pyometra may be a candidate for medical therapy.

NURSING CARE

Supportive care.

P

CLIENT EDUCATION

- Medical treatment only recommended for valuable, young (<4 years) breeding animals that are not azotemic and systemically well. For all other animals, OHE is the treatment of choice. The prognosis for successful medical treatment and future fertility in older animals and animals with evidence of uterine and ovarian pathology is poor.
- Historically, medical treatment of closed-cervix pyometra was associated with uterine rupture and peritonitis, but new pharmacologic agents and treatment protocols now make this a rare event.
- Bitches that are refractory or chronic cases that do not respond to medical treatment are candidates for OHE.
- Warn of possible recurrence of pyometra after medical therapy—important to breed at the next heat and spay when desired number of litters is achieved.

SURGICAL CONSIDERATIONS

- Complete OHE is the preferred treatment in all animals not intended for breeding, older bitches (>4 years), bitches with evidence of chronic CEH changes and/or ovarian follicular cysts, bitches that present systemically unwell and require immediate emergency care and stabilization.
- Patients should be systemically stabilized prior to anesthesia for surgery (correction of any acid-base derangements, dehydration, hypotension, shock, electrolyte abnormalities, arrhythmias) and administered IV fluids and IV broad-spectrum antibiotics.
- Closed-cervix pyometra—exercise great care in handling the enlarged and friable uterus (see Web Figure 4).
- Place saline-soaked laparotomy sponges in abdomen to prevent leakage of purulent material into peritoneal cavity.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

- Empirical, pending results of bacterial culture and sensitivity:
 - Broad-spectrum—ampicillin 22 mg/kg PO, IV q8h; amoxicillin and clavulanic acid 22 mg/kg, PO, q12h; ampicillin and sulbactam 22–30 mg/kg IV q8–12h or cefazolin 22 mg/kg IV, IM q8h combined with enrofloxacin 5–10 mg/kg PO q24h.
 - Continue for at least 14 days after resolution of vulvar discharge and fluid in uterine lumen.
- Rationale of medical therapy—remove progesterone and its effects on uterus, eliminate bacteria from uterus, promote cervical dilation and drainage of pus from the uterus.

Aglepristone

- Progesterone receptor antagonist; competitively binds to progesterone receptor with greater affinity than natural progesterone, preventing biological effect of progesterone. Will not lower progesterone levels.
- Dose—10 mg/kg SC, days 1, 2, 8, and if not cured day 14 and 28 in bitches. An additional injection at day 5 has been associated with an improved treatment success rate. In queens, 15 mg/kg SC is recommended. Minimal side effects. Excellent choice for closed pyometras as it dilates the cervix with minimal uterine contractions. Evacuation of uterus may be improved by adding prostaglandin. Aglepristone is not registered or approved by FDA in United States and not suitable for use in bitches with poor liver or kidney function.

Prostaglandins (PGF2 α)

- Doses listed here for native compound only (dinoprost tromethamine; Lutalyse *); has both luteolytic and ecabolic actions.
- Lower doses minimize side effects and ecabolic effect, especially in closed pyometras. Once the cervix is fully dilated the dose can be gradually increased if tolerated.
- Animals should be monitored in hospital for at least 1 hour after each treatment. If animal is systemically well, may be managed as outpatient.
- Side effects (dose-dependent)—tachypnea, vomiting, diarrhea, urination, anxiety; seen 20 minutes after administration and last for 15–30 minutes. Use of PGF2 α in brachycephalic breeds is contraindicated due to their predisposition to bronchospasm.
- Dogs and cats—10 μ g/kg SC q5–6h day 1, then increase to 20–25 μ g/kg q5–6h if tolerated for 1–2 days; then increase to 50 μ g/kg q5–6h for 3–4 days. Queens are more resistant to PGF2 α than bitches; often higher doses for longer periods are required.

Cloprostenol

- Synthetic PGF2 α analogue; longer action (>30 hours) than natural form of PGF2 α .
- Dogs—1 μ g/kg SC q24h for 7–14 days; convenience of once a day or every 2–3 days treatment but greater side effects, stimulates less uterine contractions and prolonged time to resolution compared to natural form of PGF2 α .

Dopamine Agonists

- Cabergoline (5 μ g/kg PO q24h for 7–14 days) or bromocriptine (10–20 μ g/kg PO q8h); both given with food to reduce risk of vomiting; cabergoline has fewer side effects. Prolactin antagonists (e.g., have luteolytic action); best used in combination with PGF2 α —should see cervical opening within 24–48 hours. Only effective after 25 days post ovulation.

CONTRAINDICATIONS

High-dose PGF2 α and cloprostenol cause strong uterine contractions that may cause uterine rupture or force purulent exudate through the oviducts if used with closed-cervix pyometra.

ALTERNATIVE DRUG(S)

Misoprostol—synthetic PGE1 analogue (10 μ g/kg PO or 200 μ g tablet in <20 kg and 400 μ g in >20 kg bitch intravaginally). Side effects minimal, facilitates cervical relaxation. Best used in combination with aglepristone and PGF2 α (PGE1 does not induce luteolysis).



FOLLOW-UP

PATIENT MONITORING

- OHE—for patients not responding to medical treatment within 5 days or those refractory to medical treatment.
- Clinical improvement should be seen within 48 hours after initiation of treatment:
 - Vaginal discharge—should reduce in volume and character over 5 days.
 - Ultrasonography—to assess response to treatment; reduction in uterine wall thickness and intraluminal fluid should be seen within 3 days after start of treatment; fluid in lumen should be absent within 5–7 days.
- Serum progesterone concentrations decline within 48 hours of treatment with PGF2 α and should be <2 ng/mL at 5–7 days; recurrence of pyometra can occur if complete luteolysis not achieved.
- CBC should return to normal within 2 weeks.
- Continue treatment until no vulvar discharge is present and no fluid is seen within uterus on ultrasound. Prolonged treatment correlated with poor fertility.

PREVENTION/AVOIDANCE

- Animals not intended for breeding should be spayed.

(CONTINUED)

PYOMETRA

- Exogenous progestagens for estrus suppression should be used with caution.
- Breeding females should be bred while they are young (<4 years) and spayed as soon as the desired number of litters has been obtained; a pregnant uterus reduces the risk of developing pyometra and maximizes uterine health.
- Animals that have been medically treated for pyometra should be bred on the very next estrus; gravid uterus is less susceptible to reinfection.
- Antimicrobial therapy at subsequent heat may or may not be helpful (controversial). Antibiotic selection based on culture and sensitivity of uterine fluid until 21 days of gestation.
- Mibolerone (androgen-receptor agonist) may be helpful following medical treatment of pyometra to postpone subsequent heat and allow endometrium to repair.

POSSIBLE COMPLICATIONS

- Recurrence of pyometra at subsequent heats.
- Uterine rupture leading to sepsis.
- Bacteremia-associated infection affecting various organs (i.e., uveitis, septic arthritis, osteomyelitis, etc.).

EXPECTED COURSE AND PROGNOSIS

- Prognosis for survival is good if uterine rupture does not occur; 4% mortality rate in bitches and 8% in queens.
- Prognosis for response to medical therapy is good, especially if young, healthy animals (average 86% in bitches; 95% in queens).
- Recurrence rate of pyometra is dependent on age, parity, and preexisting uterine pathology (reported range 20–65%).
- Variable pregnancy rates reported after treatment for pyometra (50–90%).

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Pyometra of the uterine stump in spayed animals—may develop any time after ovariohysterectomy; associated with ovarian remnant.

PREGNANCY/FERTILITY/BREEDING

Drugs used for treatment of pyometra are abortifacients—always rule out pregnancy before administration, caution while handling.

SEE ALSO

- Breeding, Timing.
- Infertility, Female—Dogs.
- Ovarian Remnant Syndrome.

ABBREVIATIONS

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

Suggested Reading

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**Client Education Handout
available online**

PYOTHORAX



BASICS

DEFINITION

Accumulation of septic suppurative inflammation in the pleural cavity.

PATHOPHYSIOLOGY

- Infectious—from transpulmonary, transesophageal, or transthoracic inoculation of bacteria into the pleural space, with subsequent suppurative pleuritis.
- Dogs—often associated with an inhaled grass awn or other foreign object or a penetrating wound to the thorax.
- Other causes include extension of discospondylitis, esophageal perforation, parasitic migration, hematogenous spread, previous thoracic surgery, and neoplasia with abscess formation.
- Cats—most commonly associated with penetrating bite wounds, foreign bodies, or aspiration of oropharyngeal flora and extension of subsequent pneumonia into the pleural space.

P

SYSTEMS AFFECTED

- Respiratory.
- Cardiovascular.
- Renal—protein-losing nephropathy.

GEOGRAPHIC DISTRIBUTION

Etiology is regionally dependent. For example, inhaled grass awn or foxtails are common in the western United States. *Spirocercus lupi* should be considered as a predisposing cause in endemic areas (Africa, Asia, southeastern United States).

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Dogs—hunting and sporting breeds; for example, Labrador retrievers, German shorthaired pointers, springer spaniels, and border collies.

Mean Age and Range

Median ~4 years, although there is wide variation.

Predominant Sex

Male animals overrepresented.

SIGNS

General Comments

- Often insidious in onset, with few clinical signs until late in the course of disease.
- Respiratory compromise—often not severe unless disease is advanced.
- Vomiting/diarrhea may be initial presenting complaint in 25% of canine cases.

Historical Findings

- Diminished activity.
- Collapse after exercising and slow recovery.
- Weight loss and partial anorexia can be the only clinical signs.

Physical Examination Findings

- Tachypnea.
- Cachexia.
- Cough.
- Pyrexia.
- Thoracic auscultation—muffled heart and lung sounds.
- Cats—may show few clinical signs before onset of apparently acute respiratory distress, collapse, and septic shock; bradycardia and hypersalivation associated with poor outcome.
- Injury to the thoracic wall—may not be apparent or may be healed at the time of examination.

CAUSES

- Infectious—Dogs: *Actinomyces* spp., *Nocardia* spp., anaerobes (*Bacteroides*, *Peptostreptococcus*, *Fusobacterium*), *Corynebacterium*, *Escherichia coli*, *Pasteurella*, and *Streptococcus* spp.; fungal agents. Cats: oral commensals (e.g., *Pasteurella multocida* and *Bacteroides* spp.) most common; obligate anaerobes (*Peptostreptococcus*, *Fusobacterium*) common.
- Parasitic—Dogs: esophageal rupture of *S. lupi* granuloma.
- Neoplastic—rarely with intrathoracic tumors secondary to tumor necrosis.

RISK FACTORS

- Dogs—hunting, field trials, and other strenuous outdoor sporting activities; *S. lupi* endemic areas.
- Cats—multiple cat households, outdoor cats, pneumonia, upper respiratory infection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other pleural effusions—chylothorax and hemothorax; nonseptic exudates (feline infectious peritonitis or neoplasia); transudative effusions; differentiated via cytologic examination.
- Diseases associated with fever of unknown origin should be considered for animals with nonlocalizing signs.

CBC/BIOCHEMISTRY/URINALYSIS

- Marked neutrophilic leukocytosis with left shift, monocytosis, and anemia of chronic disease.
- Regenerative anemia—can be seen with substantial hemorrhage into the pleural cavity.
- Hyperglobulinemia—possible due to chronic inflammation.
- Hypoalbuminemia as a negative acute-phase reactant or due to renal loss, if glomerulonephritis results from chronic antigenic stimulation.
- Azotemia—prerenal and/or renal.

IMAGING

- Radiography—unilateral or bilateral pleural effusion with pleural fissure lines; pulmonary parenchymal lesions (consolidation, atelectasis, masses) common; mediastinal lesions possible.
- Ultrasonography—pleural effusion; may show marked amount of fibrinous deposition in the pleural space; may

identify consolidated lung masses, mediastinal masses, and abscessed or neoplastic lung nodules.

CT—focal interstitial to alveolar pulmonary opacities; pleural thickening;

enlarged intrathoracic lymph nodes; pleural effusion; pneumothorax; and foreign body identification.

DIAGNOSTIC PROCEDURES

Thoracocentesis

- Cytologic evaluation—necessary to confirm the diagnosis; many effusions appear grossly hemorrhagic.
- Gram stains—can facilitate early identification of pathogenic organisms.
- Sulfa granules (small accumulations of purulent debris) in the exudate—characteristic of infection by filamentous organisms (e.g., *Actinomyces* and *Nocardia*).
- Organisms are often seen on cytologic examination, often within degenerative neutrophils.

Microbiology

- Culture fluid samples aerobically and anaerobically. Consider *Mycoplasma* culture if standard cultures are negative.
- Filamentous, anaerobic organisms are slow-growing or difficult to grow; cultures should be maintained longer than standard samples.
- Sulfa granules—maceration may enhance culturing; contain higher concentrations of bacteria.
- Fungal organisms—culture depends on history and geographic location.
- Urine samples—culture with suspected pyelonephritis.

Esophagoscopy

If *S. lupi* is suspected.

PATHOLOGIC FINDINGS

- Fibrinous and suppurative pleuritis, with or without pulmonary abscessation.
- Organisms may be identified on histopathology.
- Glomerulonephritis.



TREATMENT

APPROPRIATE HEALTH CARE

- Inpatient—often for several days to weeks.
- Treat like any abscess; drainage is critical—without it resolution is highly unlikely.
- Surgical exploration, debridement, and potential lobectomy required in some cases.

NURSING CARE

- Continuous evacuation via tube thoracostomy with low-pressure suction through a perforated tube; use a large-bore tube to minimize occlusion; continue until net drainage is <2–3 mL/kg/day and intracellular bacteria are no longer visible on Gram stain; drainage may be slightly higher with red rubber tubes because they are more irritating.
- Cats—usually require general anesthesia for tube placement.
- Dogs with severe respiratory compromise—may

(CONTINUED)

PYOTHORAX

substitute local anesthesia and regional analgesia for general anesthesia. • Periodic thoracic radiography—to ensure proper tube placement, and lack of pocketing or loculation of exudate, determine whether bilateral tube placement is necessary; document primary pulmonary pathology that may not have been apparent on initial examination. • Thoracic lavage—every 6–8 hours with warm, sterile saline; may help break down consolidated debris. Consider addition of heparin (1,500 units/L) to lavage fluid. • Coupage (rapid thoracic percussion)—may help remove consolidated debris. • Repeat bacterial culture if the patient fails to improve.

ACTIVITY

- Inpatient—encourage light exercise (10 minutes every 6–8 hours); promotes ventilatory efforts and helps break down pleural adhesions. • After discharge, gradually increase exercise over 2–4 months.

DIET

- High-calorie food. • Consider feeding tube placement if prolonged anorexia.

CLIENT EDUCATION

Warn client that the duration of treatment (inpatient and outpatient) is long and expensive; recurrence is possible with either medical or surgical management.

SURGICAL CONSIDERATIONS

- Surgery—higher cure rate expected with surgery if pulmonary abscessation, pleural fibrosis, lung lobe torsion, extensive loculation of pus is present, or if mediastinum is involved.
- Thoracoscopy can be utilized as an intermediate step to assess degree of severity and need for more aggressive intervention.
- Identified foreign body via thoracic imaging (radiography, ultrasound, or CT)—thoracotomy and retrieval indicated; grass awns are uncommonly found, even during surgery.

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

- Ultimately, choice determined by results of *in vitro* sensitivity testing. • Suspected specific pathogen—initiate treatment before culture results are available; choose on the basis of common antibiotic sensitivities of particular organisms; *Actinomyces* spp. and *Bacteroides* (*non-fragilis*) spp. often susceptible to beta-lactams or lincosamides; *Nocardia* spp. often susceptible to potentiated sulfonamides; obligate anaerobic bacteria (including *B. fragilis*) susceptible to

amoxicillin-clavulanic acid, chloramphenicol, and usually metronidazole; *Pasteurella* spp. often susceptible to potentiated penicillins.

- Ampicillin or amoxicillin with a β-lactamase inhibitor—ampicillin and sulbactam 20–30 mg/kg IV q8h followed by amoxicillin-clavulanic acid 12–25 mg/kg PO q8h when medications can be given orally.
- Clindamycin 5.5–11.0 mg/kg IV or PO q12h. • Multiple antibiotics occasionally necessary.

Analgesics

- Required following thoracotomy or during thoracocentesis. • Consider multimodal analgesia—systemic opioids, nonsteroidal anti-inflammatory drugs; intrapleural analgesia.

CONTRAINDICATIONS

Glucocorticoids and immunosuppressive agents—avoid with infectious pyothorax.

PRECAUTIONS

Potentiated sulfas—can be associated with keratoconjunctivitis sicca, polyarthropathy, hypothyroidism, thrombocytopenia, and anemia, especially with prolonged use.

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

- Decreasing thoracic fluid production, decrease in cell count in pleural fluid, and absence of bacteria usually noted within 4–7 days indicate that drains can be removed. Fluid should be submitted for aerobic and anaerobic culture at the time of drain removal. • Evaluate thoracic radiographs—ensure adequate evacuation of fluid.
- Antibiotics—continue for 1 month after the patient is clinically normal, the hemogram is normal, and there is no radiographic evidence of fluid reaccumulation; average duration of therapy is 3–4 months but may continue for 6–12 months or longer. • Assess CBC and radiographs monthly—residual radiographic changes may be permanent, but fluid should be absent.

POSSIBLE COMPLICATIONS

- Incorrect insertion of the thoracostomy tube—may prevent adequate drainage or produce pneumothorax; placement too far cranially may put pressure on brachial arteries and veins, resulting in unilateral limb edema or lameness; lung laceration during placement.
- Persistent, recurrent pyothorax—compartmentalization of exudate; premature discontinuation of treatment; pulmonary lesions. • Chronic fibrosing pleuritis and poor

performance after apparent recovery—may occasionally respond to further surgery.

- Persistent granulomatous mediastinitis.

EXPECTED COURSE AND PROGNOSIS

- With aggressive management—prognosis fair to excellent (60–90% survival).
- Dependent on severity of clinical signs.
- Overall better prognosis in dogs (83%) than in cats (62%). • Return to performance—dependent on chronicity of disease and level of management.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Retroperitoneal abscessation and discospondylitis caused by migration of a foreign body through the diaphragm into the retroperitoneal space—occasionally seen.
- Glomerulonephropathy—can be reversible with successful resolution of pyothorax.

SYNOMYNS

- Empyema. • Pleurisy. • Suppurative pleuritis.

SEE ALSO

- Chylothorax.
- Dyspnea and Respiratory Distress.
- Panting and Tachypnea.
- Pleural Effusion.

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Client Education Handout
available online

RABIES



BASICS

DEFINITION

A severe, fatal, viral polioencephalitis of warm-blooded animals, including humans.

PATHOPHYSIOLOGY

Virus—enters body through a wound (usually from a bite of rabid animal) or via mucous membranes, replicates in myocytes, spreads to the neuromuscular junction and neurotendinal spindles, travels to the central nervous system (CNS) via intra-axonal fluid within peripheral nerves, spreads throughout the CNS; finally spreads centrifugally within peripheral, sensory, and motor neurons.

SYSTEMS AFFECTED

- Nervous—brain, spinal cord, ± peripheral nervous system (PNS).
- Salivary glands—contain large quantities of infectious virus particles that are shed in saliva.

GENETICS

None

INCIDENCE/PREVALENCE

- Incidence of disease within infected animals—high (approaches 100%).
- Prevalence—overall low; can be significant in enzootic areas; especially high in countries where vaccination of dogs and cats is not routine.

GEOGRAPHIC DISTRIBUTION

- Worldwide.
- Exceptions—New Zealand, Hawaii, Japan, Iceland, and parts of Scandinavia.
- Species-adapted strains—specific geographic distributions within endemic countries.

SIGNALMENT

Species

- All warm-blooded mammals, including dogs, cats, and humans.
- United States—five strains endemic within fox, raccoon, skunk, coyote, and insectivorous bat populations; all five strains can be transmitted to dogs and cats.

Breed Predilections

None

Mean Age and Range

All ages, but animals that come in contact with wildlife at highest risk.

Predominant Sex

None

SIGNS

General Comments

- Variable; atypical presentation is the rule rather than the exception.
- Can present with focal or multifocal signs affecting either brain, spinal cord, PNS, or any combination.

- Three classical progressive stages of disease described:

- Prodromal—mentation change (more docile or more agitated) ± fever.
- Furious—prosencephalon signs including hyperactivity, aggression, seizures ± ataxia; 90% of rabid cats have furious form.
- Paralytic—lower motor neuron (LMN) paresis or paralysis starting near site of inoculation then spreading through nervous system; paralytic form can follow furious form, especially in cats.

Historical Findings

- Mentation/behavior change—variable; can include unusual shyness, excitability, aggression.
- Seizures.
- Gait change—lameness, ataxia, paralysis.
- Licking or chewing at site of inoculation, although wound not always identified.
- Change in tone of bark.
- Excess salivation or frothing at the mouth.

Physical Examination Findings

- All or some of the historical findings
- Fever.
- Cranial nerve deficits—myosis, anisocoria, absent pupillary light reflex (PLR); dropped jaw; absent gag reflex (assess by compressing larynx and avoid hand in mouth if rabies suspected).
- Hypersalivation.
- Laryngeal paralysis.

CAUSES

Rabies virus—a single-stranded, enveloped, bullet-shaped RNA virus; genus *Lyssavirus*; family *Rhabdoviridae*.

RISK FACTORS

- Exposure to wildlife, especially skunks, raccoons, bats, and foxes.
- Inadequate vaccination against rabies.
- Bite or scratch wounds from unvaccinated dogs, cats, or wildlife.
- Exposure to aerosols in bat caves.
- Immunocompromised animal—use of modified live virus rabies vaccine.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Must seriously consider rabies for any dog or cat showing acute behavior change or unaccountable neurological signs, especially those not previously vaccinated for rabies. Caution: handle with considerable care to prevent possible transmission of the virus to individuals caring for or treating the animal.
- Acute, progressive CNS and/or PNS disease—*infectious* (e.g., viral encephalitis or myelitis), *immune-mediated* (e.g., granulomatous or necrotizing meningoencephalitis, necrotizing leukoencephalitis, polymyositis), *metabolic* (e.g., hepatic

encephalopathy, hypoadrenocorticism), neoplastic, degenerative.

CBC/BIOCHEMISTRY/URINALYSIS

No characteristic hematologic or biochemical changes.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- There are no definitive premortem diagnostics. Diagnostics performed on rabies suspects should be done with extreme caution to prevent exposure to infective tissues. Consider consultation with a neurologist.
- Direct immunofluorescent antibody (DFA) test of nervous tissue—rapid and sensitive; collect head or entire body following death or euthanasia, chill sample immediately. Submit to a state-approved laboratory for rabies diagnosis. Caution: use extreme care when collecting, handling, and shipping these specimens to prevent exposure of veterinarians, staff or handlers.
- DFA test of dermal tissue—skin biopsy of the sensory vibrissae of the maxillary area, including deeper subcutaneous hair follicles; approved for human diagnostics, but not for animal diagnostics; accurate if positive, but negative test does not rule out rabies.
- Rabies antibody titer—a serologic antibody titer of 0.5 IU/mL is considered adequate for protection in vaccinated people and animals. In most states in the United States, titers are not considered a legal replacement for vaccination.

PATHOLOGIC FINDINGS

- Gross changes—generally absent.
- Histopathologic changes—acute to chronic polioencephalitis; gradual increase in the severity of the nonsuppurative inflammatory process in the CNS as disease progresses; large neurons within the brain may contain classic intracytoplasmic inclusions (Negri bodies).



TREATMENT

APPROPRIATE HEALTH CARE

Strictly inpatient.

NURSING CARE

Administer with extreme caution.

ACTIVITY

- Confine to secured quarantine area with clearly posted signs indicating suspected rabies.
- Runs or cages should be locked; only designated people should have access.
- Feed and water without opening the cage or run door.

(CONTINUED)

RABIES**DIET**

Soft, moist food; most patients will not eat.

CLIENT EDUCATION

- Thoroughly inform client of the seriousness of rabies to the animal and the zoonotic potential.
- Ask client about any human exposure (e.g., contact, bite) and strongly urge client to see a physician immediately.
- Local public health official must be notified.

SURGICAL CONSIDERATIONS

- Generally none.
- Skin biopsy—may help establish antemortem diagnosis; must be confirmed by identification from CNS tissue.

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

- No treatment.
- Once the diagnosis is likely, euthanasia is indicated.

CONTRAINDICATIONS

None

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

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

- All suspected rabies patients should be securely isolated and monitored for any development of mood change, attitude change, or clinical signs that might suggest the diagnosis.
- An apparently healthy dog or cat that bites or scratches a person should be monitored for a period of 10 days; if no signs of illness occur in the animal within 10 days, the person has had no exposure to the virus; dogs and cats do not shed virus for more than 3 days before development of clinical disease.

- An unvaccinated dog or cat that is bitten or exposed to a known rabid animal must be quarantined according to local or state regulations, often for up to 6 months.

PREVENTION/AVOIDANCE

- Vaccines (dogs and cats)—vaccinate according to standard recommendations and state and local requirements; all dogs and cats with any potential exposure to wildlife or other dogs; vaccinate after 12 weeks of age, then 12 months later, then every 3 years using a vaccine approved for 3 years; use only inactivated or recombinant vector vaccines for cats.
- Vaccinated animals exposed to possible or confirmed rabies suspect should receive booster vaccine, according to applicable local laws.
- Rabies-free countries—entering dogs and cats are quarantined for long periods, usually 6 months.
- Disinfection—any contaminated area, cage, food dish, or instrument must be thoroughly disinfected; use a 1:32 dilution (4 ounces/gallon) of household bleach to quickly inactivate the virus.

POSSIBLE COMPLICATIONS

- Development of acute neurological signs, death.
- Difficulty of antemortem diagnosis may lead to humans and other animals being exposed to virus.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—grave; almost invariably fatal.
- Dogs and cats with clinical infection usually succumb within 1–10 days of onset of clinical signs; often within 3–4 days.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

None

AGE-RELATED FACTORS

None

ZOONOTIC POTENTIAL

- Extreme.
- Humans must avoid bites and contact with saliva or CNS tissue from a rabid animal or

an asymptomatic animal that is incubating the disease.

- Suspected rabies cases must be strictly quarantined and confined to prevent exposure to humans and other animals. Full personal protective equipment should be worn if interaction is necessary.
- Local and state regulations must be adhered to carefully and completely.

PREGNANCY/FERTILITY/BREEDING
Infection during pregnancy is fatal to dam.**SYNONYMS**

N/A

ABBREVIATIONS

- CNS = central nervous system
- DFA = direct immunofluorescent antibody.
- LMN = lower motor neuron.
- PLR = pupillary light reflex.
- PNS = peripheral nervous system.

INTERNET RESOURCES

www.cdc.gov/rabies/

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Fred W. Scott.



Client Education Handout
available online

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RED EYE



BASICS

DEFINITION

Erythema of the eyelids, increased or hyperemic ocular surface vasculature, or hemorrhage within the eye.

PATHOPHYSIOLOGY

- Active dilation of ocular vessels—in response to extraocular or intraocular inflammation or passive congestion.
- Hemorrhage from existing or newly formed blood vessels.

SYSTEMS AFFECTED

Ophthalmic—eye and/or ocular adnexa.

SIGNALMENT

Dog and cat.

SIGNS

Historical Findings

Depends on cause.

Physical Examination Findings

- Depends on cause.
- May affect one or both eyes.
- Result of systemic disease—abnormalities in other organ systems common.

CAUSES

- Blepharitis.
- Conjunctivitis.
- Keratitis.
- Episcleritis or scleritis.
- Anterior uveitis.
- Glaucoma.
- Hyphema.
- Orbital disease—usually the orbital abnormality is more prominent.

RISK FACTORS

- Systemic infectious or inflammatory diseases.
- Immunocompromise.
- Coagulopathy.
- Systemic hypertension.
- Irritation by potentially any topical ophthalmic medication.
- Neoplasia.
- Trauma.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

More than one cause may occur simultaneously.

Similar Signs

- Rule out normal variations.
- Palpebral conjunctiva—normally redder than bulbar conjunctiva.
- One or two large episcleral vessels—may be normal if the eye is otherwise quiet.

- Transient mild hyperemia—with excitement, exercise, and straining.
- Horner's syndrome—may cause mild conjunctival vascular dilation; differentiated by other signs and pharmacologic testing.

Causes

- Superficial (conjunctival) vessels—originate near the fornix, move with the conjunctiva, branch repeatedly, and blanch quickly with topical 2.5% phenylephrine or 1:100,000 epinephrine. Suggests ocular surface disorders (e.g., conjunctivitis, superficial keratitis, blepharitis).
- Deep (episcleral) vessels—originate near the limbus, branch infrequently, do not move with the conjunctiva, and blanch slowly or incompletely with topical sympathomimetics. Suggests episcleritis or intraocular disease (e.g., anterior uveitis or glaucoma).
- Discharge—mucopurulent to purulent: typical of ocular surface disorders and blepharitis; serous or none: typical of intraocular disorders.
- Swollen or inflamed eyelids—suggest blepharitis.
- Corneal opacification, neovascularization, or fluorescein stain retention—suggest keratitis.
- Aqueous flare or cell (increased protein or cells in the anterior chamber)—confirms diagnosis of anterior uveitis.
- Pupil—miotic: common with anterior uveitis; dilated: common with glaucoma; normal: with blepharitis and conjunctivitis.
- Abnormally shaped or colored irides—suggest anterior uveitis.
- Luxated or cataractous lenses—suggest glaucoma or anterior uveitis.
- Intraocular pressure (IOP)—high: diagnostic for glaucoma; low: suggests anterior uveitis.
- Loss of vision—suggests glaucoma, anterior uveitis, or severe keratitis.
- Glaucoma and anterior uveitis—may complicate hyphema.

CBC/BIOCHEMISTRY/URINALYSIS

Typically normal, except with anterior uveitis, glaucoma, or hyphema secondary to systemic disease.

OTHER LABORATORY TESTS

Depends on cause—see specific types of red eye (conjunctivitis, uveitis, etc.).

IMAGING

- Chest radiographs—consider with anterior uveitis or if intraocular neoplasia is a possibility.
- Abdominal radiography or ultrasonography—may rule out infectious or neoplastic causes.
- Ocular ultrasonography—if the ocular media are opaque; may define the extent and nature of intraocular disease or identify intraocular tumor.

DIAGNOSTIC PROCEDURES

Tonometry—must perform in every patient with an unexplained red eye.

Ocular Surface Disorders

- Aerobic bacterial culture and sensitivity—with a purulent discharge, chronic disease, or poor response to treatment.
- Schirmer tear test.
- Cytologic examination of affected tissue.
- Cats—consider PCR or immunofluorescent antibody (IFA) test on corneal or conjunctival scrapings for feline herpesvirus and *Chlamydia*; collect sample before fluorescein staining to avoid false-positive results on IFA.
- Fluorescein stain.
- Conjunctival biopsies—with chronic conjunctivitis or with a mass lesion.
- See specific disease—Conjunctivitis—Cats; Conjunctivitis—Dogs; Blepharitis; Keratitis chapters.

Intraocular Disorders

- Fluorescein stain.
- See specific disease: Anterior Uveitis—Cats; Anterior Uveitis—Dogs; Hyphema; Glaucoma.



TREATMENT

- Usually outpatient.
- Elizabethan collar—to prevent self-trauma
- Avoid dirty environments or those that may lead to ocular trauma, especially if topical corticosteroids are used.
- Because there is a narrow margin for error, consider referral if the diagnosis is uncertain and/or glaucoma cannot be ruled out.
- Few causes are fatal; however, a workup may be indicated (especially with anterior uveitis and hyphema) to rule out potentially fatal systemic diseases.
- Deep corneal ulcers and glaucoma—may be best treated surgically.



MEDICATIONS

DRUG(S) OF CHOICE

- Depends on specific cause.
- Generally, control ocular pain, inflammation, infection, and IOP.
- Carprofen 2.2 mg/kg PO q12h or 4.4 mg/kg PO q24h to control mild inflammation and reduce pain

CONTRAINDICATIONS

- Topical corticosteroids—contraindicated if the cornea retains fluorescein stain.
- Systemic corticosteroids—avoid until infectious systemic causes have been ruled out.

RED EYE

(CONTINUED)

PRECAUTIONS

- Topical aminoglycosides—may be irritating; may impede reepithelialization if used frequently or at high concentrations.
- Topical solutions—may be preferable to ointments if corneal perforation is possible.
- Atropine—may exacerbate keratoconjunctivitis sicca (KCS) and glaucoma.
- Nonsteroidal anti-inflammatory drugs (NSAIDs)—use with caution in hyphema.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

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

- Depends on cause.
- Repeat ophthalmic examinations—as required to ensure that IOP, ocular pain, and inflammation are well controlled.

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- The greater the risk of loss of vision, the more closely the patient needs to be followed; may require daily or more frequent examination.

POSSIBLE COMPLICATIONS

- Loss of the eye or permanent vision loss.
- Chronic ocular inflammation and pain.
- Death.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

Numerous systemic diseases.

AGE-RELATED FACTORS

N/A

PREGNANCY/FERTILITY/BREEDING

Systemic corticosteroids may complicate pregnancy.

SEE ALSO

- Anterior Uveitis—Dogs.
- Anterior Uveitis—Cats.

- Conjunctivitis—Dogs.
- Conjunctivitis—Cats.
- Episcleritis.
- Glaucoma.
- Keratitis, Ulcerative.

ABBREVIATIONS

- IFA = immunofluorescent antibody.
- IOP = intraocular pressure.
- KCS = keratoconjunctivitis sicca.
- NSAID = nonsteroidal anti-inflammatory drug.

Suggested Reading

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**Client Education Handout
available online**

REGURGITATION



BASICS

DEFINITION

Passive, retrograde movement of undigested gastric or esophageal contents into the oral cavity. Reflux refers to the retrograde movement of gastric juice across the gastroesophageal sphincter into the esophagus.

PATOPHYSIOLOGY

Regurgitation results from a loss of normal esophageal motility. In the normal esophagus, the presence of a food bolus in the proximal esophagus stimulates afferent sensory neurons. Signals are transferred centrally, via the vagus and glossopharyngeal nerves, to the tractus solitarius and nucleus ambiguus. Motor impulses travel back via the vagus nerve to stimulate striated muscle (canine) and striated and smooth muscle (feline) to cause esophageal peristalsis. Lesions anywhere along this pathway may lead to regurgitation. Esophagitis secondary to reflux can cause esophageal dysmotility and subsequent regurgitation. Delayed gastric emptying is a common and underappreciated cause of reflux and possible regurgitation.

SYSTEMS AFFECTED

- Gastrointestinal—dysphagia, weight loss.
- Musculoskeletal—weakness, weight loss.
- Nervous—polyneuropathies, CNS disease.
- Respiratory—aspiration pneumonia.

GENETICS

• Regurgitation due to megaesophagus can be inherited in smooth fox terriers (autosomal recessive) and miniature schnauzers (autosomal dominant or 60% penetrance autosomal recessive). In addition, Jack Russell terriers, springer spaniels, long-haired miniature dachshunds, golden retrievers, Labrador retrievers, and Samoyeds are predisposed to the congenital form of myasthenia gravis. A breed predisposition for acquired megaesophagus also exists for the German shepherd dog, Great Dane, Irish setter, Labrador retriever, pug, and Chinese Shar-Pei. The site and pathogenesis of the lesion in idiopathic megaesophagus is unknown. Suggested hypotheses include abnormalities of the afferent limb of the reflex arc (receptors, neurons) or of the swallowing center in the CNS. • Boxers and Newfoundlands have a genetic predisposition for inflammatory myopathy that is associated with esophageal dysmotility. • Brachycephalic breeds are predisposed to sliding hiatal hernias (type I) that is typically associated with gastroesophageal reflux and regurgitation.

INCIDENCE/PREVALENCE

N/A

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

Species

Dog (more commonly) and cat.

Breed Predilections

- Smooth fox terriers, miniature schnauzers. Other predisposed breeds include Great Dane, German shepherd dog, Irish setter, Labrador retriever, Newfoundland, and boxer, brachycephalic breeds (shar-pei, pug, Boston terrier, English bulldog, French bulldog).
- Siamese and Siamese-related cats.

Mean Age and Range

- Congenital cases present soon after birth (congenital megaesophagus) or at weaning (vascular ring anomalies) during the transition from liquid diet to solid foods.
- Acquired cases may be seen at any age, depending on the etiology.

Predominant Sex

No gender predilection has been identified.

SIGNS

General Comments

- Clients often report vomiting; the veterinarian must differentiate vomiting from regurgitation using a comprehensive history. Having owner videotape events may be helpful. • Regurgitation—passive process; little to no abdominal effort; no prodromal phase; regurgitated material has increased amounts of thick mucus. • Vomiting—active process; prodromal phase is identified; vomited material may have increased amounts of bile staining. • The shape of the expelled material (i.e., tube-like), presence of undigested food, and length of time from ingestion to regurgitation or vomiting are less helpful to differentiate.

Historical Findings

- Vomiting (as perceived by owner).
- Dysphagia. • Coughing. • Ravenous appetite. • Weight loss. • Ptyalism. • Other signs, depending upon underlying etiology.

Physical Examination Findings

- Cervical swelling may be noted. • Ptyalism.
- Halitosis. • Increased respiratory noises.
- Nasal discharge and fever (if concurrent pneumonia). • Cachexia. • Weakness.

CAUSES

Congenital Pharyngeal or Pharyngoesophageal

- Cleft or short palate (typically associated with nasal reflux). • Cricopharyngeal muscle achalasia (typically associated with nasal reflux and dysphagia). • Myasthenia gravis.

Congenital Esophageal

- Vascular ring anomaly (e.g., persistent right aortic arch). • Megaesophagus. • Glycogen storage disease. • Esophageal diverticulum.
- Bronchoesophageal fistula.

Acquired Pharyngeal or Pharyngoesophageal

- Cricopharyngeal dysphagia. • Foreign bodies. • Neoplasia. • Rabies. • Toxicity

(botulism). • Myopathy/neuropathy/junctionopathy.

Acquired Esophageal

- Megaeophagus. • Myasthenia gravis. • Stricture. • Neoplasia.
- Hypoadrenocorticism. • Hypothyroidism.
- Hiatal hernia. • Dysmotility.
- Gastroesophageal intussusception.
- Gastroesophageal reflux. • Periesophageal masses. • Dysautonomia. • Myopathy/neuropathy.
- Foreign bodies. • Granulomatous disease. • Toxicity (lead). • Idiopathic.
- Gastric dilatation/volvulus. • Parasitic infection (*Spirocerca lupi*). • Bronchoesophageal fistula.

Congenital or Acquired Gastric (Increase Gastroesophageal Reflux)

- Pyloric outflow obstruction. • Gastric foreign body. • Gastric hypomotility.

RISK FACTORS

- Increased risk of gastroesophageal reflux with general anesthesia; the resultant esophagitis may lead to stricture formation and regurgitation. • Administration of doxycycline or clindamycin have been associated with esophagitis and stricture formation. • Esophageal foreign body.
- Swallowing caustic agents causing esophagitis.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Regurgitation is a clinical sign, not a diagnosis, and is the hallmark of esophageal disease. • It is important to differentiate vomiting from regurgitation.

CBC/BIOCHEMISTRY/URINALYSIS

- There are no pathognomonic changes for regurgitation. • Inflammatory leukogram may be seen if aspiration pneumonia is present. • Most helpful for evaluation of possible underlying etiologies: e.g., erythrocyte changes with lead toxicosis, elevated creatine kinase (CK) with myopathy, hyperkalemia and hyponatremia with hypoadrenocorticism, hypercholesterolemia with hypothyroidism.

OTHER LABORATORY TESTS

These elucidate etiologies of acquired conditions causing regurgitation and include adrenocorticotrophic hormone (ACTH) stimulation test or baseline cortisol level (hypoadrenocorticism); thyroid serology (hypothyroidism); acetylcholine receptor antibody level (myasthenia gravis); blood lead levels (toxicosis).

IMAGING

- Thoracic and cervical radiography—evidence of a gas-, fluid-, or ingesta-filled esophagus with megaesophagus; may also show aspiration pneumonia, neoplasia, foreign bodies, hiatal

REGURGITATION

hernia, etc. • Contrast studies—both liquid barium and barium-coated food for radiolucent foreign bodies or esophageal strictures. Iohexol may also be used. Esophagram does not allow one to evaluate functional disorders such as intestinal dysmotility or cricopharyngeal muscle achalasia. Caution: contrast studies may increase the risk for aspiration pneumonia with regurgitation. • Videofluoroscopy—for pharyngeal weakness, cricopharyngeal muscle dysfunction, esophageal motility disorders, hiatal hernia, or gastroesophageal reflux. • Other imaging studies include scintigraphy and high-resolution manometry for motility evaluation and ultrasound for pharyngeal or cervical masses. • Cervical and thoracic CT scans may also be utilized.

DIAGNOSTIC PROCEDURES

- Esophagoscopy can be useful for esophagitis, strictures, vascular ring anomalies, neoplasia, and foreign bodies. • Electromyography and nerve/muscle biopsies may be used for neuro-pathic or myopathic conditions. • Transtracheal wash or bronchoalveolar lavage if aspiration pneumonia is present or suspected.

PATHOLOGIC FINDINGS

Gross and histologic findings depend upon the underlying etiology and the presence of complicating factors.

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TREATMENT

APPROPRIATE HEALTH CARE

- Therapy for underlying etiology should be instituted. • Important to meet nutritional requirements and treat or prevent aspiration pneumonia.

NURSING CARE

- Aspiration pneumonia may require supplemental oxygen therapy, nebulization/coupage, and fluid therapy with balanced electrolyte solution. • These animals may be recumbent and require soft bedding. They should be maintained in sternal recumbency or turned to alternate down sides every 4 hours.

ACTIVITY

Depending on etiology, restricted activity is not necessary.

DIET

- Experimentation with different food consistencies is essential. Liquid gruel, small meatballs, or blenderized slurries may be used.
- Some cases benefit from gastrostomy feedings, though regurgitation may still occur.
- Both food and water should be elevated, and animal should be maintained in an upright position for 10–15 minutes after eating or drinking. Use of a Bailey chair facilitates keeping the dog upright for 10–15 minutes after a meal. • The recommend caloric requirement amount should be calculated and the diet should be monitored so that metabolizable energy requirements are met.

CLIENT EDUCATION

- If regurgitation is due to megaesophagus, most cases require lifelong therapy, even if an underlying etiology is found. Client dedication is important for long-term management.
- Most animals succumb to aspiration pneumonia or intractable regurgitation.
- Placement of a percutaneous gastrostomy tube (PEG) tube in dogs with megaesophagus can reduce the frequency of aspiration pneumonia, leading to prolonged survival.

SURGICAL CONSIDERATIONS

- Surgical intervention is indicated for vascular ring anomalies, cricopharyngeal muscle achalasia, bronchoesophageal fistula, and others. • Esophageal dysfunction is permanent in most cases. • Balloon dilation is indicated for cases of esophageal stricture.



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotics for aspiration pneumonia (broad-spectrum or based on culture and sensitivity from transtracheal wash or bronchoalveolar lavage). • Specific therapy for underlying etiology if indicated. • Prokinetics—metoclopramide 0.2–0.4 mg/kg SC or PO q6–12h, or 1–2 mg/kg q24h as a CRI increases lower esophageal sphincter (LES) tone and increases gastric motility. Cisapride 0.5 mg/kg PO q8–12h is more effective for esophageal reflux than metoclopramide and has been documented to enhance gastric emptying and increase LES tone in dogs. • Other motility agents (e.g., erythromycin) can enhance gastric emptying and possibly increase LES tone. • H₂ receptor antagonists can be used for the short term to manage mild to moderate esophagitis—ranitidine 1–2 mg/kg PO, IV q12h, famotidine 0.5–1 mg/kg PO, SC, IM, IV q12h; however, are subject to tachyphylaxis (tolerance) when used for >4–5 days and are less potent compared to proton-pump inhibitors. Proton-pump inhibitors may be used in moderate to severe cases, and are also effective when administered for prolonged periods of time—omeprazole 0.7–1.5 mg/kg PO q12h. • Sucralfate caplets or suspension can be administered to help reduce esophageal pain and promote healing of esophagitis and esophageal erosions or ulcerations.

CONTRAINDICATIONS

N/A

PRECAUTIONS

- Absorption of orally administered drugs may be compromised when coadministered with sucralfate. • Injectable forms of acid suppressants should be used when applicable to avoid concerns with regurgitation of the drug before absorption.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Animals with aspiration pneumonia should have thoracic radiographs and complete blood counts checked until resolution, or if recurrence is suspected. • Animals should be monitored, weighed, and body condition scores applied to ensure adequate caloric intake.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Aspiration pneumonia. • Others depending on presence of underlying diseases (e.g., hypothyroidism).

EXPECTED COURSE AND PROGNOSIS

- Older animals with idiopathic megaesophagus have a poor prognosis. • Aspiration pneumonia is the typical cause of death or euthanasia.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Aspiration pneumonia. • Megaesophagus.

AGE-RELATED FACTORS

Young animals may regain some esophageal function with appropriate therapy, depending on etiology.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Dysautonomia (Key-Gaskell Syndrome).
- Dysphagia. • Esophagitis.
- Megaesophagus. • Myasthenia Gravis.
- Pneumonia, Bacterial.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- CK = creatine kinase. • LES = lower esophageal sphincter. • PEG = percutaneous endoscopic gastrostomy tube.

Suggested Reading

Guilford G, Strombeck D. Diseases of swallowing. In: Strombeck's Small Animal Gastroenterology, 3rd ed. Philadelphia, PA: Saunders, 1996, pp. 211–235.

Author Stanley L. Marks

Consulting Editor Mark P. Rondeau



Client Education Handout
available online

RETAINED PLACENTA



BASICS

OVERVIEW

- Dogs—placenta retained beyond the immediate postpartum period; placentas usually passed within 15 minutes of birth of a puppy; may develop acute metritis secondary to retained placenta.
- Cats—may retain placentas for days without signs of illness.
- Extremely uncommon.

SIGNALMENT

- Dog—rare, most common in toy dog breeds.
- Cat—rare.

SIGNS

Historical Findings

- Recent parturition.
- Continued vulvar discharge of lochia.
- Owner may note number of placentas passed, although this information is frequently unreliable.

Physical Examination Findings

- Green lochia vulvar discharge.
- Palpation of firm mass in uterus—not always possible.
- Concurrent clinical signs of postpartum metritis.

CAUSES & RISK FACTORS

- Toy breed.
- Large litter size.
- Dystocia.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Postpartum metritis—physical examination and vaginal cytologic examination show no signs of infection with uncomplicated retained placenta; metritis may develop concurrently.
- Retained fetus—differentiated by radiography or ultrasonography.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal when uncomplicated.

OTHER LABORATORY TESTS

Vaginal cytologic examination—parabasal epithelial cells; may note erythrocytes; biliverdin clumps.

IMAGING

Ultrasonography—echogenic but nonfetal mass within the uterus.

DIAGNOSTIC PROCEDURES

Celiotomy or hysterotomy—may be required for diagnosis.



TREATMENT

- Outpatient for healthy bitch or queen.
- Instruct owner to monitor rectal temperature and observe for signs of systemic illness.
- Ovariohysterectomy—curative; recommended if future breeding is not a consideration.
- Surgical removal—indicated if medical treatment is unsuccessful and the bitch develops metritis.



MEDICATIONS

DRUG(S) OF CHOICE

- Oxytocin—known or suspected condition in otherwise healthy cats and dogs; dogs: 0.5 IU/kg IM, up to 5 IU total dose; cats: 0.5–1 IU IM. Oxytocin may be ineffective after 48 hours postpartum.
- Can precede oxytocin treatment with calcium gluconate (10%); dogs and cats, 0.5–1.5 mL/kg IV slowly over 15 minutes; monitor for bradycardia during injection.
- Metritis—treat accordingly (see Metritis).

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

Do not give progestational drugs.



FOLLOW-UP

- Monitor temperature and physical condition.
- Acute metritis (dogs)—may develop if the placenta is not passed; fair to good prognosis for recovery with treatment.
- Prognosis for future reproduction—good without metritis; fair to poor with metritis.



MISCELLANEOUS

SEE ALSO

Metritis

Suggested Reading

Feldman EC, Nelson RW. Periparturient diseases. In: Feldman EC, Nelson RW, eds., Canine and Feline Endocrinology and Reproduction, 3rd ed. Philadelphia, PA: Saunders, 2004, pp. 808–834.

Grundy SG, Davidson AP. Theriogenology question of the month. Acute metritis secondary to retained fetal membranes and a retained nonviable fetus. J Am Vet Med Assoc 2004, 224(6):844–847.

Author Joni L. Freshman

Consulting Editor Erin E. Runcan

ROUNDWORMS (ASCARIASIS)



BASICS

OVERVIEW

- Ascariasis caused by *Toxocara canis* (dogs), *T. cati* (cats), and *Toxascaris leonina* (dogs, cats); *Baylisascaris* (raccoons) can infect dogs and causes neural larval migrans in people.
- Transplacental transmission of *T. canis* larvae from bitch to pups causes prenatal infection; transmammary transmission of larvae occurs with both *Toxocara* spp.; no transplacental or transmammary transmission with *Toxascaris*.
- In first month of life, infected neonatal pups may develop abdominal pain and rapidly deteriorate before *Toxocara* eggs appear in feces.
- Older pups and kittens can acquire by ingesting eggs spread by dams with postgestational infection; dams can be infected by ingesting immature worm stages in pups' feces or vomitus or by predation on vertebrate transport hosts.
- Adult ascarids occur in lumen of small intestine; larval stages of *Toxocara* spp. may migrate in liver and lungs.
- If numerous, ascarids (up to 10–12 cm long) can distend intestine and cause colic, interference with gut motility, inability to utilize food, intestinal rupture.

SIGNALMENT

- Dog and cat.
- Important in puppies/kittens due to *in utero*/transmammary transmission.

SIGNS

- Abdominal distension; often with palpable intestinal distension.
- Colic.
- Weakness, loss of condition, cachexia; poor nursing or appetite; scant feces.
- Coughing due to larval lung migration.
- Entire litter may be affected.

CAUSES & RISK FACTORS

- Dormant *Toxocara* larvae in dam's tissues is infection reservoir for puppies during gestation; queen becomes infected during late pregnancy or lactation and transfers to kittens via transmammary route.
- Access to infected transport hosts.
- Concurrent enteric infections.
- Toxocara* larvae undergo extensive migration and can cause granulomatous inflammation (visceral larva migrans). Visceral larva migrans caused by ascarids is cause of human morbidity.
- Somatically arrested larvae in small vertebrates are source of infection for dogs/cats that hunt.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Transmammary perinatal infection of neonates with hookworms (anemia, melena,

weakness, lethargy, pallor, enteritis) or *Strongyloides* (diarrhea); coccidiosis, giardiasis; examine feces for eggs or larvae.

- Physaloptera*.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal.

OTHER LABORATORY TESTS

N/A

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Fecal flotation to detect eggs:
 - Toxocara* eggs spherical pitted outer shell membrane, single dark cell filling interior, 80–85 µm (*T. canis*), ~75 µm (*T. cati*).
 - Baylisascaris* eggs similar to *T. canis* eggs but smaller (~76 × 60 µm), more finely pitted shell.
- Toxascaris* eggs ovoid, smooth exterior shell membrane, 1–2 cells with light-colored cytoplasm; cells do not fill interior of egg: 80 × 70 µm in diameter.
- Necropsy of siblings—identify ascarids by size, appearance.
- Fecal ELISA—commercial test detects antigen produced by adult and immature roundworms of both sexes; can detect prepatent infection.



TREATMENT

- Generally outpatient.
- Acute severe cases treated as inpatients; provide parenteral fluids.
- Alert client to possibility of sudden death or chronic debilitation.
- Treat dam with adulticide/larvicide anthelmintic to remove intestinal stages and limit transmission to subsequent litters.



MEDICATIONS

DRUG(S) OF CHOICE

Adulticide/Larvicide Anthelmintics

- Fenbendazole 50 mg/kg PO q24h for 3 days.
- Milbemycin oxime 0.5 mg/kg (dogs) or 2 mg/kg (cats) PO q30 days.
- Moxidectin (dogs) 2.5 mg/kg, topically, q30 days.
- Moxidectin (in combination with imidacloprid) 10 mg/kg, topically, q30 days.
- Emodepside 3 mg/kg, or praziquantel 12 mg/kg, topically once for cats ≥8 weeks old; repeat in 30 days if cat is reinfected.

Adulticide Anthelmintics

- Pyrantel pamoate 5 mg/kg PO (dogs) or 10–20 mg/kg PO (cats, extra-label).
- Pyrantel/praziquantel, label dose for cats.
- Febantel/praziquantel/pyrantel, label dose for dogs.
- Ivermectin/pyrantel, label dose for

dogs.

- Selamectin 6 mg/kg, topically, once (*T. cati*, cats): dogs, extra-label.

CONTRAINDICATIONS/POSSIBLE INTERACTIONS

N/A



FOLLOW-UP

PATIENT MONITORING

Repeat post-treatment fecal exams on puppies/kittens and/or repeat anthelmintic treatment every 2–3 weeks until old enough for monthly anthelmintic product.

PREVENTION/AVOIDANCE

- Minimize environmental contamination, treat infected dogs/cats with anthelmintic, dispose of feces promptly.
- Prevent dogs/cats from hunting or ingesting transport hosts.
- Extra-label treatment of dam with adulticide/larvicide anthelmintic to remove intestinal stages and decrease vertical transmission.

POSSIBLE COMPLICATIONS

Transplacental transmission of large numbers of larvae can result in fetal death or birth of weak, nonviable offspring.

EXPECTED COURSE AND PROGNOSIS

Prognosis good after anthelmintic treatment; guarded with severe prenatal *T. canis* infection.



MISCELLANEOUS

AGE-RELATED FACTORS

Greater concern in neonates.

ZOONOTIC POTENTIAL

- Visceral larva migrans, ocular larva migrans, neural larva migrans, chronic abdominal or cutaneous problems may follow ingestion of infective *Toxocara* spp. or *Baylisascaris* eggs by humans; advise clients to practice good hygiene after handling feces.
- Most likely cause of neural larva migrans is *Baylisascaris*; virtually all raccoons become infected with *Baylisascaris* and therefore extreme caution should be exercised with clients having raccoons as "pets."

INTERNET RESOURCES

- <http://www.capcvet.org> • <http://www.cdc.gov>

Suggested Reading

Bowman DD. Georgis' Parasitology for Veterinarians, 9th ed. St. Louis, MO: Saunders, 2009, pp. 197–198, 201–208.

Authors Matt Brewer and Jeba R.J. Jesudoss Chelladurai

Consulting Editor Amie Koenig

SALMONELLOSIS



BASICS

DEFINITION

Infection caused by many different serotypes of *Salmonella*, causing enteritis, septicemia, and abortions.

PATHOPHYSIOLOGY

- *Salmonella*—Gram-negative bacterium; colonizes small intestine (ileum); adheres to and invades enterocytes; enters and multiplies in lamina propria and local mesenteric lymph nodes; cytotoxin and enterotoxin are produced; inflammation and prostaglandin synthesis ensue; results in secretory diarrhea, mucosal sloughing.
- Uncomplicated gastroenteritis—organisms are stopped at the mesenteric lymph node stage; patient has only diarrhea, vomiting, dehydration.
- Bacteremia and septicemia following gastroenteritis—more serious; focal extra-intestinal infections (abortion, joint disease) or endotoxemia may result; may cause thrombosis, disseminated intravascular coagulation (DIC), death.
- Some patients recover from septicemia but have prolonged recovery.

SYSTEMS AFFECTED

- Gastrointestinal—enterocolitis; inflammation, mucosal sloughing, secretory diarrhea.
- Systemic disease (e.g., bacteremia, focal infections, septicemia)—multiorgan infarction, thrombosis, abscesses, meningitis, osteomyelitis, abortion.

GENETICS

N/A

INCIDENCE/PREVALENCE

- True incidence unknown; prevalence in healthy dogs/cats similar to diarrheic animals.
- Most infections subclinical.
- Dogs—clinical disease most often seen in the young and pregnant bitches. Common in racing greyhounds and sled dogs due to raw meat diets; presence of *Salmonella* in feces does not necessarily imply infection.
- Cats—natural resistance; stressed, hospitalized, and shelter cats at risk. Pandemics of salmonellosis in migrating songbirds (usually *Salmonella Typhimurium*) in spring lead to epidemics in bird-hunting cats.
- Raw meat diet (especially chicken) risks—*Campylobacter* spp. in addition to *Salmonella* spp. and *Listeria* spp. Outbreaks linked to pet foods/treats common.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Dog and cat.

Mean Age and Range

- Dogs—neonatal/immature puppies, pregnant bitches. Most adult carrier dogs clinically normal.
- Cats—adults highly resistant unless treated with an antimicrobial prior to exposure.

SIGNS

General Comments

Disease severity—subclinical (carrier state, more common) to severe clinical cases in neonatal and stressed adult animals.

Historical Findings

- Diarrhea, can be hemorrhagic.
- Vomiting.
- Fever.
- Malaise.
- Anorexia.
- Vaginal discharge/abortion—dogs.
- Chronic febrile illness—persistent fever, anorexia, malaise without diarrhea.

Physical Examination Findings

- Asymptomatic carrier states—no clinical signs.
- Gastroenteritis—fever (102–104°F/39–40°C), diarrhea with mucus and/or blood, dehydration, abdominal pain, tenesmus, pale mucous membranes, weight loss.
- Gastroenteritis with bacteremia, septic shock, or endotoxemia—brick-red mucous membranes, tachycardia, bounding pulses, rapid capillary refill time (unless decompensatory shock), tachypnea, abdominal pain, weakness.
- Focal extraintestinal infections—conjunctivitis, cellulitis, pyothorax, diskospondylitis.
- Cats—chronic febrile illness, vague, nonspecific clinical signs.
- Recovering patients—chronic intermittent diarrhea for 3–4 weeks (may shed *Salmonella* in stool ≥6 weeks).

CAUSES

- Any one of more than 2,000 serotypes of salmonellae.
- Two or more simultaneous serotypes in host animal can occur:
 - Most common serotypes—Newport, Typhimurium, Albany, 4,5,12:i:, Dublin, Heidelberg.

RISK FACTORS

Disease Agent

- *Salmonella* serotype determines virulence, infectious dose, and route of exposure.
- Host factors that increase susceptibility:
 - Age—neonatal/young dogs and cats; immature immune system.
 - Health—debilitated young animals (immature gastrointestinal tract, poorly developed normal microbial flora) or adults with concurrent disease.
 - Disrupted gastrointestinal flora (adult cats)—antimicrobial treatment; exposure to salmonellae during hospitalization.

Environmental Factors

- Diet:
 - Raw food diet is major risk factor.
 - Contaminated dog treats (e.g., pig ears).
 - Dehydrated (dry) pet food; semi-moist foods usually not as risky.
- Coprophagy.
- Grooming habits—can contaminate environment, feed and water dishes.
- Dense population—colonies, boarding facilities, shelters:
 - Build up of *Salmonella* in environment, more efficient fecal-oral cycling.
 - Stress.
 - Exposure to infected (or carrier) animals.
- Unsanitary environment.

Hospitalized Animals

Nosocomial exposure (plus stress) or activation (by stress) of preexisting asymptomatic (carrier) *Salmonella* infection, especially in animals treated with antimicrobial drugs.

Vaccinated Cats

Death reported in kittens (likely to be subclinically infected by *Salmonella*) post vaccination, with high titers of modified live panleukopenia vaccine.



DIAGNOSIS

S

DIFFERENTIAL DIAGNOSIS

- Acute gastroenteritis—infectious, foreign body, neoplasia:
 - Viral gastroenteritis—canine enteric coronavirus, canine parvovirus, rotavirus, canine distemper.
 - Bacterial gastroenteritis—*Escherichia coli*, *Campylobacter jejuni*, *Yersinia enterocolitica*.
- Bacterial overgrowth syndrome—*Clostridium difficile*, *C. perfringens*.
- Parasites—helminths, protozoa (*Giardia*, *Coccidia*, *Cryptosporidium*), salmon poisoning.
- Acute gastritis—erosions or ulcers.
- Diet-related—allergy or food intolerance.
- Drug- or toxin-induced distress.
- Extraintestinal disorders (metabolic disease).

CBC/BIOCHEMISTRY/URINALYSIS

- CBC—variable; depends on stage of illness: initially neutropenia, left-shifted neutrophils, lymphopenia, thrombocytopenia, non-regenerative anemia.
- Hypoalbuminemia, electrolyte abnormalities related to gastrointestinal losses.

DIAGNOSTIC PROCEDURES

- Fecal/rectal bacterial culture—special media needed:
 - Subclinical carriers may have intermittent positive fecal culture (≥6 weeks).
 - Use of antimicrobials before sampling may yield false-negative culture.
 - Serotyping of cultured organisms—helpful to define outbreak.

SALMONELLOSIS

(CONTINUED)

- Cultures of blood and joint fluid, ileum, mesenteric lymph node, liver/spleen, bone marrow.
- Fecal cytology—leukocytes present.
- Fecal *Salmonella* PCR.
- Abdominal ultrasound (clinical gastroenteritis)—lymphadenomegaly, enterocolitis, typhlitis, peritonitis.

PATHOLOGIC FINDINGS

Lymphoplasmacytic, neutrophilic typhlitis/enteritis with ulceration, crypt abscessation, lymphoid hyperplasia, pyogranulomas; lymphadenitis.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—uncomplicated gastroenteritis.
- Inpatient—with bacteremia/septicemia, gastroenteritis in neonatal/immature animals (rapidly debilitated).

NURSING CARE

- Varies according to severity of illness—assess dehydration, body weight, ongoing fluid loss, shock, hematocrit, albumin, electrolytes, acid-base status.
- Supportive care—fluid and electrolyte replacement:
 - Parentral, balanced, polyionic isotonic replacement solution (lactated Ringer's).
 - Oral fluids—hypertonic glucose solutions; for secretory diarrhea.
 - Plasma transfusions—if serum albumin <2 g/dL.

ACTIVITY

- Isolate patients.
- Cage rest, provide warmth during illness.

DIET

Restrict food 24 hours in adults; gradually introduce highly digestible, low-fat diet.

CLIENT EDUCATION

Instruct client to wash hands frequently and to restrict access to patient in acute stages of disease; large numbers of salmonellae may be shed in stool.



MEDICATIONS

DRUG(S) OF CHOICE

Asymptomatic Carrier State

- Antimicrobials—contraindicated:
 - Quinolones—clear carrier states in humans; controlled trials in animals needed before this can be recommended.

Uncomplicated Gastroenteritis

- Antimicrobials not indicated.
- Locally acting intestinal adsorbents and supportive therapy.

Neonates, Aged, and Debilitated Animals

- Antimicrobial therapy—indicated; culture and susceptibility testing with minimal inhibitory concentration recommended:
 - Trimethoprim-sulfa: 15 mg/kg PO, SC q12h.
 - Enrofloxacin: 5 mg/kg q24h (cat); 10 mg/kg PO, IM, q24h (dog).
 - Chloramphenicol: dogs, 50 mg/kg PO, IV, IM, SC q8h; cats, 50 mg/kg total PO, IV, IM, SC q12h.
- Recent strains of *Salmonella* are multidrug-resistant; adjust empirical therapy based on antimicrobial susceptibility testing.

PRECAUTIONS

- Chloramphenicol, trimethoprim-sulfa—use cautiously in neonatal and pregnant patients.
- Fluoroquinolones—avoid use in pregnant, neonatal, or growing animals because of concern for adverse effects on cartilage; do not administer to cats at dosages higher than 5 mg/kg q24h.



FOLLOW-UP

PATIENT MONITORING

- Fecal culture—repeat monthly for few months to assess development of carrier state.
- Other animals—monitor for secondary spread of infection.
- Advise client to contact veterinarian if patient shows signs of recurring disease.

PREVENTION/AVOIDANCE

- Keep animals healthy—proper nutrition; avoid raw meat diets; vaccinate for other infectious diseases; clean, disinfect cages, runs, and food/water dishes frequently; store food, feeding utensils properly.
- Reduce overcrowding.
- New arrivals—isolate and screen; monitor for sickness before mixing with other animals.
- Protect animals being treated with antimicrobial drugs from exposure to *Salmonella*-contaminated environment (e.g., animal hospital).
- Experimental live attenuated vaccine shows promise, especially for racing dogs.

POSSIBLE COMPLICATIONS

- Spread of infection to other animals or humans within household.

- Development of chronic infection with diarrhea.
- Recurrence of disease with stress.

EXPECTED COURSE AND PROGNOSIS

- Uncomplicated gastroenteritis—prognosis excellent; frequently self-limited; patients recover with good nursing care.
- Recovered animals may shed *Salmonella* intermittently for months or longer.
- Neonatal, aged, pregnant, stressed animals—can develop sepsis or abortion; can be severe, debilitating; may lead to death if untreated.



MISCELLANEOUS

AGE-RELATED FACTORS

Clinical disease is frequently seen in neonatal, or aged animals.

ZOONOTIC POTENTIAL

- High potential, especially in children, elderly, immunosuppressed, and antimicrobial drug users.
- Multidrug-resistant salmonellae have been reported.

PREGNANCY/FERTILITY/BREEDING

- May complicate disease.
- Abortion—may be a sequela to infection.
- Antimicrobial therapy—consider the effect on the fetus.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation.

INTERNET RESOURCES

- <http://www.cfsph.iastate.edu/DiseaseInfo/disease.php?name=salmonella-nontyphoidal&lang=en>
- <https://www.cdc.gov/healthypets/index.html>

Suggested Reading

Marks S, Rankin S, Byrne B, et al.

Enteropathogenic bacteria in dogs and cats: diagnosis, epidemiology, treatment, and control. J Vet Intern Med 2011, 25:1195–1208.

Author Patrick L. McDonough

Consulting Editor Amie Koenig

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—CATS



BASICS

DEFINITION

- Epilepsy—recurrence of seizures from primary brain origin.
- Genetic epilepsy—syndrome that is only epilepsy, with no demonstrable underlying brain lesion or other neurologic signs; the genetic origin must be proven through family studies, gene isolation, or other specific forms of evidence (International League Against Epilepsy); rare in cats.
- Structural epilepsy—syndrome in which the epileptic seizures are the result of identifiable structural brain lesions; frequent in cats.
- Epilepsy of unknown cause—structural epilepsy suspected but a lesion cannot be demonstrated; frequent in cats.
- Cluster seizures— ≥ 1 seizure/24 hours.
- Status epilepticus (SE)—continuous seizure activity, or seizures repeated at brief intervals without complete recovery between seizures. Can be nonconvulsive.
- Convulsive SE—life-threatening medical emergency.

PATOPHYSIOLOGY

- Paroxysmal disorganization of one or several brain functions originating from the thalamocortex. Any thalamocortical disturbance or disease process may lead to seizure activity.
- Not all cortical regions have the same propensity to seize; from the most to the least likely to cause seizures—temporal, frontal, parietal, and occipital lobes.
- As more seizures occur, the tendency for neuronal damage and propensity for more seizures or SE increases; this kindling effect does not occur in all cortical regions.
- The clinical appearance of the seizure is directly related to the location of the neuronal hyperactivity. If the electrical abnormality remains regional, the seizure is focal. If there is recruitment of both hemispheres, the seizure is generalized.
- Great majority of seizures and SE in cats are secondary to structural brain lesions.

SYSTEMS AFFECTED

Nervous

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Cats of any breed, age, or sex.

SIGNS

General Comments

- Nonconvulsive generalized seizures—frequent in cats; movements of facial musculature predominate, such as bilateral twitches of eyelids, whiskers and ears, salivation, lip smacking; may be associated with whole body trembling/shaking, piloerection, dilated pupils. Nonconvulsive SE frequent in cats.

- Focal seizure—when limited to one hemisphere; frantic running and colliding with objects (aura), unilateral facial twitches or eyelid blinks, unilateral limb motions or head/neck turning to one side. Focal seizures often generalize.
- Generalized convulsive seizures—bilateral symmetrical tonic-clonic contractions of limb muscles and dorsiflexion of the head, often associated with autonomic signs such as salivation, urination, defecation. At time of admission, the gross motor activity may have stopped, but there may still be twitching of the lids and body/limb jerks.
- Mutilation frequent—biting of tongue, nail avulsion.

Historical Findings

- Confirm that seizure activity has indeed occurred.
- Pattern of seizures (age at seizure onset, type and frequency of seizures)—most important factor in listing the possible causes.
- Metabolic diseases may cause generalized seizures (GS). • With most seizurogenic toxins, there is a crescendo of hyperexcitability, shaking, trembling, with ultimately GS and death.
- Asymmetry in the signs (eyelid twitches, limb movements primarily on one side, circling) before, during, or after the seizure suggests focal cortical lesion.
- Overdose of insulin, postrenal transplant, or bilateral thyroidectomy lead to GS shortly after the fact.
- Presence of abnormal behavior in the days/weeks preceding the seizure activity indicates structural brain disease.
- Presence of concomitant gastrointestinal (GI), respiratory, or other systemic signs indicates multisystem disease.

Physical Examination Findings

- If chorioretinitis present, look for infectious diseases.
- Dark red mucous membranes suggest polycythemia vera.

Neurologic Examination Findings

- Mental status, menace responses, responses to nasal septum stimulation, and proprioceptive positioning are neurologic tests that evaluate the cerebral cortex. Asymmetry indicates structural brain lesion on the contralateral side of the deficits.
- In most cases of structural epilepsy, neurologic deficits are present at presentation.

CAUSES

Extracranial

Metabolic—hypoglycemia from insulin overdose, hypocalcemia from bilateral thyroidectomy, severe hyperthyroidism, hypertension secondary to renal transplant, hepatic encephalopathy, uremia, polycythemia vera, severe hypertriglyceridemia.

Toxins; Intracranial

- Anatomic—congenital malformation.
- Metabolic—cell storage disease (e.g., neuronal ceroid-lipofuscinosis reported in one cat with myoclonus and seizure activity).
- Neoplastic—meningioma, astrocytoma, lymphoma.
- Inflammatory infectious—viral

non-feline infectious peritonitis (FIP), FIP, toxoplasmosis, cryptococcosis.

- Toxicity—organochlorines, pyrethrins, and pyrethroids; seizures usually observed at end stage; chlorambucil in lymphoma treatment.
- Vascular—polycythemia vera secondary to hyperviscosity, feline ischemic encephalopathy secondary to *Cuterebra* larva.
- Trauma has not been linked to seizures in cats.

RISK FACTORS

- Any forebrain lesion.
- Diabetes mellitus.
- Treatment with chlorambucil.
- Renal failure.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Sleep disorders—the cat does not wake up, or has a normal waking behavior following the episode.
- Syncope—the body is limp with a rapid recovery phase, with no abnormal behavior.
- When seizures are preceded by 2–3 weeks of vague transient systemic illness (decreased appetite, GI signs) in an otherwise healthy cat—viral non-FIP encephalitis or epilepsy of unknown cause.
- When seizures are preceded by systemic signs that persist (>3 weeks)—FIP, cryptococcosis.
- Insidious abnormal behavior with/without circling in a cat >10 years old presented for seizure activity suggests meningioma.
- Cats with hepatic encephalopathy drool excessively.
- Cats with polycythemia vera have GI signs and dark mucous membranes.

S

CBC/BIOCHEMISTRY/URINALYSIS

- Extracranial metabolic causes are diagnosed on history, physical examination, and blood test results.
- High packed cell volume ($>60\%$) in polycythemia vera.
- Low blood glucose in insulin overdose.
- Low calcium in bilateral post thyroidectomy.
- High BUN and creatinine with low specific gravity in acute renal failure.
- Creatine kinase—mild to markedly elevated in cats with SE, even nonconvulsive; with or without myoglobinuria; indicates muscle necrosis.

OTHER LABORATORY TESTS

- Serologic testing—feline immunodeficiency virus, feline leukemia virus titers often noncontributory to diagnosis; FIP and *Toxoplasma gondii* titers nonreliable by themselves.
- Bile acid testing—in cats with suspected hepatic encephalopathy.

IMAGING

- Thoracic radiographs and abdominal ultrasound—if infectious disease suspected; to evaluate lung pathology if SE; to look for neoplasia if tumor suspected.
- MRI—best to define location, extent, and nature of lesion.

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—CATS

(CONTINUED)

DIAGNOSTIC PROCEDURES

CSF—sensitive to detect structural disease; unspecific in itself to reach diagnosis except when organism is seen (e.g., cryptococcosis).

PATHOLOGIC FINDINGS

- Findings reflect etiology.
- It is unknown if hippocampal necrosis is a cause or the consequence of seizures.
- Small lesions may be easily missed in cats diagnosed with epilepsy of unknown cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—isolated recurrent seizures in an otherwise healthy cat.
- Inpatient—cluster seizures and SE. Isolated recurrent seizures in an ill cat.

NURSING CARE

- Constant supervision.
- Install IV line for drug and fluid administration.
- Draw blood for rapid measurement of blood gases, glucose, calcium, and antiepileptic drug levels if pertinent.
- Cool if hyperthermia.

CLIENT EDUCATION

Antiepileptic treatment in structural epilepsy may not help until the primary cause is addressed. Seizures can be difficult to stop in cases of SE, especially with nonconvulsive status.

SURGICAL CONSIDERATIONS

Craniotomy—tumor excision with meningioma or other accessible mass.



MEDICATIONS

DRUG(S) OF CHOICE

Seizure type and frequency determine therapeutic approach.

Isolated Recurrent Generalized Seizures

- First line—phenobarbital 7.5–15 mg/cat q12h; optimal therapeutic serum levels 100–130 µmol/L (23–30 µg/L).
- Second line— gabapentin 3–8 mg/cat q8–12h.
- Levetiracetam—20 mg/kg q8h (serum levels humans 10–40 µg/mL).
- Initiate gradually to avoid overt sedation.

Convulsive Cluster and Status Epilepticus

- Treat cluster and generalized SE early—the more seizures in a given time, and the more drugs for seizure control, time for recovery, and cost for treatment.
- No ongoing seizure activity at presentation and patient naïve to the drug—phenobarbital IV bolus 10 mg/kg to a maximum of 60 mg/cat over 15 minutes, continued with phenobarbital maintenance dosage PO 12 hours later.
- Ongoing seizure activity at presentation—diazepam IV bolus

0.5–1 mg/kg, continuing with CRI at 0.25–0.5 mg/cat/h in an inline burette using a fluid pump; IV bolus of diazepam can be repeated 5 minutes after the first bolus if gross seizure activity persists; in this case, add phenobarbital to CRI at 4 mg/cat/h.

- Start oral phenobarbital at maintenance dose as soon as patient can swallow.
- After 6 hours seizures-free, wean CRI gradually over 4–6 hours.

Persistent Seizures

Subanesthetic doses of IV propofol 1–3.5 mg/kg bolus and 0.01–0.25 mg/kg/minute CRI titrated to effect.

Non-Antiepileptic Drug Treatment

- Dexamethasone 0.25 mg/kg IV q24h for 1–3 days, to improve edema secondary to SE and treat the primary cause if systemic infectious disease is not suspected; dexamethasone alters CSF results.
- Thiamine—5–50 mg/cat in any cat presented with acute neurologic signs, including seizures.

CONTRAINdications

- Do not use KBr in cats; side effects include life-threatening respiratory disease.
- Avoid giving aminophylline, theophylline, ketamine, and fentanyl to epileptic cats.

PRECAUTIONS

- Prolonged use of propofol (>24 hours) may cause Heinz body anemia in cats.
- Cats on CRI of antiepileptic drug(s) are often overtly sedated; cardiovascular and respiratory depression may occur; close monitoring necessary; lubricate eyes, express bladder manually, correct hypothermia.
- Close monitoring necessary to observe if mild ongoing seizure activity persists.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

- Zonisamide—5–10 mg/kg PO q24h (serum levels humans 15–45 µg/mL).
- Diazepam—0.5–2.0 mg/kg/day PO divided q12h.



FOLLOW-UP

PATIENT MONITORING

- CBC, biochemistry, urinalysis prior to initiating antiepileptic drug.
- Phenobarbital-induced hepatotoxicity is not a problem in the cat.
- Creatine kinase to evaluate muscular necrosis and indirectly subtle ongoing seizure activity in cats presented in SE.
- Measure phenobarbital serum level 2 weeks after initiation; correct dosage accordingly; it is difficult to titrate phenobarbital in cats, i.e., a mild increase in dosage often leads to a major increment of the serum levels.
- CBC and biochemistry—

repeat every 6–12 months.

- If structural epileptic patient has recovered from primary disease and remains seizure-free for 6 months—seizures may recur when drug is weaned off.

POSSIBLE COMPLICATIONS

- SE—seizure control may not be reached despite polypharmacy.
- Rare hypersensitivity to phenobarbital—thrombocytopenia, neutropenia, pruritus, swollen feet; do CBC 4–6 weeks after onset of phenobarbital.
- Diazepam rarely may cause acute hepatic necrosis and death.
- Cardiovascular and respiratory collapse from overdose during SE treatment.

EXPECTED COURSE AND PROGNOSIS

- Depends on the underlying cause and response to treatment.
- Cats with epilepsy of unknown cause have good long-term prognosis.
- Cats can recover despite episode of severe cluster-seizures and generalized SE.



MISCELLANEOUS

AGE-RELATED FACTORS

Cats with seizure onset prior to 1 year of age and diagnosed with epilepsy of unknown cause have guarded prognosis for seizure control.

SEE ALSO

- Feline Ischemic Encephalopathy.
- Meningioma—Cats and Dogs.

ABBREVIATIONS

- FIP = feline infectious peritonitis.
- GI = gastrointestinal.
- GS = generalized seizures.
- SE = status epilepticus.

Suggested Reading

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Client Education Handout
available online

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—DOGS



BASICS

DEFINITION

- Epilepsy—recurrence of seizures from primary brain origin.
- Genetic epilepsy—epilepsy with no observable underlying brain lesion or other neurologic signs or symptoms.
- Structural epilepsy—seizures are the result of identifiable structural brain lesions.
- Epilepsy of unknown cause—structural epilepsy is suspected but a lesion cannot be demonstrated.
- Cluster seizures—>1 seizure/24 hours.
- Status epilepticus (SE)—continuous seizure activity or seizures repeated at brief intervals without complete recovery between seizures.
- SE can be convulsive or nonconvulsive.
- Seizures are classified as focal (limited to one hemisphere), generalized (involve both hemispheres), and focal with secondary generalization.

PATHOPHYSIOLOGY

- Any thalamocortical disturbance may lead to seizure activity.
- Not all cortical regions have equal propensity to seize; from the most to the least likely to cause seizures—temporal, frontal, parietal, and occipital lobes.
- As more seizures occur, the tendency for neuronal damage and propensity for more seizures or SE increases; this kindling effect does not occur in all cortical regions.
- The clinical appearance of a seizure is related to the location of the neuronal hyperactivity.

SIGNALMENT

- Dogs of any breed, age, or sex.
- SE—overrepresentation of German shepherd dog, English foxhound, pug, teacup poodle, Boston terrier, Lakeland terrier.

Mean Age and Range

SE—4.2–5 years (0.15–15 years).

SIGNS

General Comments

- Prodrome—hours to days prior to the seizure; no electroencephalogram (EEG) changes.
- Aura—short period (seconds) prior to generalization of a seizure where the dog seeks help, looks lost, frightened or has a glazed look. Focal seizure. If it precedes the tonic-clonic generalized seizure, the seizure has a focal onset.
- Ictus—may start with an aura and progress to generalized seizure (GS); lateral recumbency with bilateral symmetrical tonic-clonic contractions of limb muscles; often with autonomic signs, e.g., salivation, urination, defecation.

- GS—may be mild, the animal remaining sternal or even standing during the event; may be long-lasting, 20 minutes or more. Convulsive or nonconvulsive.

- Post-ictal phase—disorientation, confusion, aimless pacing, blindness, polydipsia, polyphagia.
- A seizure lasts <2 minutes.
- Most seizures occur when dog is resting or sleeping.

Historical Findings

- Confirm that seizure has occurred.
- Seizure pattern (age at onset of seizure, seizure type and frequency)—most important factor in establishing list of possible causes.
- Metabolic diseases usually cause generalized seizures.
- Asymmetric neurologic signs before, during, or after the seizure suggest structural brain lesion.
- Presence of behavioral changes in the days/weeks preceding seizure onset indicates structural brain disease.

Neurologic Examination Findings

- Mental status, menace responses, responses to nasal septum stimulation, and proprioceptive positioning—neurologic tests that evaluate the cerebral cortex. Asymmetry indicates structural brain lesion contralateral to deficits.
- Compensated SE, first 30 minutes—salivation, hyperthermia, tachycardia, arrhythmia, increased blood pressure.
- Decompensated SE—difficulty breathing, weak pulse, low blood pressure, poor capillary refill.

CAUSES

Extracranial

- Metabolic—electrolyte disturbances, hypoglycemia (insulinoma); hypocalcemia; acute renal failure; hepatic encephalopathy.
- Toxicities—metaldehyde, pyrethrins/pyrethroids, lead, hexachlorophene, chlorinated hydrocarbons, organophosphates, bromethalin, mycotoxins, macadamia nut, theobromine (chocolate), 5-fluorouracil.

Intracranial

- Degenerative—encephalopathy.
- Malformations—cortical dysplasia.
- Genetic epilepsy.
- Metabolic—cell storage diseases.
- Neoplasia—primary (meningioma, gliomas); secondary (metastatic).
- Inflammatory infectious—viral (e.g., canine distemper); fungal; protozoal (*Neospora*, *Toxoplasma*); rickettsial (ehrlichiosis, Rocky Mountain spotted fever).
- Inflammatory noninfectious—meningoencephalomyelitis of unknown origin, eosinophilic meningoencephalomyelitis; breed-related encephalitis (pug, Maltese, Yorkshire terriers, etc.).
- Trauma.
- Vascular—cerebrovascular accident.

- Epilepsy of unknown cause—post-encephalitic glial scar.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Syncope—body is limp, rapid recovery with no abnormal behavior; occurs at exercise, cough, excitement.
- Insulinoma—seizures occur at exercise, excitement.
- Obsessive compulsive behaviors or stereotypes—complex and goal-directed behaviors; behavior can be stopped.
- Seizurogenic toxins—progression from whole body tremor to SE and death if left untreated.
- Metabolic encephalopathy—seizures unusual and accompanied with obtunded mental state and abnormal behavior; no lateralizing signs.
- Structural brain disease likely—if acute onset of >2 GS within first week of onset, acute onset of focal seizures with gradual progression to GS, or presence of interictal neurologic deficits including behavioral changes.
- Genetic epilepsy—differentiated on age, breed, and seizure pattern; progressive onset of GS with/without aura.
- Cervical pain/spasms—may be mistaken for focal seizures.
- Head bobbing or idiopathic head tremor—dog remains active; can eat, drink, walk.

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CBC/BIOCHEMISTRY/URINALYSIS

- Infectious CNS diseases—may reflect multisystem involvement.
- Hypoglycemia—small/toy breeds during SE; insulinoma.
- Hepatic and renal dysfunction—advanced SE.
- Urinalysis—rule out myoglobinuria.

OTHER LABORATORY TESTS

- Blood gases—metabolic acidosis frequent with SE. Respiratory acidosis needs immediate treatment.
- Coagulation profile—disseminated intravascular coagulation (DIC) in advanced SE.
- Bile acids—suspected hepatic encephalopathy.
- Fasting blood glucose and amended insulin: glucose ratio—dogs >5 years with occasional seizures during exercise.
- Serology (infectious diseases)—as suggested by systemic signs and laboratory abnormalities.
- Toxicity screen—cholinesterase levels.

IMAGING

- Thoracic radiographs and abdominal ultrasound—to identify metastatic or systemic illness, or lung pathology from SE.
- MRI—best to define location, extent, and nature of lesion.

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—DOGS

(CONTINUED)

DIAGNOSTIC PROCEDURES

Electrocardiogram (ECG)—arrhythmias can occur in SE due to myocardial damage. CSF—if intracranial structural cause is suspected; CSF and serum titers and PCR for diagnosing infectious diseases. EEG—to document ongoing seizure activity once physical manifestations have ceased.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient—isolated seizures in an otherwise healthy dog.
- Inpatient—cluster seizures and SE.

NURSING CARE

- SE and cluster-seizures—constant supervision.
- Ensure airway patency. May need to be suctioned due to excessive salivation.
- Administer 100% oxygen via non-rebreathing mask.
- Cool down if hyperthermia.
- Install IV line for drug and fluid administration.
- Draw blood for rapid measurement of blood gases, glucose, calcium, renal and hepatic function, and antiepileptic drug (AED) levels if pertinent.
- Monitor urine output with indwelling urinary catheter.

S

CLIENT EDUCATION

- Treat cluster of GS and generalized status epilepticus (GSE) early—the more seizures in a given time, and the more drugs for seizure control, time for recovery, and cost for treatment.
- Antiepileptic treatment in structural epilepsy may not help until the primary cause is addressed.
- Client to keep a seizure calendar noting date, time, severity, and length of seizures to objectively evaluate response to treatment.
- Outline an in-home treatment emergency plan for cluster-seizures.



MEDICATIONS

- Electrolytes imbalance—treat immediately with fluid therapy.
- Low glucose—50% dextrose diluted to 25% (500 mg/kg IV) over 15 minutes or treat with oral glucose syrup.

DRUG(S) OF CHOICE

Seizure type and frequency determine the therapeutic approach. Important to seek and treat primary cause.

Convulsive Cluster Seizures or Status Epilepticus

Diazepam

- Administer 0.5–1 mg/kg IV bolus; repeat 5 minutes later if gross motor activity has not subsided; follow with CRI of 0.5–1 mg/kg/h added to hourly maintenance fluids in an inline burette or through syringe pump.
- Rectal—only where IV access cannot be obtained; may diminish or stop gross motor seizure activity to allow IV catheter placement.
- Refractoriness may rapidly develop, necessitating the addition of phenobarbital CRI.

Phenobarbital

- Add if seizures persist after second diazepam bolus or during diazepam CRI; administer CRI phenobarbital (2–6 mg/dog/h added to diazepam infusion) if patient already treated with phenobarbital, or loading dose if patient naïve to phenobarbital.
- Loading dose—12–24 mg/kg given as boluses of 4 mg/kg IV, 20 minutes apart until desired effect is reached, to a maximum of 24 mg/kg. Optimal therapeutic range—100–120 µmol/L (23–28 mg/L).
- If patient already on phenobarbital, obtain serum level prior to initiating phenobarbital CRI. IV bolus 2–6 mg/kg can be administered once while awaiting results if serum levels believed inadequate.
- Once seizures have been controlled for 4–6 hours, gradually wean the patient off CRI over as many hours.
- Start/resume oral maintenance AED using phenobarbital and/or other GS AED as soon as patient can swallow.

Other

- If seizures continue, propofol at 1–2 mg/kg IV slowly over 60 seconds, followed by CRI at 0.1–0.6 mg/kg/min to effect; monitor anesthetized patient with EEG to evaluate treatment response.
- Ketamine is also used occasionally at 5 mg/kg IV bolus followed by CRI at 5 mg/kg/h.
- Dexamethasone—0.2 mg/kg q24h for 1–3 days; reduce cerebral edema.
- Dexamethasone—for acute treatment of cerebral edema secondary to severe inflammatory CNS disease, even if infectious.

Acute Focal Status Epilepticus

- Often harbors brain lesion.
- Diazepam and phenobarbital CRI—effective for focal and GS.
- Frequently difficult to reach seizure control.
- Instances of chronic nonconvulsive generalized or focal SE—owner unaware it is occurring (e.g., senile encephalopathy); if seizures remain focal and patient's quality of life not significantly altered, no treatment necessary. Long-term antiepileptic treatment if necessary—phenobarbital 3–5 mg/kg q12h PO, levetiracetam 20 mg/kg q8h PO, or zonisamide 5 mg/kg q12h PO.

CONTRAINdications

- Potassium bromide—do not use to treat SE; too long half-life; loading dose not recommended.
- Aminophylline, theophylline—CNS excitement; may cause seizure.
- Steroids—alter CSF parameters; avoid if considering CSF analysis.

PRECAUTIONS

- Phenobarbital—liver disease, lower dose; monitor levels closely; for SE, add cautiously to diazepam because the drugs potentiate each other, cardiac/respiratory depression may ensue.
- Steroids—contraindicated in infectious diseases, but one dose of dexamethasone 0.2 mg/kg IV may decrease brain edema when impending brain herniation or life-threatening edema is suspected.

POSSIBLE INTERACTIONS

- Cimetidine, ranitidine, and chloramphenicol—interfere with phenobarbital metabolism; may lead to phenobarbital toxic level.
- Phenobarbital decreases zonisamide serum levels. Dosage recommended when drugs are used simultaneously—10 mg/kg q12h.
- If levetiracetam used concomitantly with phenobarbital—measure serum levels (humans 10–40 µg/mL).

ALTERNATIVE DRUG(S)

Levetiracetam—20–60 mg/kg IV; use upper end dosage if patient already on oral phenobarbital. Good alternative in liver disease or portosystemic shunts, as the drug is not metabolized in the liver. Use with caution in patients with renal disease.



FOLLOW-UP

PATIENT MONITORING

- Inpatients—constant supervision for seizure monitoring.
- Eyelid or lip twitching in a heavily sedated patient is sign of ongoing seizure activity.
- Monitor heart rate, respiratory rate, oxygenation/ventilation, body temperature, blood pressure, urine production, neurologic examination.
- EEG monitoring for ongoing seizure activity.
- Patient may need 7–10 days before returning to normal after SE.

POSSIBLE COMPLICATIONS

- Phenobarbital—hepatotoxicity after long-term treatment with serum levels >140 µmol/L (>33 µg/L); acute neutropenia (rare) in the first few weeks of use requires permanent withdrawal.
- Paradoxical hyperexcitability.
- Permanent neurologic deficits (e.g., blindness, abnormal behavior, cerebellar signs) may follow severe SE.

(CONTINUED)

SEIZURES (CONVULSIONS, STATUS EPILEPTICUS)—DOGS

- GSE may lead to hyperthermia, acid-base and electrolyte imbalances, pulmonary edema, cardiovascular collapse, and death.

EXPECTED COURSE AND PROGNOSIS

- Genetic epilepsy or epilepsy of unknown cause represents a large proportion of dogs with GSE or cluster-seizures. In-home emergency measure using diazepam rectal/nasal should be provided.
- Dogs with encephalitis and GSE—poor outcome.
- Structural epileptic dogs recovered from primary disease (e.g., *Ehrlichia canis*)—slowly (over months) wean patient off AEDs

after 6 months seizure-free; if seizures recur, reinstate AED.

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

- The immature brain has a higher propensity to seize.
- Genetic epilepsy—6 months–5 years; often epilepsy refractory when onset at <2 years.
- Phenobarbital—higher dose needed in puppies (<5 months) to reach therapeutic range.

ABBREVIATIONS

- AED = antiepileptic drug.
- DIC = disseminated intravascular coagulation.
- ECG = electrocardiogram.
- EEG = electroencephalogram.
- GS = generalized seizure.
- GSE = generalized status epilepticus.
- SE = status epilepticus.

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Client Education Handout available online



BASICS

DEFINITION

- Sepsis—life-threatening organ dysfunction caused by dysregulated host response to severe infection.
- Bacteremia—presence of viable bacterial organisms in the bloodstream.
- Terms are not synonymous, although often used interchangeably.

PATHOPHYSIOLOGY

- With severe infection, immune system is stimulated by pathogen-associated products such as lipopolysaccharide (LPS) (Gram-negative bacteria); lipoteichoic acid, peptidoglycan, bacterial DNA, exotoxins (Gram-positive bacteria); fungal cell walls; flagellin (protozoans).
- Macrophage-derived cytokines activate and recruit neutrophils and other inflammatory cells, activate coagulation cascade, increase capillary permeability.
- Activation of inducible nitric oxide synthase (iNOS) produces large quantities of nitric oxide, causing diffuse, profound vasodilation; refractory hypotension or vasodilatory shock may result.
- White blood cells (WBCs) and platelets at sites of inflammation activate coagulation, produce thrombin, and activate platelets; anticoagulant and fibrinolytic pathways inhibited. Procoagulant state favors microthrombi that can lead to decreased tissue oxygen delivery, multiple organ dysfunction, and organ failure. Progression to a hypocoagulable state can occur.
- Cryptic shock—decreased microcirculatory perfusion despite normal global hemodynamic parameters; results from decreased functional capillary density.
- Endothelial cell dysfunction—disruption of endothelial glycocalyx, changes in deformability of red blood cells (RBCs), WBC activation, microthrombosis, loss of vascular smooth muscle autoregulation, changes in capillary permeability.
- Cytopathic hypoxia—sepsis-induced mitochondrial dysfunction renders cells unable to use oxygen to make ATP.
- Bacteremia—may be transient and subclinical or escalate to overt sepsis when immune system overwhelmed; generally of more pathologic significance when source is venous or lymphatic drainage sites.

SYSTEMS AFFECTED

- Cardiovascular—increased or decreased cardiac output, decreased systemic vascular resistance, and increased vascular permeability.
- Hemic/lymphatic/immune—procoagulant state favors formation of microthrombi, may progress to hypocoagulable state (consumption).
- Endocrine—relative adrenal insufficiency (critical illness-related corticosteroid insufficiency [CIRCI]).
- Respiratory.
- Gastrointestinal.
- Hepatobiliary.
- Renal.
- All systems can be affected by sepsis via systemic inflammatory

response syndrome and multiple organ dysfunction syndrome.

SIGNALMENT

Species

- Dog and cat.
- No age, sex, or breed predispositions.
- Large-breed male dogs—predisposed to bacterial endocarditis, discospondylitis.

SIGNS

General Comments

- May be acute or occur in vague or episodic fashion.
- May involve single or multiple organ systems.

Historical Findings

Historical findings variable depend on underlying cause.

Physical Examination Findings

- Signs of sepsis vary with stage.
- Dog:
 - Early sepsis—hyperdynamic state: tachycardia, bounding pulses, rapid capillary refill time, red mucous membranes, fever.
 - Late sepsis—thready pulses, prolonged capillary refill time, pale mucous membranes, cool extremities, stupor, hypothermia.
 - Cat:
 - Lethargy, pale mucous membranes, tachypnea, weak pulses, hypotension, hypothermia, icterus, diffuse abdominal pain (even in absence of primary abdominal problem).
 - May present with tachycardia or a relative bradycardia (heart rate inappropriately low given illness, e.g., 120–150 bpm).
 - Specific clinical signs relate to site of infection or secondary organ dysfunction:
 - Lameness.
 - Heart murmur—diastolic murmur may indicate aortic valve endocarditis.
 - Abdominal pain, peritoneal effusion.
 - Dyspnea.
 - Dysuria, prostatomegaly.
 - Neurologic deficits—primary deficit or secondary to hypoglycemia, hypotension.

CAUSES

- Infection from bacterial (most common), viral, protozoal, fungal, or parasitic organisms.
- Specific causes include:
 - Cardiovascular—endocarditis.
 - Cutaneous—bite wounds, deep pyoderma, infected burns, surgical site infection, abscess.
 - Gastrointestinal—septic peritonitis, gastrointestinal perforation, translocation, gastroenteritis, colitis.
 - Genitourinary—pyelonephritis, pyometra, prostatitis/prostatic abscess.
 - Hemic/immune—blood-borne parasites, vector-borne infections.
 - Hepatobiliary—hepatitis, hepatic abscess, cholangitis, cholangiohepatitis.
 - Musculoskeletal—necrotizing fasciitis, osteomyelitis, septic arthritis.
 - Neurologic—discospondylitis.
 - Respiratory—pneumonia, pyothorax.
- Dogs: Gram-negative organisms (especially *E. coli*) most common; polymicrobial infection reported in ~20% of dogs with positive blood cultures.
- Cats—bloodstream pathogens usually Gram-

SEPSIS AND BACTEREMIA

negative bacteria from *Enterobacteriaceae* family or obligate anaerobes; *E. coli* and *Salmonella* most common Gram-negative organisms cultured.

RISK FACTORS

- Predisposing factors—hyperadrenocorticism, diabetes mellitus, liver or renal failure, splenectomy, malignancy, burns.
- Immunodeficient state—chemotherapy, feline leukemia virus or feline immunodeficiency virus infection, splenectomy, endogenous or exogenous corticosteroids.
- IV catheters.
- Indwelling urinary catheters or other drainage devices.
- Surgical implants.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Other causes of fever, heart murmur, joint or back pain, or hypotension.
- Clinical signs of chronic bacteremia may be similar to immune-mediated disease.
- Other causes of distributive/vasodilatory shock—hypoadrenocorticism, anaphylaxis or mast cell tumor degranulation, antihypertensive drug overdose.

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CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilic leukocytosis with a left shift and moncytosis.
- Neutropenia may develop.
- Hypoalbuminemia and a high alkaline phosphatase activity (2 times upper limit of normal)—50% of affected dogs.
- Hypoglycemia—~25% of affected dogs; hyperglycemia or hypoglycemia in cats.
- Blood lactate concentration—persistent lactate elevation despite therapy portends poor prognosis.

OTHER LABORATORY TESTS

- Aerobic and anaerobic cultures of site of infection—recommended but *should not delay timely antibiotic therapy*.
- Suspected catheter-induced sepsis—culture catheter tip.
- Urine culture—urinary tract may be primary or secondary source of infection.
- Endocarditis—consider *Bartonella* testing (see Bartonellosis).
- PCR, serology for tick-borne disease, as indicated.
- PCR, serology or for organisms of interest, as indicated (e.g., *Leptospira*, influenza, *Babesia*).
- Fungal antigen testing.
- Coagulation parameters should be monitored in most cases.

IMAGING

- Radiographs and ultrasound—may identify source of sepsis (e.g., pyometra, pneumonia) or secondarily infected organs (e.g., discospondylitis).
- Ultrasound may help guide fine-needle aspiration for cytology/culture.
- Echocardiography—for suspected endocarditis.
- CT, MRI—may identify some sources of sepsis or for surgical planning.

SEPSIS AND BACTEREMIA

(CONTINUED)

DIAGNOSTIC PROCEDURES

- Abdominocentesis, thoracocentesis, fine-needle aspirate—for cytology, culture/sensitivity of effusion, masses:
 - Neutrophilic or pyogranulomatous inflammation, eosinophilic.
 - Diagnostic peritoneal lavage if strong suspicion for abdominal sepsis without effusion.
- Endo- or transtracheal wash, bronchoalveolar lavage—samples for cytology, culture/sensitivity, PCR.
- Fecal cytology, fecal PCR.
- Blood cultures—in any patient that develops fever (or hypothermia), leukocytosis (especially with a left shift), neutropenia, shifting leg lameness, recent onset or changing heart murmur, or any sign of sepsis for which the source cannot be identified.

PATHOLOGIC FINDINGS

Varies with underlying cause.



TREATMENT

APPROPRIATE HEALTH CARE

- S**
- Success requires early identification of the problem and aggressive intervention; careful monitoring is essential, patient status may change rapidly.
 - Start IV antibiotics within 1 hour of identifying sepsis or septic shock.
 - Fluid therapy—IV bolus isotonic replacement crystalloids (cat, 10–15 mL/kg; dog, 20–30 mL/kg), repeat as necessary; then administer crystalloids to provide maintenance needs, replace dehydration deficits and meet ongoing losses; provide albumin and plasma for hypoalbuminemia and coagulation abnormalities, respectively; consider synthetic colloids if clinical hypoproteinemia and hypotension are ongoing and biologic colloid sources unavailable.
 - Add dextrose to IV fluids if hypoglycemic.
 - Electrolytes and acid-base balance—correct abnormalities.
 - Pressor, inotropic therapy for persistent hypotension; refer early.
 - Source control—should be completed after patient is normotensive and stable; provide appropriate wound care, bandage changes, or surgical intervention, as indicated.

NURSING CARE

- Goals—systolic blood pressure >90 mmHg, heart rate 80–140 bpm (dogs) and 160–225 bpm (cats), capillary refill time 1.5 seconds, urine output >1–2 mL/kg/h, blood lactate <2.5 mmol/L in dogs.
- Inadequate response to therapy prompts vasopressor administration (norepinephrine, dopamine, vasopressin). Most commonly recommended

vasopressor is norepinephrine. Dopamine may be a good choice for cats with relative bradycardia.

- As appropriate for each patient's situation.

DIET

Nutritional support—provide by assisted feeding or feeding tube.

CLIENT EDUCATION

Prognosis should be discussed with client.

SURGICAL CONSIDERATIONS

Any identifiable focus of infection such as an abscess should be located and removed where possible.



MEDICATIONS

DRUG(S) OF CHOICE

Antibiotics

- IV antibiotics should be started within 1 hour of recognizing sepsis, septic shock.
- Pending culture and sensitivity results, treat for organisms commonly isolated from presumed source of infection, or empirically cover Gram-positive, Gram-negative, aerobic, anaerobic organisms:
 - Initial therapy—Gram-negative (enrofloxacin, cefotaxime, amikacin); Gram-positive (ampicillin, clindamycin); anaerobes (metronidazole).
 - Ampicillin 22 mg/kg IV q6–8h.
 - Ampicillin/sulbactam 25–30 mg/kg IV q6–8h.
 - Clindamycin 12 mg/kg IV q12h.
 - Cefotaxime 20–80 mg/kg IV q8h.
 - Enrofloxacin 10–15 mg/kg IV q24h (dogs); 5 mg/kg/day IV (cats).
 - Amikacin 10–15 mg/kg IV q24h.
 - Metronidazole 10 mg/kg IV q8–12h.
- De-escalate (reduce unnecessary antibiotics) once sensitivity results are available.
- For many bacterial infections, total duration of therapy can be limited to 7–10 days; longer if source cannot be eliminated/drained or immune deficiencies are present.

Corticosteroids

Physiologic doses (e.g., 0.25 mg/kg prednisone or 0.05 mg/kg of dexamethasone) may be indicated if patient has persistent hypotension unresponsive to fluid therapy and catecholamines.

CONTRAINDICATIONS

NSAIDs—high risk of renal failure (acute kidney injury) or gastrointestinal ulceration in patient with sepsis/septic shock.

PRECAUTIONS

Aminoglycosides—use with caution in patient with renal impairment.



FOLLOW-UP

PATIENT MONITORING

- Aminoglycoside therapy—monitor renal function.
- Blood pressure, ECG, electrolytes, blood lactate.

POSSIBLE COMPLICATIONS

Multiple organ failure.

EXPECTED COURSE AND PROGNOSIS

Sepsis has a mortality rate of ~50%, with higher mortality for animals with multiorgan failure.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Discospondylitis (dogs)—screen for *Brucella* spp.
- See Risk Factors.

SYNOMYMS

- Septic shock.
- Septicemia.

SEE ALSO

- Abscessation.
- Anaerobic Infections.
- Endocarditis, Infective.
- Shock, Septic.

ABBREVIATIONS

- CIRCI = critical illness-related corticosteroid insufficiency.
- iNOS = inducible nitric oxide synthase.
- LPS = lipopolysaccharide.
- NSAID = nonsteroidal anti-inflammatory drug.
- RBCs = red blood cells.
- WBCs = white blood cells.

Suggested Reading

Burkitt JM, Haskins SC, Nelson RW, et al. Relative adrenal insufficiency in dogs with sepsis. J Vet Intern Med 2007; 21:226–231.

Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock: 2016. Crit Care Med 2017; 45(3):486–552.

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Acknowledgment The author/editor acknowledges the prior contribution of Sharon Fooshee Grace.



Client Education Handout
available online

SHOCK, CARDIOGENIC



BASICS

DEFINITION

- Severe manifestation of forward heart failure in which patients have both clinical and biochemical evidence of inadequate tissue perfusion.
- Profound impairment of cardiac function resulting in poor cardiac output and life-threatening end-organ hypoperfusion and hypoxia in the presence of adequate intravascular volume and systemic vascular resistance.
- Cardiac impairment may result from systolic dysfunction (dilated cardiomyopathy, sepsis, myocarditis, ischemia), diastolic dysfunction (hypertrophic cardiomyopathy, restrictive cardiomyopathy, tension pneumothorax/mediastinum, restrictive pericarditis, pericardial tamponade), conduction defects and arrhythmias, valvular diseases, obstructive diseases, pulmonary thromboembolism, and structural defects. Understanding the underlying defect and its hemodynamic consequences is imperative to institute appropriate therapy.
- In congestive heart failure (CHF), sometimes referred to as backward heart failure, the ventricle cannot adequately pump out the returning blood, resulting in systemic and/or pulmonary edema. This is in contrast to forward heart failure, when the heart is not pumping enough blood out to meet the needs of the body. Most, but not all, veterinary patients that present in cardiogenic shock will have concurrent CHF.

PATHOPHYSIOLOGY

- Decreased cardiac output leads to hypotension and systemic hypoperfusion.
- Hypotension decreases coronary perfusion, resulting in ischemia that provokes further myocardial dysfunction.
- Peripheral vasoconstriction increases myocardial work and exacerbates tissue ischemia and energy depletion, resulting in organ dysfunction.

SYSTEMS AFFECTED

- Cardiovascular—cardiac dysfunction is causative, myocardial ischemia exacerbates cardiac dysfunction.
- Musculoskeletal—weakness.
- Nervous—altered mental status.
- Respiratory—as cardiac dysfunction progresses and atrial pressure increases, pulmonary edema and/or pleural effusion develop and hypoxemia ensues.
- Endocrine—hyperglycemia and insulin resistance.
- Gastrointestinal—mucosal necrosis and sloughing, hemorrhage, bacterial translocation.
- Hepatobiliary—hepatocellular enzyme leakage, cholestasis, reduced clearance of bacteria and bacterial by-products, and abnormal synthetic function; hepatic congestion may result from right-sided CHF.
- Renal—ischemic tubular damage, oliguria, development of acute kidney injury.
- Hemic—homeostatic imbalances lead to microvascular thrombosis.

GENETICS

Many breeds are predisposed to specific cardiac diseases.

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

Unknown

SIGNALMENT

- Dog and cat.
- Any breed, age, or sex.

SIGNS

Historical Findings

- Cardiac decompensation may be associated with a history of previously compensated heart disease and cardiac drug administration.
- A suspicion of previously undiagnosed cardiac disease may result from a history of coughing, exercise intolerance, weakness, or syncope.

Physical Examination Findings

- Markers of poor perfusion:
 - Weakness.
 - Altered mental status.
 - Cool extremities and hypothermia.
 - Pale mucous membranes.
 - Prolonged capillary refill time.
 - Weak femoral pulse quality.
 - Oliguria.
 - Muffled heart sounds if pericardial or pleural effusion is present.
 - Variable heart rate with possible cardiac arrhythmia, murmur or gallop sound.
 - Variable respiratory rate with possible increased bronchovesicular sounds, crackles, or moist cough.

CAUSES

Primary Cardiac Disease

- All cardiomyopathies (e.g., dilated, hypertrophic, unclassified, restrictive).
- Severe mitral insufficiency or other end-stage valvular disease.
- Chordae tendineae rupture.
- Tachy- or bradyarrhythmias.
- Myocarditis.
- Endomyocarditis (cats).
- Structural defects (e.g. congenital heart disease).

Secondary Cardiac Dysfunction

- Cardiac tamponade.
- Sepsis.
- Severe electrolyte derangement.
- Pulmonary thromboembolism.
- Tension pneumothorax/mediastinum.
- Caval syndrome.

RISK FACTORS

- Underlying cardiac disease.
- Concurrent illness causing hypoxemia, acidosis, electrolyte imbalances, or as in sepsis, release of myocardial depressant factors.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Cardiogenic shock is differentiated from other causes of circulatory shock when there is evidence of decreased cardiac output and tissue hypoxia in the face of adequate intravascular volume and systemic vascular resistance.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

Mature neutrophilia and lymphopenia secondary to stress.

Biochemistry Panel

- Hyperglycemia—stress.
- Elevated anion gap—accumulation of lactic and renal acids.
- Elevated hepatocellular enzyme activity—hepatic hypoxia.
- Elevated phosphorus—decreased glomerular filtration rate (GFR).
- Azotemia—decreased GFR or hypoxia induced renal injury.
- Hyponatremia and mild hypoalbuminemia—suggestive of chronic CHF.

Urinalysis

Isosthenuria—concomitant diuretic therapy or acute kidney injury.

OTHER LABORATORY TESTS

- Blood gas analysis—metabolic acidosis, respiratory alkalosis or acidosis, hypoxemia, and evidence of increased tissue oxygen extraction (widened arteriovenous oxygen difference and/or decreased venous oxygen concentration in the absence of hypoxemia or anemia).
- Hyperlactatemia—tissue hypoperfusion.
- Increased cardiac troponin I levels—sensitive and specific marker of myocardial injury.
- B-type natriuretic peptide (NT-proBNP)—useful in ruling out intrinsic cardiac dysfunction.

IMAGING

Radiographs

Thoracic radiography may reveal cardiomegaly and evidence of CHF (pulmonary edema, pleural effusion).

Cageside Focused Pulmonary and Cardiac Ultrasound

- Lung ultrasound may reveal pleural effusion and/or B-lines (CHF).
- Cardiac ultrasound to detect pericardial tamponade; patients with cardiogenic shock secondary to primary cardiac disease and some with secondary causes will have an increased left atrial size.

Echocardiography

To characterize cardiomyopathy, valvular disease, myocardial contractility, structural disease, pericardial disease, and heartworm infection.

DIAGNOSTIC PROCEDURES

Thoraco-, abdomino-, and pericardiocentesis when indicated may elucidate underlying etiology.

PATHOLOGIC FINDINGS

Cardiac abnormalities consistent with various underlying etiologies; abnormalities consistent with tissue hypoxia and CHF.



TREATMENT

APPROPRIATE HEALTH CARE

Emergency inpatient intensive care management.

SHOCK, CARDIOGENIC

(CONTINUED)

NURSING CARE

- Minimize stress—patients are extremely fragile and at risk of cardiac arrest.
- Oxygen supplementation.
- Pleural effusion—relieve with thoracocentesis.
- Respiratory failure—may require mechanical ventilation.
- Patients should *not* receive *any* fluid therapy until the etiology of the underlying cardiac dysfunction is understood and cardiac function improved; exceptions include cardiogenic shock secondary to pericardial tamponade, tension pneumothorax and mediastinum, and pulmonary thromboembolism.
- Pericardial tamponade—relieve with pericardiocentesis.

ACTIVITY

Minimize patient exertion.

DIET

Free choice access to water; withhold food until shock is resolved.

CLIENT EDUCATION

Discuss risk of imminent cardiac arrest and confirm “code status” in advance if possible.

SURGICAL CONSIDERATIONS

- Bradyarrhythmia may require pacemaker implantation.
- Tension pneumothorax may require thoracostomy tube placement or exploratory thoracotomy.
- Caval syndrome secondary to *Dirofilaria immitis* infection requires worm extraction.

S

MEDICATIONS

DRUG(S) OF CHOICE

- Fast-acting positive inotropes to improve cardiac function and preserve end-organ perfusion in patients with reduced myocardial contractility (pimobendan 0.25–0.3 mg/kg PO q12h in dogs and cats [IV formulation available in some countries]; dobutamine 5–20 µg/kg/min CRI in dogs; 2.5–15 µg/kg/min CRI in cats). While dobutamine can be used safely in many feline patients, seizures have been observed in some cats at doses exceeding 5 µg/kg/min.
- Arrhythmias and conduction abnormalities should be corrected promptly with antiarrhythmic therapy, cardioversion, or pacemaker implantation.
- Ventricular tachycardia: o Dogs—lidocaine (2–4 mg/kg slow IV loading dose then 25–100 µg/kg/min CRI) or procainamide (5–15 mg/kg slow IV loading dose then 25–50 µg/kg/min CRI). Due to many common adverse effects, amiodarone (2–5 mg/kg IV, infused over 30–60 minutes) should only be used short term and the formulation should not contain polysorbate-80.
- Sotalol (1–2.5 mg/kg PO, bid). Use with caution and at the lower end of the dosage range in dogs with concurrent CHF or DCM.
- Cat procainamide (1–2 mg/kg IV slowly over 20 minutes) or lidocaine (0.25–0.5 mg/kg slow IV bolus then if needed 10–20 µg/kg/min).
- Caution when using lidocaine in cats

as they may be at higher risk of toxicosis.

- Supraventricular tachyarrhythmia:
 - Treatments to slow the heart rate include vagal maneuvers, calcium channel blockers (diltiazem 0.125–0.35 mg/kg IV over 2–3 minutes or 0.125–0.35 mg/kg/h CRI), beta-blockers (esmolol 0.5 mg/kg IV over 1 minute), and procainamide (6–8 mg/kg IV over 5–10 minutes then 20–40 µg/kg/min CRI).
 - Patients unresponsive to vagal maneuvers or emergency drug therapy may require DC cardioversion or overdrive pacing.
- Bradyarrhythmia: o Cardiac pacing.
- Some patients may benefit from atropine (0.02–0.04 mg/kg IV) or isoproterenol (0.4 mg in 250 mL D₅W slowly to effect).
- Concurrent CHF:
 - Furosemide to treat pulmonary edema in dogs and cats (2–8 mg/kg IV or IM; or 0.5–1.0 mg/kg/h CRI); IV route is preferable, but IM is appropriate when manual restraint to obtain IV access puts the patient at risk.
 - Relief of pain or anxiety with morphine sulfate (0.1–0.5 mg/kg/h IV CRI, or 0.2–2 mg/kg IM) can reduce excessive sympathetic activity and decrease oxygen demand, preload, and afterload.

CONTRAINdications

- Avoid diuretic therapy in patients with pericardial tamponade, tension pneumothorax/mediastinum, and pulmonary thromboembolism.
- Avoid beta-blockers and calcium channel blockers in patients with reduced myocardial contractility.

PRECAUTIONS

- Catecholamine infusions must be carefully titrated to maximize coronary perfusion with the least possible increase in myocardial oxygen demand.
- Afterload reducers and vasodilators (angiotensin-converting enzyme inhibitors, nitroglycerin, and nitrprusside) should be used with caution because of the risk for worsening hypotension and decreasing coronary blood flow.

ALTERNATIVE DRUG(S)

Dopamine may be used to improve systolic function as an alternative to dobutamine at a dose of 5–10 µg/kg/min (dogs and cats).



FOLLOW-UP

PATIENT MONITORING

- Serial assessment of perfusion (mentation, mucous membrane color, capillary refill time, pulse quality, muscle strength, temperature, serum lactate, urine output, heart rate, BP, and oxygenation indices), respiratory rate and effort, and pulmonary auscultation is required to optimize therapy.
- Blood gas analysis and pulse oximetry to assess tissue oxygenation, ventilation, and acid–base balance.
- Packed cell volume, serum total protein, serum electrolytes, hepatocellular enzymes, BUN, and serum creatinine to monitor effects of systemic tissue hypoxia.
- Daily cardiac

troponin I levels to assess degree of myocardial injury in some cases.

- BP measurement may document hypotension.
- Electrocardiography may aid detection and characterization of arrhythmias.
- Pulse oximetry may document low oxygen saturation.
- Central venous pressure monitoring may aid in assessment of cardiac preload and central venous oxygen saturation.
- Hemodynamic monitoring to assess mixed venous oxygen saturation, cardiac output and systemic vascular resistance.

PREVENTION/AVOIDANCE

Prevention strategies aimed at the various underlying etiologies.

POSSIBLE COMPLICATIONS

- CHF.
- Cardiac arrhythmias.
- Syncope.
- Acid–base and electrolyte disturbances.
- Renal dysfunction.
- Cardiac arrest.

EXPECTED COURSE AND PROGNOSIS

Dependent on underlying etiology. Patients with primary cardiac disease have generally worse prognosis (poor to grave) as compared to those with secondary cardiac dysfunction.



MISCELLANEOUS

ASSOCIATED CONDITIONS

CHF

AGE-RELATED FACTORS

Variable, depending on underlying etiology.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

Variable, depending on underling etiology.

SEE ALSO

- Atrioventricular Block.
- Cardiomyopathy.
- Congestive Heart Failure, Left-Sided.
- Congestive Heart Failure, Right-Sided.
- Endomyocardial Diseases—Cats.
- Myocarditis.
- Pericardial Disease.
- Pneumothorax.
- Pulmonary Thromboembolism.
- Sepsis and Bacteremia.
- Shock, Hypovolemic.
- Shock, Septic.
- Sick Sinus Syndrome.
- Supraventricular Tachycardia.
- Ventricular Tachycardia.

ABBREVIATIONS

- BP = blood pressure.
- CHF = congestive heart failure.
- GFR = glomerular filtration rate.

Suggested Reading

- De Laforcade A, Silverstein DC. Shock. In: Silverstein DC, Hopper K, ed., Small Animal Critical Care Medicine, 2nd ed. St. Louis, MO: Saunders, 2015, pp. 26–30.
- Hopper K, Silverstein D, Bateman S. Shock syndromes. In: Dibartola SP, ed., Fluid Therapy in Small Animal Practice, 4th ed. Philadelphia, PA: Saunders, 2011, pp. 557–583.

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SHOCK, HYPOVOLEMIC



BASICS

DEFINITION

Inadequate circulating volume and perfusion due to fluid loss.

PATHOPHYSIOLOGY

- Hemorrhage or other fluid loss results in a critical decrease in intravascular volume, diminished venous return, and decreased cardiac output.
- Compensatory neuroendocrine responses lead to peripheral vasoconstriction thus exacerbating tissue ischemia and energy depletion, resulting in organ dysfunction.

SYSTEMS AFFECTED

- Cardiovascular—increased heart rate, increased cardiac contractility, and peripheral vasoconstriction; increased cardiac oxygen demand in the face of reduced oxygen delivery may cause arrhythmias.
- Respiratory—hyperventilation to compensate for metabolic acidosis.
- Musculoskeletal—weakness.
- Nervous—altered mental status.
- Endocrine—hyperglycemia and insulin resistance.
- Gastrointestinal (GI)—mucosal necrosis and sloughing, hemorrhage, bacterial translocation.
- Hepatobiliary—hepatocellular enzyme leakage, cholestasis, reduced clearance of bacteria and their by-products, abnormal synthetic function.
- Renal—ischemic tubular damage, oliguria, acute kidney injury.
- Hemic—homeostatic imbalances lead to microvascular thrombosis as well as hyper- and hypocoagulability.

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

- Dog and cat.
- Any breed, age, or sex.

SIGNS

Historical Findings

May have history of trauma, weakness, collapse, surgery, vomiting, diarrhea, decreased water intake, and polyuria.

Physical Examination Findings

- Compensated shock/warm shock/preshock:
 - Compensatory mechanisms may allow an otherwise healthy pet to be relatively asymptomatic despite a 10% reduction in total effective blood volume. When

homeostatic mechanisms fail, decompensated shock ensues.

• Decompensated shock:

- Poor perfusion (pale mucous membranes [may be compounded by anemia], prolonged capillary refill time, weak peripheral pulses, weakness, altered mental status, hypothermia/cool extremities, oliguria).
- Absent/minimal jugular vein distension.
- Tachycardia ± arrhythmia.
- Tachypnea.
- Clinical dehydration (decreased skin turgor, tacky mucous membranes, and sunken eyes) more common in patients with fluid loss than hemorrhage.

CAUSES

Hemorrhage

- Trauma.
- Ruptured neoplasm.
- GI bleeding (e.g., ulcerative disease, neoplasia, severe thrombocytopenia).
- Coagulopathy (e.g., severe thrombocytopenia/thrombocytopathy, von Willebrand factor deficiency, anticoagulant rodenticide intoxication, synthetic liver failure, disseminated intravascular coagulation, hemophilia, other bleeding disorders).

Fluid Loss

- GI (vomiting and diarrhea).
- Urinary (renal failure, diabetes mellitus, diabetes insipidus, hypercalcemia, Addison's, and Cushing's diseases).
- Burns.
- Third spacing (any disease resulting in significant effusion).

RISK FACTORS

No specific risk factors; caused by another condition.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Hypovolemic shock differentiated from other causes of circulatory shock when inadequate circulating volume results in decreased cardiac output in the face of normal or increased cardiac function and normal or increased systemic vascular resistance.

CBC/BIOCHEMISTRY/URINALYSIS

CBC

- Stress leukogram.
- Hematocrit and platelet count are variable (may be decreased with hemorrhage).

Biochemistry Panel

- Hyperglycemia.
- Variabile total protein (TP) and albumin (decreased with hemorrhage; increased in fluid loss).
- Elevated hepatocellular enzyme activity (alanine aminotransferase, aspartate aminotransferase).

- Variable electrolyte derangements (more likely in fluid loss).
- Variable anion gap.
- Azotemia due to decreased glomerular filtration rate.

Urinalysis

- Urine specific gravity may be increased; however, acute tubular injury due to renal hypoxia may cause isosthenuria.

OTHER LABORATORY TESTS

- Blood gas analysis may reveal metabolic acidosis and evidence of increased tissue oxygen extraction (widened arteriovenous oxygen difference and/or decreased venous oxygen concentration in a patient without hypoxemia or anemia).
- Hyperlactatemia reflects decreased clearance and increased production of lactate.
- Coagulation testing if critically ill or if evidence of significant hemorrhage.

IMAGING

- Thoracic radiography may reveal microcardia and pulmonary vascular underperfusion.
- May have radiographic or ultrasonographic findings of pleural or abdominal effusion.

DIAGNOSTIC PROCEDURES

Thoracocentesis, abdominocentesis, or pericardiocentesis, if indicated, may provide insight into underlying etiology.

PATHOLOGIC FINDINGS

Consistent with tissue hypoxia and underlying etiology.



TREATMENT

APPROPRIATE HEALTH CARE

Emergency inpatient intensive care management.

NURSING CARE

- Maximize blood oxygen content:
 - Assess and stabilize airway and breathing as necessary.
 - Supplemental oxygen and ventilatory support as needed.
 - Significant anemia (packed cell volume [PCV] <25–30%) in a hypovolemic patient is concerning and should be corrected.
- Control further fluid loss:
 - External bleeding controlled with direct pressure; internal bleeding may require surgical intervention.
- Control of fluid loss, other than hemorrhage, aimed at control of signs (e.g., antiemetics) and correcting underlying disorder.
- Fluid resuscitation:
 - Once IV or IO access obtained, initial fluid resuscitation performed with isotonic crystalloid such as lactated Ringer's solution, normal saline, Plasmalyte-A, and

SHOCK, HYPOVOLEMIC

(CONTINUED)

Normosol-R (20–30 mL/kg, dog; 15–20 mL/kg, cat; over 15 minutes). If no significant dehydration and no other contraindications, addition of 7.5% hypertonic saline (4 mL/kg over 15 minutes) may expedite resuscitation.

- Assess response to initial bolus. If vital signs and other resuscitation parameters return to normal, monitoring must be continued to ensure stability. If vital signs and other resuscitation parameters transiently improve or if little or no improvement seen, another crystalloid bolus should be infused and colloids such as hydroxyethylstarch (dose variable, dependent on type) or appropriate blood products (10–20 mL/kg) considered.
- Process is repeated until resuscitation parameters normalize. When bolusing fluids to correct perfusion deficits, monitor not only for response to therapy, but also for potential complications.
- While fluid boluses are used to correct perfusion deficits, hydration deficits must be corrected more slowly. After perfusion has normalized, patient is reassessed and fluid therapy targeted to correct hydration deficits over 12–24 hours.

S Traditional endpoints of resuscitation (restoration of normal vital signs, blood pressure, and urine output) remain the standard of care; however, it has been documented that critically ill patients have evidence of ongoing tissue hypoxia despite normalization of these parameters, suggesting occult oxygen debt and the presence of compensated shock. There is evidence that normalization of vital signs, blood lactate, base deficit, and oxygen transport indices such as cardiac index, oxygen delivery, oxygen consumption, and mixed venous oxygen and central venous oxygen saturation in concert are more sensitive markers for adequacy of tissue perfusion than any of these variables alone. Until stronger support exists for preferential selection of one endpoint over others, utilization of as many of these markers as are available seems advisable.

ACTIVITY

Minimize patient exertion.

DIET

Withhold oral intake until shock is resolved.

CLIENT EDUCATION

Discuss risk of cardiac arrest and confirm "code status" in advance if possible.

SURGICAL CONSIDERATIONS

Identify and repair source of fluid loss (most common in hemorrhage-induced).



MEDICATIONS

DRUG(S) OF CHOICE

- For patients with refractory hypovolemic shock, rule out ongoing losses (especially if hemorrhage-induced); administer blood products as needed.
- If adequate circulating volume is assured and patient is still demonstrating clinical signs of shock (not very common with hypovolemic shock), consider:
 - Pressors such as dopamine (5–20 µg/kg/min), norepinephrine (0.05–2 µg/kg/min), or vasopressin (0.5–2 mU/kg/min). These can be used for vasopressor support in dogs and cats. Monitor for tachyarrhythmia and excessive peripheral vasoconstriction.
 - Positive inotropes such as dobutamine (2–20 µg/kg/min) may be beneficial in patients with decreased contractility or myocardial depression. Monitor for tachyarrhythmia. While dobutamine can generally be used safely in dogs, seizures have been observed in some cats at doses exceeding 5 µg/kg/min.
- For bleeding dogs, antifibrinolytic medications such as ϵ -aminocaproic acid (50–100 mg/kg IV or PO q6h) or tranexamic acid (10 mg/kg IV bolus over 20 minutes, followed by 10 mg/kg/h IV CRI for 3 hours, then 10 mg/kg over 20 minutes q6h) may be considered.

CONTRAINdicATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Serial assessment of perfusion:
 - Physical exam including mentation, mucous membrane color, capillary refill time, pulse quality, muscle strength, temperature, and heart rate.
 - Hemodynamic monitoring to include arterial blood pressure (frequently reveals disproportionately low diastolic pressure), and in a subset of patients central venous pressure, cardiac output and tissue oxygenation.
 - Laboratory data including serum lactate and base deficit; patients with hemorrhage-induced

hypovolemic shock should have minimum of daily PCV, and TP assessed more frequently.

- Serial assessment of respiratory rate and effort, and pulmonary auscultation is required to optimize therapy.
- Urine output as indicator of glomerular filtration rate and renal blood flow.
- ECG may aid in characterization of arrhythmias.
- Minimum of daily PCV, serum TP, blood glucose, blood gas, serum electrolytes, hepatocellular enzymes, BUN, and serum creatinine to monitor effects of systemic tissue hypoxia and to guide clinical management.

PREVENTION/AVOIDANCE

Prevention strategies aimed at the various underlying etiologies.

POSSIBLE COMPLICATIONS

- Acid–base disturbances.
- Anemia and thrombocytopenia.
- Multiple organ dysfunction.
- Low colloid oncotic pressure.
- Volume overload with clinical signs of pulmonary and/or peripheral edema.
- Dilutional coagulopathy can occur in patients receiving very large resuscitation volumes (more than 1–2 blood volumes), due to dilution of clotting factors and proteins respectively, but is rare within the first hour of resuscitation. Coagulation times should be used to guide the administration of fresh frozen plasma.
- Cardiac arrest.

EXPECTED COURSE AND PROGNOSIS

Depends on underlying etiology and ability to institute appropriate therapy.



MISCELLANEOUS

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Shock, Cardiogenic.
- Shock, Septic.

ABBREVIATIONS

- GI = gastrointestinal.
- PCV = packed cell volume.
- TP = total protein.

Suggested Reading

Hopper K, Silverstein D, Bateman S. Shock syndromes. In: Dibartola SP, ed., Fluid Therapy in Small Animal Practice, 4th ed. Philadelphia, PA: Saunders, 2011, pp. 557–583.

Author Gretchen L. Schoeffler

Consulting Editor Michael Aherne

SHOCK, SEPTIC**BASICS****DEFINITION**

Sepsis-induced hypotension, attributable to low systemic vascular resistance that persists despite adequate intravascular volume and cardiac output.

PATHOPHYSIOLOGY

- In sepsis, an elaborate interaction of inflammatory cells and mediators decreases systemic vascular resistance and provokes maldistribution of blood flow (distributive effect). Vasodilation is primarily mediated by increased nitric oxide and prostacyclin synthesis induced by endotoxin and inflammatory cytokine interaction with vascular endothelial cells. In the face of severe arterial vasodilation, cardiac output is insufficient to maintain tissue oxygen delivery.
- Infectious agents trigger large-scale activation of monocytes, macrophages, and neutrophils that interact with endothelial cells, inducing a generalized inflammatory response. Endothelial injury is a universal feature, mediated by cellular and humoral factors that increase capillary permeability, and fluid shifts out of the intravascular space. Presence of interstitial edema and microvascular sludging further compound oxygen delivery, and tissue hypoxia leads to organ failure and death.

SYSTEMS AFFECTED

- Cardiovascular**—arterial vasodilation and maldistribution of blood flow with hypotension predominates; cardiac output frequently normal or high; however, myocardial dysfunction due to circulating factors can be important.
- Nervous**—altered mental status.
- Endocrine**—may have hyperglycemia and insulin resistance, or insufficient production of either corticosteroids or vasopressin.
- Gastrointestinal**—mucosal necrosis, hemorrhage, bacterial translocation.
- Respiratory**—interstitial and alveolar edema due to enhanced microvascular permeability; hypercoagulopathy may result in pulmonary thromboembolism.
- Hepatobiliary**—hepatocellular enzyme leakage, cholestasis, reduced bacterial clearance, hypoglycemia and abnormal synthesis.
- Hemic**—microvascular thrombosis, hyper- and hypocoagulopathy.
- Renal**—ischemic tubular damage, oliguria, acute kidney injury.

GENETICS

N/A

INCIDENCE/PREVALENCE

Unknown

GEOGRAPHIC DISTRIBUTION

N/A

SIGNALMENT

- Dog and cat.
- Any breed, age, or sex.

SIGNS**Historical Findings**

Recent infection, injury, serious illness, surgery, or immunosuppression.

Physical Examination Findings

- Dogs may have a hyperdynamic form, typified by altered mental status, weakness, hypotension, tachycardia, tachypnea, hyperemia, fast capillary refill time (CRT), bounding pulses, and fever. Cats rarely have hyperdynamic signs.
- Patients with the hypodynamic form are more likely to exhibit altered mental status, weakness, hypotension, bradycardia, tachypnea, pale mucous membranes, prolonged CRT, weak pulses, and hypothermia.

CAUSES

- Septic peritonitis—ruptured viscus; penetrating wound.
- Respiratory and pleural space—pneumonia, pyothorax.
- Skin or soft tissue—wounds, burns, cellulitis, abscess.
- Urinary tract—pyelonephritis.
- Reproductive—prostatitis, metritis, pyometra.
- Cardiovascular—endocarditis, bacteremia.
- Musculoskeletal—septic arthritis, osteomyelitis.
- Iatrogenic—catheters, implants, surgical sites.
- CNS—meningitis, encephalitis.

RISK FACTORS

- Extremes of age.
- Concurrent disease (e.g., diabetes mellitus, Cushing's disease, malignancy).
- Immunosuppression.
- Surgery, trauma, burns.
- Prior antibiotics.

**DIAGNOSIS****DIFFERENTIAL DIAGNOSIS**

- Other causes of distributive shock (e.g., drug/toxin reaction, anaphylaxis, adrenal insufficiency).
- Hypovolemic shock.
- Cardiogenic shock.
- Heatstroke.

CBC/BIOCHEMISTRY/URINALYSIS

- Neutrophilia or neutropenia, left shift, and toxic change.
- Lymphopenia.
- Thrombocytopenia.
- Variable hematocrit and blood glucose.
- Hypoalbuminemia.
- Elevated bilirubin and liver enzyme activity.
- Electrolyte derangements.
- Azotemia.
- Isthmenuria and variably active urine sediment.

OTHER LABORATORY TESTS

- Prolonged activated partial thromboplastin and prothrombin times, increased D-dimers and fibrin degradation products, and decreased levels of antithrombin and protein C.
- Blood gases may reveal hypoxemia and acid-base disturbances.
- Hyperlactatemia.
- Cytology, Gram stain, and culture and sensitivity on samples obtained from potential sites of infection may reveal etiologic organisms.
- Culture and sensitivity of urine

and blood may be useful when the source of sepsis is unknown.

- Adrenocorticotrophic hormone (ACTH) stimulation test in patients unresponsive to standard therapy.

IMAGING

- Thoracic radiographs and CT may reveal septic focus or cause for respiratory dysfunction; may also provide insights into volume status.
- Echocardiography may document a vegetative valvular lesion and/or characterize cardiac function and volume status.
- Abdominal ultrasonography and CT may detect source of infection.

DIAGNOSTIC PROCEDURES

When indicated, tissue aspirates, thoraco-, abdomino-, and arthrocentesis may provide insight into underlying etiology.

PATHOLOGIC FINDINGS

Consistent with inflammation, tissue hypoxia, and underlying etiology.

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

Emergency inpatient intensive care management. Early surgical intervention when possible to control source of infection.

NURSING CARE**Maximize Blood Oxygen Content**

- Assess and stabilize the airway and breathing as necessary.
- Administer supplemental oxygen and provide ventilatory support as needed.
- Significant anemia (packed cell volume [PCV] <25%) should be corrected.

Resuscitation

Most septic patients are hypovolemic and require initial fluid resuscitation with isotonic crystalloids such as lactated Ringer's solution, normal saline, Plasmalyte-A, and Normosol-R (20–30 mL/kg, dog; 15–20 mL/kg, cat, over 15 minutes). If no significant dehydration, addition of 7.5% hypertonic saline (4 mL/kg over 15 minutes) may expedite resuscitation:

- After the initial bolus, patient is reassessed. If vital signs and other resuscitation parameters normalize, continue monitoring to ensure stability. If vital signs and other resuscitation parameters transiently improve or if little or no improvement is seen and patient is still deemed hypovolemic, sequential crystalloid boluses should be infused and colloids (dose variable, dependent on type) may be considered.
- Septic patients receiving large fluid volumes may achieve adequate circulating volume without normalization of BP and other perfusion parameters.

Continued aggressive fluid therapy in these patients will result in volume overload and vasoconstrictors and/or positive inotropes are indicated. Monitor closely since infusion of large volumes may precipitate pulmonary

SHOCK, SEPTIC

edema in patients with capillary leak. • IV fluids, vasopressors, and positive inotropes are titrated until resuscitation endpoints have been achieved. Traditional endpoints of resuscitation (restoration of normal vital signs, BP, and urine output) remain the standard of care; however, it has been documented that critically ill patients have evidence of ongoing tissue hypoxia despite normalization of these parameters, suggesting occult oxygen debt and presence of compensated shock. There is evidence that normalization of vital signs, blood lactate, base deficit, and oxygen transport indices are more sensitive markers for adequacy of tissue perfusion than any of these variables alone. Until stronger support exists for preferential selection of one endpoint over others, utilization of as many of these markers as are available seems advisable. • Blood products should be administered based on patient need. Packed red blood cells are administered to anemic patients to improve oxygen-carrying capacity and plasma products are used to correct coagulation deficits.

ACTIVITY

Minimize patient exertion.

DIET

Withhold oral intake until shock is resolved.

CLIENT EDUCATION

Discuss risk of cardiac arrest and confirm "code status" in advance if possible.

SURGICAL CONSIDERATIONS

Identify and eliminate infection source when, and as early as, possible.



MEDICATIONS

DRUG(S) OF CHOICE

- Once adequate circulating volume is achieved, improvement in systemic BP and other clinical resuscitation parameters may require one or more vasopressors and/or positive inotropes:
 - Norepinephrine (0.05–2 µg/kg/min), vasopressin (0.5–2 mU/kg/min), or dopamine (5–20 µg/kg/min) can be used for vasopressor support (dogs and cats). Monitor for tachyarrhythmia and excessive peripheral vasoconstriction.
 - Dobutamine (2–20 µg/kg/min) is primarily used as a positive inotrope in canine septic shock patients with decreased contractility or myocardial depression. Monitor for tachyarrhythmia. While dobutamine can be used safely in many feline patients, seizures have been observed in some cats at doses exceeding 5 µg/kg/min.
 - It is essential that IV, empiric,

broad-spectrum antibiotic therapy be instituted early in septic patients; the spectrum should be narrowed when culture results become available. Empiric selection based on patient's underlying immune status, suspected source and organism(s) responsible, specific antibiotic properties (tissue penetration, cidal versus static activity), and considerations for resistance (previous antibiotic use, hospital- or community-acquired infection). • It is not unreasonable to empirically treat patients not responding adequately to standard therapy with 0.75–1.0 mg/kg q6h IV hydrocortisone after undergoing a standard ACTH stimulation test. Therapy should be continued in patients in whom relative adrenal insufficiency is documented.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

- Serial assessment of perfusion to optimize titration of fluids and vasoactive drugs:
 - Physical exam including mentation, mucous membrane color, CRT, pulse quality, muscle strength, temperature, and heart rate.
 - Hemodynamic monitoring to include arterial BP (frequently reveals disproportionately low diastolic pressure), and in some patients central venous pressure, cardiac output, and tissue oxygenation.
 - Thoracic ultrasound to monitor for pulmonary changes and to aid in assessing patient volume status and cardiac systolic function.
 - Laboratory data including serum lactate and base deficit.
- Blood gas analysis and pulse oximetry to follow tissue oxygenation, ventilation, and acid–base status.
- Serial assessment of respiratory rate and effort, and pulmonary auscultation.
- Continuous ECG to detect arrhythmia.
- Urine output as an indicator of glomerular filtration rate and renal blood flow.
- Minimum of twice daily PCV, serum total protein, blood glucose, and serum electrolytes; once daily hepatocellular enzymes, blood urea nitrogen, and serum creatinine to monitor effects of systemic tissue hypoxia.
- Patients with coagulopathy should

have coagulation indices, PCV and total protein assessed as needed.

PREVENTION/AVOIDANCE

- Timely and effective wound treatment.
- Appropriate antimicrobial therapy.

POSSIBLE COMPLICATIONS

- Volume overload. • Pulmonary edema.
- Vasculitis and peripheral edema. • Acid–base disturbances. • Anemia. • Thrombocytopenia and other coagulopathy. • Multiple organ dysfunction. • Cardiac arrest.

EXPECTED COURSE AND PROGNOSIS

Dependent on underlying etiology and ability to institute appropriate therapy.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Sepsis

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Variable infectious agent etiologies have zoonotic potential.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNOMYS

N/A

SEE ALSO

- Disseminated Intravascular Coagulation.
- Hyperadrenocorticism (Cushing's Syndrome)—Cats.
- Hyperadrenocorticism (Cushing's Syndrome)—Dogs.
- Hypoadrenocorticism (Addison's Disease).
- Shock, Cardiogenic.
- Shock, Hypovolemic.

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone.
- CRT = capillary refill time.
- PCV = packed cell volume.

Suggested Reading

De Laforcade A, Silverstein DC. Shock. In: Silverstein DC, Hopper K, ed., Small Animal Critical Care Medicine, 2nd ed., St. Louis, MO: Saunders, 2015, pp. 26–30.

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Author Gretchen L. Schoeffler

Consulting Editor Michael Aherne



Client Education Handout
available online

SINUS ARRHYTHMIA



BASICS

DEFINITION

- Normal sinus impulse formation characterized by a phasic variation in sinus cycle length. An irregular R-R interval is present that has more than 10% variation in sinus cycle length (or variability of 0.12 seconds [dog], 0.10 seconds [cat], or more exists between successive P waves) (Figure 1).
- Two basic forms exist—respiratory sinus arrhythmia (RSA): P-P interval cyclically shortens during inspiration due primarily to reflex inhibition of vagal tone and lengthens during expiration; nonrespiratory sinus arrhythmia: phasic variation in P-P interval unrelated to the respiratory cycle.

ECG Features

- Other than the irregular rhythm, all other criteria for sinus rhythm are present.
- Normal heart rate.
- Positive P wave in leads I, II, III, and aVF, unless a wandering pacemaker is present, where the P waves may be positive, diphasic, or negative temporarily.
- A P wave is present for every QRS complex.
- A QRS complex is present for every P wave.
- PR interval is relatively constant.

S

PATHOPHYSIOLOGY

Sinus node discharge rate depends on the two opposing influences of the autonomic nervous system. Vagal stimulation decreases spontaneous sinus nodal discharge rate and predominates over sympathetic stimulation. Negative intrathoracic pressure occurring with inspiration causes decreased pressure on the vagus nerves. Feedback from the cardiorespiratory and vasomotor centers in the medulla produces cardiac acceleration by decreasing vagal restraint on the sinus node; the opposite occurs during exhalation. The genesis of sinus arrhythmia also depends on reflexes involving pulmonary stretch receptors (Hering–Breuer

reflex), pressure–volume sensory receptors in the heart (Bainbridge reflex whereby atrial stretch stimulates receptors in the atrial wall, causing vagal inhibition and increase in heart rate; baroreceptors in the carotid sinus and aortic arch elicit inverse changes in heart rate with acute changes in arterial blood pressure), blood vessels, and chemical factors of the blood.

- RSA is measured as a high-frequency component of heart rate variability (HRV) and is used as an index of cardiac vagal control. HRV measures beat to beat changes in heart rate and R-R variability from the ECG. HRV is a widely accepted clinical and research tool for evaluation of cardiac autonomic changes.

SYSTEMS AFFECTED

Cardiovascular—generally no hemodynamic consequence, but marked sinus arrhythmia may produce a long enough sinus pause to produce syncope if not accompanied by an escape rhythm.

GENETICS

N/A

INCIDENCE/PREVALENCE

Most frequent form of arrhythmia in dogs.

SIGNALMENT

Species

- RSA frequent normal finding in dogs.
- While common in cats asleep and in home environment, in a clinical setting sympathetic dominance occurs and RSA is rare without underlying pathology.

Breed Predilections

- Brachycephalic breeds predisposed.
- Dogs—bulldog, Lhasa apso, Pekingese, pug, shar-pei, shih tzu, boxer.
- Cats—Persian, Himalayan.

Mean Age and Range

N/A

Predominant Sex

N/A

SIGNS

General Comments

- Uncommon, but weakness may develop if pauses between beats are excessively long; syncope can occur when a marked sinus arrhythmia and sinus bradycardia develop.
- In general, symptoms more common in nonrespiratory than in respiratory form.

Historical Findings

- RSA—none.
- Nonrespiratory sinus arrhythmia—may be findings related to underlying disease.

Physical Examination Findings

- May be normal.
- Irregular rhythm on auscultation.
- May be findings related to specific disease accentuating vagal tone (e.g., stertor and stridor in a patient with brachycephalic airway syndrome).

CAUSES

- Normal cyclic change in vagal tone associated with respiration in the dog; heart rate increases with inspiration and decreases with expiration.
- Underlying conditions that increase vagal tone—high intracranial pressure, gastrointestinal disease, respiratory disease, cerebral disorders, digitalis toxicity, organophosphates.
- Carotid sinus massage or ocular pressure (vagal maneuver) may accentuate.

RISK FACTORS

- Brachycephalic conformation.
- Digoxin therapy.
- Any disease that increases vagal tone.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Auscultation of sinus arrhythmia is often confusing; ECG helps differentiate normal

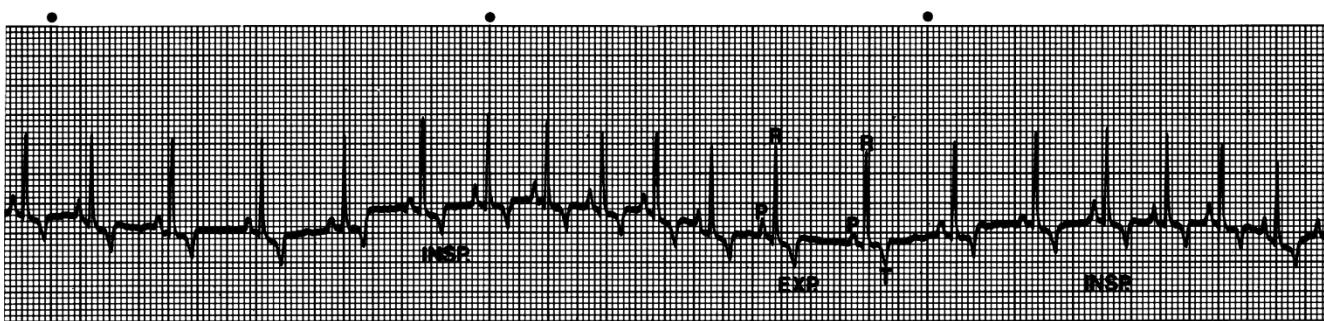


Figure 1.

Respiratory sinus arrhythmia with an average rate of 120 bpm (6 complexes between 1 set of time lines or 3 seconds × 20) (paper speed, 25 mm/s; 10 mm/mV). The rate increases during inspiration (INSPIRATION) and decreases during expiration (EXHALATION). The fluctuation of the baseline correlates with the movement of the electrodes by the thoracic cavity. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

(CONTINUED)

SINUS ARRHYTHMIA**S**

sinus arrhythmia from true pathologic arrhythmia.

- Wandering sinus pacemaker frequently associated and a variant of sinus arrhythmia. Site of impulse formation shifts within the sinoatrial node or to an atrial focus or atrioventricular (AV) node, changing the configuration of the P wave.
- Important to differentiate normal sinus arrhythmia from pathologic arrhythmias including atrial premature complexes, sick sinus syndrome, slow atrial fibrillation, and AV dissociation.

CBC/BIOCHEMISTRY/URINALYSIS

N/A

OTHER LABORATORY TESTS

Cats with chronic respiratory disease may be positive for feline leukemia virus or feline immunodeficiency virus.

IMAGING

Radiographs, CT, or MRI of head and neck to assess for abnormal anatomic conformation that might predispose to airway problems.

DIAGNOSTIC PROCEDURES

- Pharyngoscopy/laryngoscopy if upper airway disease suspected.
- Atropine challenge test (administer atropine 0.04 mg/kg IM followed by ECG in 30 minutes or 0.04 mg/kg atropine IV followed by ECG in 10 minutes) if associated with sinus bradycardia and primary dysfunction of sinus node is suspected. Subsequent heart rate should be greater than 150 bpm.

PATHOLOGIC FINDINGS

See specific disease.

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

Generally, specific treatment required only when associated with symptomatic sinus bradycardia; if not related to respiration, underlying cause is treated. If patient is suffering respiratory distress, appropriate inpatient management indicated until patient is stable.

NURSING CARE

None unless associated with underlying disease.

ACTIVITY

Not restricted unless associated with specific disease (e.g., brachycephalic animals may need to limit exercise, especially in high ambient temperatures).

DIET

Caloric restriction for obese animals with airway compromise.

CLIENT EDUCATION

None unless associated with specific disease.

SURGICAL CONSIDERATIONS

None unless associated with specific disease.

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

- Generally no therapy indicated; this is a normal rhythm.
- Infectious respiratory diseases require appropriate antibiotic therapy.
- If associated with symptomatic sinus bradycardia or sinus arrest or block, anticholinergics may be indicated—atropine 0.02–0.04 mg/kg IV, IM, SC or glycopyrrolate 5–10 µg/kg IV, IM, SC.

CONTRAINdications

Discontinue digoxin if toxicity is a problem.

PRECAUTIONS

Avoid atropine in patients with respiratory disease; an adverse effect is drying of secretions.

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A

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

Only if associated with specific disease.

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

N/A

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Sick sinus syndrome.
- Brachycephalic airway syndrome.
- Asthma.
- Chronic obstructive pulmonary disease.

AGE-RELATED FACTORS

Generally more pronounced in young adult.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

Increased incidence of arrhythmias.

SYNOMYS

- Nonrespiratory sinus arrhythmia = nonphasic sinus arrhythmia; sinus irregularity.
- Respiratory sinus arrhythmia = phasic sinus arrhythmia.
- Ventriculophasic sinus arrhythmia—form of nonphasic sinus arrhythmia in which atrial cycles containing ventricular complexes are shorter than those in which they are absent. That is, the P-P interval that includes the QRS complex is shorter than the P-P interval without a QRS complex. This can be seen with second-degree AV block, complete AV block or in the presence of ventricular premature complexes with a full compensatory pause.

SEE ALSO

- Brachycephalic Airway Syndrome.
- Sick Sinus Syndrome.
- Sinus Arrest and Sinoatrial Block.

ABBREVIATIONS

- AV = atrioventricular.
- HRV = heart rate variability.
- RSA = respiratory sinus arrhythmia.

Suggested Reading

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Author Deborah J. Hadlock

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SINUS BRADYCARDIA



BASICS

DEFINITION

Sinus rhythm in which impulses arise from the sinoatrial (SA) node at slower than normal rate for an animal's signalment and activity (Figure 1).

ECG Features

- Dogs—sinus rate <60 bpm.
- Cats—sinus rate <110 bpm at home or <130 bpm at the clinic.
- Rhythm regular, often with a slight variation in R-R interval; may be irregular; often coexists with sinus arrhythmia.
- Normal P wave for each QRS complex.
- P-R interval constant.

PATHOPHYSIOLOGY

Can be an incidental finding in healthy animals or during sleep. May represent normal physiologic response to athletic training; may result from enhanced cardiac parasympathetic tone or decreased sympathetic tone as well as from intrinsic changes in the sinus node. Automaticity of the heterogeneous sinus node is a very complex phenomenon invoking the calcium and voltage clock mechanisms. More than 16 autonomically influenced currents with the I_f (funny) channel predominating and Ca^{2+} release from the sarcoplasmic reticulum critical to maintain autonomic balance and changes in heart rate. May represent pathophysiologic response due to high vagal tone, change in blood pH, Pco_2 , Po_2 , or serum electrolyte disorders, hypothyroidism, increased intracranial pressure, toxins and certain drugs. May be a result of sick sinus syndrome (SSS).

SYSTEMS AFFECTED

Cardiovascular—most instances benign arrhythmia; may be beneficial by producing a longer period of diastole and increased ventricular filling time; can be associated with syncope if due to abnormal reflex (neurocardiogenic) or intrinsic disease of sinus node.

GENETICS

Female miniature schnauzer, West Highland white terrier, boxer, cocker spaniel, dachshund, and pug predisposed to SSS—may cause bradycardia.

INCIDENCE/PREVALENCE

Common in the dog; less common in cat. Clinical interpretation of sinus node rate also depends on environment and type of patient. For example, a sinus rate can be as low as 20 bpm in a normal dog that is sleeping.

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Bradycardia associated with SSS—miniature schnauzer, cocker spaniel, dachshund, pug, and West Highland white terrier.

Mean Age and Range

- Decreased prevalence with advancing age unless associated with intrinsic disease of SA node.
- SSS typically seen in middle-aged to geriatric patients.

Predominant Sex

With SSS, older female miniature schnauzers.

SIGNS

Historical Findings

- Often asymptomatic.
- Lethargy.
- Weakness.
- Exercise intolerance.
- Syncope.
- Episodic ataxia.

Physical Examination Findings

- Pulse rate slow.
- Hypothermia may be present.
- Poor perfusion.
- Syncope.
- Decreased level of consciousness.

CAUSES

Physiologic

- Athletic conditioning.
- Hypothermia.
- Intubation with pharyngeal or soft palate tension.
- Sleep.
- Cushing's reflex with increased intracranial pressure.
- Gastrointestinal distension.
- Activation of baroreceptor reflex with increase in systemic blood pressure (BP).

Pathophysiology

- High vagal tone associated with gastrointestinal, respiratory, neurologic, and pharyngeal diseases.
- Reflex-mediated/neurocardiogenic/vasovagal—e.g., carotid sinus hyperactivity; situational (micturition, defecation, cough, swallowing).

Pathologic

- High intracranial pressure.
- Hyperkalemia.
- Hyper- or hypocalcemia.
- Hypermagnesemia.
- Hypoxemia.
- Hypothyroidism.
- Hypoglycemia.
- May precede cardiac arrest.
- SSS (rare in the cat).
- Feline dilated cardiomyopathy.
- Viral myocarditis.
- SA block.
- In humans, mutations in the I_f channel and drugs which block I_f (such as ivabradine) have been associated with bradycardia.

Pharmacologic

- General anesthesia.
- Any negative chronotropic including:
 - Phenothiazines.
 - Beta-adrenergic blockers.
 - Digitalis glycosides.
 - Calcium channel blockers.
 - α_2 -Adrenergic agonists.
 - Sotalol.
 - Amiodarone.
 - Centrally acting opioids: morphine, hydromorphone, butorphanol, fentanyl.

RISK FACTORS

- Any situation or disease that may increase parasympathetic tone.
- Oversedation.
- Hypoventilation under anesthesia.
- Breeds predisposed to SSS.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Persistent and marked sinus bradycardia (SB) should raise possibility of SSS.
- Clinical signs may mimic cerebral dysfunction.

CBC/BIOCHEMISTRY/URINALYSIS

- Hyperkalemia, hypercalcemia, hypocalcemia, or hypermagnesemia possible.
- CBC and serum chemistry profile may reveal changes associated with metabolic disease such as renal failure.

OTHER LABORATORY TESTS

- Serum thyroxine (T_4), free T_4 , and thyroid-stimulating hormone assays if hypothyroidism suspected.
- Measure trough serum digoxin concentration, if applicable, 8 hours after last dose or close to next dosing; normal therapeutic serum concentration should be 0.5–1.5 ng/mL.
- Toxicologic screen.

DIAGNOSTIC PROCEDURES

- Provocative atropine response test to assess sinus node function—administer atropine 0.04 mg/kg IV, wait 10–15 minutes, then record ECG or administer same dose IM, wait 30 minutes, then record ECG; persistent sinus tachycardia at >140 bpm is expected response. Lower doses of atropine have increased tendency to cause initial accentuation of SB and first- or second-degree atrioventricular block because of centrally mediated increase in vagal tone.
- 24-hour Holter monitoring or ECG event recorder, an owner-triggered device, useful if transient bradycardia is suspected cause for clinical signs.



TREATMENT

APPROPRIATE HEALTH CARE

- Many animals exhibit no clinical signs and require no treatment. In dogs without structural heart disease, heart rates as low as 40–50 bpm generally provide normal cardiac output at rest.
- Therapeutic approaches—vary markedly; depend on the mechanism for SB, the ventricular rate, and severity of clinical signs.
- Inpatient or outpatient management—depends on underlying cause and clinical status of patient.

NURSING CARE

- Provide general supportive therapy including IV fluid therapy for hypothermic and hypovolemic patients.
- Discontinue any causative drug.
- Correct any serious electrolyte imbalance with appropriate fluid therapy.

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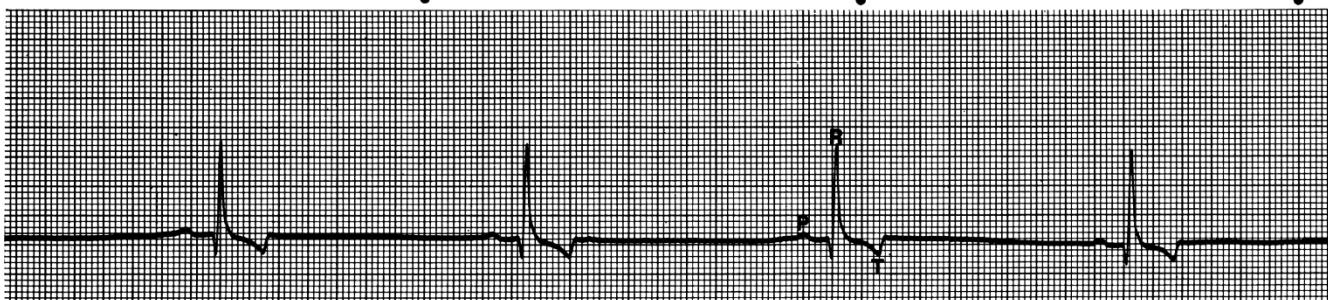
SINUS BRADYCARDIA

Figure 1.

Sinus bradycardia at a rate of 75 bpm in a cat from anesthetic complications during surgery. Note the tall R waves. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

CLIENT EDUCATION

- Discuss importance of complying with daily medical management when treating.
- Advise that persistent symptomatic bradycardia may necessitate permanent pacemaker implantation for reliable long-term management.

SURGICAL CONSIDERATIONS

- If progressive bradycardia occurs during anesthesia and is attributed to hypoventilation, immediately discontinue inhalation anesthetics and provide adequate ventilation; atropine is generally ineffective in this situation.
- If surgical manipulation triggering vagal reflexes (eye, vagus nerve, larynx) is anticipated, pretreatment with atropine 0.02 mg/kg IM, SC or glycopyrrolate 5–10 µg/kg IM, SC may prevent bradycardia.
- Severe bradycardia may precipitate cardio-pulmonary arrest; identify the causative agent or condition for effective management.

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

- If patient is hypothyroid, supplement with L-thyroxine.
- For severe hypocalcemia (<6 mg/dL) administer 10% calcium gluconate 0.5–1.5 mL/kg IV slowly over 15–30 minutes; monitor with ECG.
- For symptomatic drug-induced bradycardias, disorders causing excessive vagal tone, and initial management of bradycardia associated with SSS, administer atropine 0.04 mg/kg IV or glycopyrrolate 5–10 µg/kg IV; anticholinergic therapy may be continued short term using atropine 0.02–0.04 mg/kg IM, SC q6–8h or glycopyrrolate 0.01 mg/kg IM, SC q6–8h. Consider propantheline bromide 0.25–0.5 mg/kg PO q8–12h, hyoscyamine 3–6 µg/kg PO q8h, methylxanthine theophylline, an adenosine receptor antagonist (extended release formulation 10 mg/kg PO q12h, dogs; 12.5 mg PO q24h in the evening, cats), and/or terbutaline (0.2 mg/kg q8–12h PO, dogs; 0.625–1.25 mg/cat PO, cats) to manage symptomatic bradycardia associated with SA node disease.

- For temporary management of symptomatic persistent bradycardia until pacing can be accomplished, consider continuous IV infusion of isoproterenol 0.04–0.08 µg/kg/min IV. Temporary pacing, if available, would be the initial procedure of choice.

CONTRAINdications

- For hypothermia-induced bradycardia with a pulse, rewarming and supportive measures should be mainstay of treatment. Parasympatholytics generally not recommended.
- Parasympatholytic agents contraindicated for acidotic, hypercarbic patients under anesthesia (hypoventilation); bradycardia in this setting may protect the myocardium by decreasing oxygen consumption.

PRECAUTIONS

- Close ECG monitoring recommended when administering calcium solutions for treatment of hypocalcemia; if QT interval shortening or bradycardia, stop administration temporarily.
- In patients with heart disease, a lower initial dose of L-thyroxine is advised to allow adaptation to higher metabolic rate.
- Administer atropine selectively; rapid IV administration may predispose to ventricular arrhythmias by altering autonomic balance.
- Caution when administering parasympatholytic agent to dogs with suspect SSS—could result in tachycardias that overdrive suppress escape rhythms and thus have a potential risk of asystole after termination of the tachycardia.

ALTERNATIVE DRUG(S)

- Bradycardia associated with structural heart disease is most reliably treated by permanent pacemaker implantation.
- Glycopyrrolate may have longer vagal blocking effect and cause less frequent ventricular ectopic beats than atropine.

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

- Assess total T₄ 6 hours post pill.
- Addison's disease—assess electrolytes every 3–4 months

after patient is stable.

- ECG check of pacemaker function and pacing rate is recommended during each follow-up examination.

PREVENTION/AVOIDANCE

- Maintain normal PaO_2 under anesthesia with proper ventilation; monitor with pulse oximetry or blood gases.
- Avoid hypothermia intraoperatively.

EXPECTED COURSE**AND PROGNOSIS**

- Signs, if present, should resolve with correction of causative metabolic or endocrine problem.
- Treatment of symptomatic SB with a permanent pacemaker generally offers a good prognosis for rhythm control.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Sick sinus syndrome.
- Heart block.
- Sinus arrhythmia.

PREGNANCY/FERTILITY/BREEDING

Postparturient hypocalcemia usually develops 1–4 weeks postpartum, but can occur at term, prep partum, or late lactation.

SEE ALSO

- Digoxin Toxicity.
- Eclampsia.
- Hypercalcemia.
- Hyperkalemia.
- Hypermagnesemia.
- Hypocalcemia.
- Hypothermia.
- Hypothyroidism.
- Organophosphate and Carbamate Toxicosis.
- Sick Sinus Syndrome.

ABBREVIATIONS

- ECG = electrocardiogram.
- SA = sinoatrial.
- SB = sinus bradycardia.
- SSS = sick sinus syndrome.
- T₄ = thyroxine.

Suggested Reading

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Author Deborah J. Hadlock

Consulting Editor Michael Aherne

SINUS TACHYCARDIA



BASICS

DEFINITION

Disturbance of sinus impulse formation; acceleration of the sinoatrial node beyond its normal discharge rate (Figure 1).

ECG Features

- Dogs—heart rate (HR) >160 bpm (puppies HR >220 bpm). • Cats—HR >180 bpm; (kittens HR >240 bpm). • ECG shows a rapid regular rhythm with possible slight variation in R-R interval. • P wave of sinus origin for each QRS complex with constant P-R interval. • P waves may be partially or completely fused with preceding T waves. • Generally has a gradual onset and termination.

PATHOPHYSIOLOGY

- Accelerated phase 4 diastolic depolarization of sinus nodal cells (as a result of voltage- and calcium-dependent mechanisms) generally responsible for sinus tachycardia (ST).
- Enhanced adrenergic effect or cholinergic inhibition results in high rate of sinus impulse formation; changes in heart rate usually involve a reciprocal action of the parasympathetic and sympathetic divisions of the autonomic nervous system.

S

SYSTEMS AFFECTED

Cardiovascular—cardiac output = heart rate × stroke volume. Changes in heart rate affect preload, afterload, and contractility, which determine stroke volume; severe tachycardia can compromise cardiac output. Rapid rates shorten diastolic filling time, and particularly in diseased hearts, the increased heart rate can fail to compensate for decreased stroke volume, resulting in decreased cardiac output and coronary blood flow. Chronic tachycardias can cause cardiac dilation (tachycardiomypathy) which often resolves with control of the tachycardia. However, ST is most often present due to elevated sympathetic tone and is physiologic (because of hypovolemia, fear, pain, etc.).

GENETICS

N/A

INCIDENCE/PREVALENCE

- Most common benign arrhythmia in the dog and cat. • Most common rhythm disturbance in the postoperative patient.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat.

Breed Predilections

None

SIGNS

General Comments

Often no clinical signs because ST is almost always a consequence of a variety of physiologic or pathophysiologic stresses.

Historical Findings

- In general, ST itself does not produce any symptoms. • If associated with primary cardiac disease, weakness, exercise intolerance, or syncope may be reported. • If associated with other medical conditions, signs may be seen specific to the disease present.

Physical Examination Findings

- High HR. • May otherwise be normal if not associated with a pathologic condition.
- Pale mucous membranes if associated with anemia or congestive heart failure (CHF).
- Fever may be present. • Signs of CHF (e.g., dyspnea, cough, cyanosis, ascites) if associated with primary cardiac disease.

CAUSES

Physiologic

- Exercise. • Pain. • Restraint. • Excitement.
- Any hyperadrenergic state.

Pathologic

- Fever. • CHF. • Chronic lung disease.
- Shock. • Pericardial effusion. • Anemia.
- Pain. • Infection. • Hypoxia. • Pulmonary thromboembolism. • Hypotension.
- Hypovolemia. • Functional pheochromocytoma. • Hyperthyroidism. • Pericarditis.
- Pneumothorax. • Hypoglycemia.
- Vestibulosympathetic hypovolemia.

Pharmacologic

- Atropine. • Epinephrine. • Ketamine.
- Tiletamine (Telazol®). • Quinidine.
- Xanthine bronchodilators. • β -Adrenergic agonists.

RISK FACTORS

- Thyroid medications. • Primary cardiac diseases. • Inflammation. • Pregnancy.
- Anesthesia. • Certain toxins (*Amanita muscaria*, scorpion venom, black widow spider venom), plants (Jimson weed, mandrake), and drugs (antihistamines, tricyclic antidepressants).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Must differentiate from supraventricular tachycardia (SVT), including atrial tachycardia, atrial flutter with 2:1 AV block, and AV junctional tachycardia; as sinus rate increases, the P wave appears closer to the T wave of the previous beat. At very rapid rates, it becomes difficult to distinguish this condition from other pathologic SVT. Gradual slowing of the rate is suggestive of ST.

CBC/BIOCHEMISTRY/URINALYSIS

- Low packed cell volume if patient is anemic. • Leukocytosis with left shift if inflammation or infection is causative.

OTHER LABORATORY TESTS

- High serum thyroxine (T_4) or free T_4 concentration (cats) if secondary to hyperthyroidism. • Triiodothyronine (T_3) suppression test and thyrotropin-releasing hormone (TRH) response test if T_4 values are normal and hyperthyroidism is suspected. • Functional testing for pheochromocytoma:
 - Metanephrenes (breakdown metabolites of epinephrine and norepinephrine); measured in plasma or urine.
 - Serum inhibin, a hormone involved in reproductive physiology; undetectable levels supportive of pheochromocytoma.
- 24-hour Holter monitoring. • Cardiac

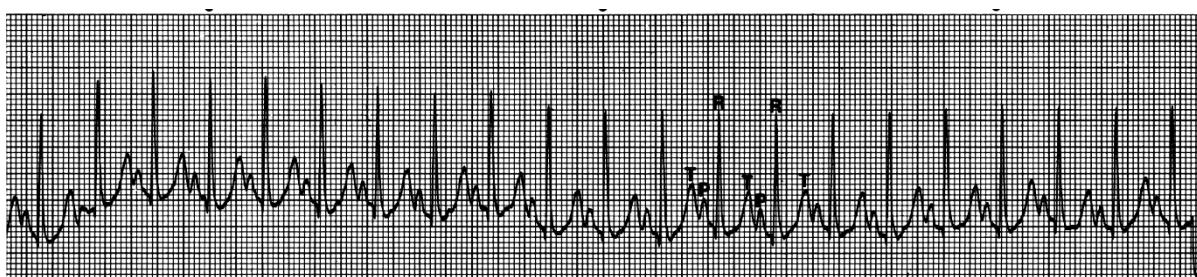


Figure 1.

Sinus tachycardia at a rate of 272 bpm in a dog in shock. The rhythm is sinus because the P waves are normal, the P-R relationship is normal, and the rhythm is regular. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

(CONTINUED)

electrophysiologic studies. • Plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) assay may be helpful if evaluating for cardiac disease.

IMAGING

- Thoracic radiographs and echocardiography to evaluate for evidence of primary cardiac disease.
- Thyroid scintigraphy to evaluate for hyperthyroidism. • Abdominal ultrasound and angiography to evaluate for adrenal mass. • CT and MRI as well as functional imaging modalities very sensitive for detecting adrenal masses.

DIAGNOSTIC PROCEDURES

- A nonpharmacologic vagal maneuver can differentiate ST from other SVTs; carotid sinus or ocular pressure may terminate ectopic SVT. With effective vagal maneuvers, the HR in ST gradually slows. Less commonly, varying degrees of AV block (usually first-degree or Wenckebach) may occur transiently. ECG monitoring is recommended during these vagal maneuvers. • Pharmacologic agents can be used if no response to the vagal maneuver. Similarly, an abrupt reduction in HR suggests SVT whereas gradual slowing suggests ST: o IV diltiazem 0.25 mg/kg administered over 2 minutes. If no response, can be repeated in 15 minutes. o IV esmolol 50–100 µg/kg bolus q5min up to 500 µg/kg; 25–200 µg/kg/min CRI.
- A precordial thump may be used to differentiate ST from other SVT. ST usually not affected, whereas the SVT may stop for at least 1 or 2 beats. • Serial arterial BP measurement may document hypertension in patients with hyperthyroidism, pheochromocytoma, or renal disease.

PATHOLOGIC FINDINGS

- None if associated with physiologic or pharmacologic cause. • Pathologic findings depend on the primary disease process.



TREATMENT

APPROPRIATE HEALTH CARE

- Identify and correct underlying disorders whenever possible. • Whether inpatient or outpatient depends on clinical status of patient and primary disease, if any (e.g., if CHF, treat as outpatient unless animal is dyspneic or severely hypotensive). • If associated with pericardial effusion, avoid drug therapy and perform pericardiocentesis.
- If associated with a certain drug (e.g., hydralazine, bronchodilators), discontinue the medication or adjust the dose. • If associated with hypovolemia, replace fluid volume.

NURSING CARE

Depends on whether associated with a specific disease.

ACTIVITY

Exercise restriction recommended if symptomatic cardiac disease.

DIET

Sodium restriction generally advised with hypertension and CHF.

CLIENT EDUCATION

Discuss importance of managing any primary disease appropriately, with medical or surgical intervention.

SURGICAL CONSIDERATIONS

- Thyroidectomy—treatment option for hyperthyroidism (cats). • Tumor removal is the definitive treatment for patients with pheochromocytoma.



MEDICATIONS

DRUG(S) OF CHOICE

- Establish underlying cause and treat appropriately; specific antiarrhythmic therapy is generally limited to patients in CHF or those with secondary cardiac disease due to hyperthyroidism or hypertension. • Dogs—if CHF is the cause, administer pimobendan along with appropriate diuretic therapy and angiotensin-converting enzyme inhibitor. Digoxin may be indicated in some cases such as CHF with atrial fibrillation. If ST persists despite above management, consider adding a calcium channel blocker (e.g., diltiazem 0.5–2.5 mg/kg PO q8h) or a beta-blocker (e.g., atenolol 0.25–1 mg/kg q12h, sotalol 1–2 mg/kg q12h PO) *only* after congestion is controlled. • Cats—if ST is associated with hyperthyroidism without CHF, a beta-blocker (e.g., atenolol 0.25–1 mg/kg PO q12–24h) may lower the HR. Consider digoxin (0.01875–0.03125 mg per average-size cat, equal to 1/8–1/4 of a 0.125 mg tablet—tablet preferred) if CHF present with atrial fibrillation and rapid ventricular response rate. Although still controversial, pimobendan (0.1–0.3 mg/kg PO q12h) has become more commonly accepted as treatment for CHF. If ST associated with hypertrophic cardiomyopathy, administer atenolol 6.25–12.5 mg/cat PO q12h or diltiazem 1.75–2.4 mg/kg PO q8h.

CONTRAINDICATIONS

Avoid drugs such as atropine or catecholamines (epinephrine) that may further increase the HR.

PRECAUTIONS

- Beta-blockers can potentially worsen signs of congestion and lower cardiac output in patients with systolic dysfunction. • Suppression of ST may be catastrophic if occurring as natural compensatory response to maintain cardiac output in a systemically ill patient.

POSSIBLE INTERACTIONS

See manufacturer's insert for specific drugs.

ALTERNATIVE DRUG(S)

N/A

SINUS TACHYCARDIA



FOLLOW-UP

PATIENT MONITORING

Depends on specific disease—for CHF, serial ECG, thoracic radiographs, BUN, creatinine, and serum electrolytes; for hyperthyroidism, serial serum T_4 , complete blood count, and biochemistry.

PREVENTION/AVOIDANCE

Minimize stress, exercise, and dietary sodium, if heart disease.

POSSIBLE COMPLICATIONS

- Weakness or syncope if associated with low cardiac output. • Development of CHF if persistent ST associated with heart disease.

EXPECTED COURSE

AND PROGNOSIS

- ST usually resolves with correction of the underlying cause. • Poor despite treatment if ST is associated with CHF. • Favorable for remission of ST when hyperthyroidism is controlled medically, surgically, or by radioactive iodine.



MISCELLANEOUS

ASSOCIATED CONDITIONS

See list of pathologic and physiologic causes.

PREGNANCY/FERTILITY/BREEDING

Increase in cardiac output in late pregnancy (third trimester) largely due to an accelerated HR.

SYNONYMS

- Inappropriate sinus tachycardia. • Postural tachycardia syndrome.

SEE ALSO

- Atrial Fibrillation and Atrial Flutter.
- Congestive Heart Failure—Left-Sided.
- Congestive Heart Failure—Right-Sided.
- Hyperthyroidism. • Pheochromocytoma.
- Supraventricular Tachycardia.

ABBREVIATIONS

- AV = atrioventricular. • CHF = congestive heart failure. • ECG = electrocardiogram. • HR = heart rate. • NT-proBNP = N-terminal pro-brain natriuretic peptide. • ST = sinus tachycardia. • SVT = supraventricular tachycardia. • T_3 = triiodothyronine. • T_4 = thyroxine. • TRH = thyrotropin-releasing hormone.

Suggested Reading

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SPLENOMEGALY



BASICS

DEFINITION

Enlargement of the spleen; characterized as either diffuse, focal, or nodular.

PATHOPHYSIOLOGY

- Splenic functions—removal of senescent and abnormal erythrocytes; filtration and phagocytosis of antigenic particles such as microorganisms, degraded cellular material, macromolecules; production of lymphocytes and plasma cells; antibody production, reservoir for erythrocytes and platelets; iron metabolism and storage, hematopoiesis, as required. • Many disorders affect function of spleen.

Diffuse Splenomegaly

Four General Pathologic Mechanisms

- Inflammation (splenitis)—associated with infectious agents; classified according to cell type (e.g., suppurative, necrotizing, eosinophilic, lymphoplasmacytic, and granulomatous-pyogranulomatous). • Lymphoreticular hyperplasia—increased proliferation of mononuclear phagocytes and lymphoid elements (in response to antigens); accelerated erythrocyte destruction. • Congestion—associated with impaired venous drainage.
- Infiltration—involves cellular invasion of the spleen or deposition of abnormal substances.

Focal or Nodular lesions

Associated with neoplastic (benign or malignant) or non-neoplastic disorders (infection, hyperplasia/regeneration, or inflammation).

SYSTEMS AFFECTED

Disorders of the spleen may also be associated with changes in the liver and lymph nodes.

SIGNALMENT

- Dog and cat; certain conditions maybe more prevalent in specific breeds or sizes of dog.
- Splenic torsion—overrepresented in large, deep-chested breeds (e.g., German shepherd dog, Great Dane). • Hemangiosarcoma—middle-aged dogs; large breeds; predilection in German shepherd dog, golden retriever, Labrador retriever, and boxer. • Prominent spleen—may be normal in certain breeds (German shepherd dog).

SIGNS

General Comments

- Splenic enlargement—often nonspecific.
- Frequently reflects an underlying disorder rather than primary disease of the spleen.

Historical Findings

- Vomiting, diarrhea, anorexia—can be seen with infiltrative diseases such as lymphoma, mast cell tumor, feline infectious peritonitis (FIP), lymphoplasmacytic enteritis (cats).
- Lethargy, anorexia, vomiting, vague abdominal pain (in acute cases pain can be severe), mild to moderate abdominal distention in deep-chested large to giant-breed

dogs (Great Dane, German shepherd dog overrepresented)—associated with splenic torsion (with or without concurrent gastric dilatation and volvulus [GDV]). • Weakness, lethargy, collapse (can be episodic), abdominal distention—can indicate a hemoabdomen secondary to bleeding/ruptured splenic tumor (hemangiosarcoma most common) or benign conditions such as a hematoma.

Physical Examination Findings

- Prominent spleen on abdominal palpation or cranial/mid-abdominal mass; nonpalpable spleen does not preclude splenomegaly.
- Dogs—smooth or irregular surface.
- Cats—usually diffuse, uniform enlargement.
- Pallor, poor capillary refill time, poor peripheral pulses and tachycardia if splenic hemorrhage or splenic torsion. • Abdominal distention if massive splenomegaly or splenic rupture (effusion). • Petechia and ecchymosis if coagulopathy secondary to primary splenic disorder or underlying disease. • Concurrent hepatomegaly, thickened intestines, and/or mesenteric lymphadenopathy imply infiltrative (neoplastic) or inflammatory (immune-mediated or infectious) disease.
- Peripheral lymphadenomegaly—suggests lymphoma/leukemia or histiocytic sarcoma.
- Cardiac arrhythmias—can be seen with primary cardiac disease affecting the spleen (congestion) or can be associated with primary splenic disorders.

CAUSES

Dogs

Inflammation (Splenitis)

- Inflammatory cell type can help prioritize differentials. • Suppurative (neutrophilic)—bacterial infections associated with penetrating abdominal wound; migrating foreign body; endocarditis; sepsis; infectious complication of splenic torsion. • Necrotizing—most commonly associated with anaerobic infections (often secondary to splenic torsion), or neoplasia.
- Eosinophilic—eosinophilic gastroenteritis, hypereosinophilic syndrome.
- Lymphoplasmacytic—subacute or chronic infectious disorders; pyometra; coexistent inflammatory bowel disease.
- Granulomatous—fungal or protozoal disease most common. • Pyogranulomatous—bacterial or fungal infections most common cause.

Hyperplasia

- Infection—chronic bacteremia (bacterial endocarditis; discospondylitis; *Brucella*).
- Immune-mediated disease—any; hemolytic anemia or thrombocytopenia, systemic lupus erythematosus (SLE).

Congestion

Tranquillizers; barbiturates; portal hypertension; right-sided heart failure; splenic torsion.

Infiltration

- Neoplasia—lymphoma; acute and chronic leukemia; (hemophagocytic) histiocytic sarcoma; multiple myeloma; systemic mastocytosis; hemangiosarcoma, other sarcoma; metastasis.

- Extramedullary hematopoiesis (EMH)—immune-mediated hemolytic anemia or thrombocytopenia; chronic anemia; infectious disease; malignancy; SLE. • Amyloidosis – part of systemic amyloidosis.

Cats

Inflammation

- Suppurative—penetrating wound or migrating foreign body; septicemia; salmonellosis. • Necrotizing—salmonellosis.
- Eosinophilic—hypereosinophilic syndrome.
- Lymphoplasmacytic—lymphoplasmacytic enteritis; hemotropic mycoplasmas; pyometra.
- Granulomatous—histoplasmosis; mycobacteriosis. • Pyogranulomatous—FIP, *Mycobacterium*.

Hyperplasia

- Infection—hemotropic mycoplasmosis.
- Immune-mediated—any; hemolytic disorders, SLE.

Congestion

Portal hypertension, congestive heart failure.

Infiltration

- Neoplasia—mast cell tumor, lymphoma; lympho- or myeloproliferative diseases; multiple myeloma; histiocytic sarcoma (rare); hemangiosarcoma (rare). • Non-neoplastic—amyloidosis, EMH.

RISK FACTORS

- Cats—feline leukemia virus (FeLV), FIP.
- Dogs—breed/age.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Other cranial organomegaly or masses.

CBC/BIOCHEMISTRY/URINALYSIS

Dogs

- Regenerative anemia secondary to splenic bleeding or hemolytic disease. • Nucleated red blood cells (RBCs)—may accompany EMH, indicates splenic dysfunction. • Spherocytes—hemolysis, microangiopathic shearing.
- Schizocytes (aka schistocytes) – disseminated intravascular coagulation (DIC), hemangiosarcoma. • Acanthocytes- hemangiosarcoma.
- Leukocytosis with a left shift—may indicate infectious or inflammatory conditions, marked regenerative response, or EMH.
- Thrombocytopenia—from increased consumption (DIC or bleeding) secondary to hemangiosarcoma or other neoplasia, increased destruction (immune-mediated), sequestration, or decreased production in the bone marrow.
- Hypercalcemia may be associated with neoplasia, especially lymphoma.
- Hyperglobulinemia may be associated with neoplasia, *Ehrlichia* infections.
- Hemoglobinemia and hyperbilirubinemia—associated with hemolysis and may occur with microangiopathic anemia, splenic torsion, hemangiosarcoma, and immune-mediated anemia.

SPLENOMEGLY

Cats

- Direct RBC examination for hemoparasites.
- Regenerative anemia and splenomegaly—may indicate hemotropic mycoplasmosis.
- Macrocytosis and nonregenerative anemia—suggests retroviral infection or myeloproliferative disease.
- Eosinophilia—suggests hypereosinophilic syndrome, systemic mastocytosis, or lymphoma.
- Circulating blast cells—suggest lympho- or myeloproliferative disorder.
- Nucleated RBCs—may accompany EMH and splenic dysfunction.
- Thrombocytopenia—from increased consumption (DIC), increased destruction (immune-mediated), sequestration, or decreased production in the bone marrow.

OTHER LABORATORY TESTS

- FeLV and feline immunodeficiency virus testing.
- Coagulation panel—DIC commonly seen with hemangiosarcoma (includes prolonged clotting times, hypofibrinogenemia, and increased fibrin degradation products [FDPs]); D-dimers not specific for clinical application in differential diagnoses.

IMAGING

Abdominal Radiography

- S**
- Confirms or detects splenomegaly.
 - Mass effect may appear in the (left) midcranial abdomen.
 - May provide evidence of an underlying cause—concurrent hepatomegaly may indicate infiltrative disease or right-sided heart disease; splenic torsion secondary to GDV.
 - Effusion—may indicate hemorrhage from splenic rupture (hemangiosarcoma, hematoma) or portal hypertension influencing splenic perfusion.
 - Visualization of the splenic tail along the ventral body wall on lateral radiographs of cats supports the diagnosis of splenomegaly.

Thoracic Radiography

- Three views (right and left lateral and dorsal-ventral views)—screen for metastasis and underlying disease in thoracic cavity and effusion.
- Evaluate sternal lymph nodes—these drain the abdominal cavity, reflecting disorders causing lymphadenomegaly. Evaluate for signs of congestive heart failure (size of the cardiac silhouette and pulmonary veins and evidence of pulmonary edema or pleural effusion).

Abdominal Ultrasonography

- Distinguishes between diffuse and focal/nodular parenchymal patterns.
- Diffuse enlargement with normal parenchyma—may occur with congestion or cellular infiltration.
- In cats splenic masses greater than 1 cm suggestive of malignancy.
- Hypoechoogenicity may occur with splenic torsion, splenic vein thrombosis, hematopoietic neoplasia or infectious agents.
- Complex, mixed echogenic mass—common with hemangiosarcoma or hematoma.
- Can identify concurrent abdominal diseases—liver, kidneys, intestines, and lymph nodes.
- Cannot differentiate between benign and malignant splenic disorders.
- Doppler color

flow interrogation of splenic vasculature may detect splenic vein thrombi or splenic torsion.

Echocardiography

Evaluate for cardiac dysfunction or cardiac tumors causing splenic congestion (based on other physical exam/imaging findings).

DIAGNOSTIC PROCEDURES

Fine-Needle Aspiration

- Assess coagulation status before any aspiration. Procedure—patient in right lateral or dorsal recumbency; using ultrasound guidance, use a 22- or smaller gauge, 2.5–3.75 cm (1–1.5 in.) length needle depending on the size of the patient.
- Non-aspiration method (needle-only method) results in higher yield of nucleated cells relative to the amount of blood than aspiration method.
- Specimens—evaluate cytologically for infectious agents (often found in macrophages); identify predominant inflammatory or infiltrative cell type.
- Neoplastic infiltrates—classified as epithelial, mesenchymal, or round cell.
- Aspiration of cavitated masses may cause rupture and is not recommended.

Bone Marrow Aspiration

- Indicated with cytopenias before splenectomy (spleen may be supporting hematopoiesis).
- May yield infectious disorder (e.g., ehrlichiosis, mycosis, toxoplasmosis, leishmaniasis) or hematopoietic neoplasia.



TREATMENT

- Depends on underlying cause; supportive nursing care as needed.
- Important to determine if splenomegaly is appropriate for systemic conditions.
- Treatment and prognosis after splenectomy—based on histopathologic features: submit the entire spleen for histopathologic evaluation (hemangiosarcoma may be missed in some tumors owing to regional necrosis with diagnosis rendered of hematoma).

SURGICAL CONSIDERATIONS

Splenectomy

- With anemia or leukopenia—rule out bone marrow aplasia/hypoplasia before surgery; spleen may be the source of hematopoiesis.
- Indicated for splenic torsion, splenic rupture, isolated splenic masses considered likely to be neoplastic, and mast cell infiltration (cats only).
- Exploratory laparotomy—permits direct evaluation of all abdominal organs.



MEDICATIONS

DRUG(S) OF CHOICE

Depend on underlying disease.



FOLLOW-UP

PATIENT MONITORING

Ventricular arrhythmias (dogs)—associated with splenic mass lesions or torsion; may occur before, during, and up to 3 days post splenectomy; evaluate (auscultation and electrocardiogram) surgical candidates before anesthesia; continuous cardiac monitoring during surgery and postoperatively.

POSSIBLE COMPLICATIONS

- Asplenic patient—increased risk of infection and red cell parasitism.
- Postoperative sepsis—uncommon complication.
- Antibiotics—indicated in asplenic patients receiving immunosuppressive therapy, if any sign of infection apparent.



MISCELLANEOUS

AGE-RELATED FACTORS

Neoplastic causes more likely in geriatric animals.

ZOONOTIC POTENTIAL

A variety of infectious diseases may involve the spleen.

SEE ALSO

See Causes.

ABBREVIATIONS

- DIC = disseminated intravascular coagulation.
- GDV = gastric dilatation and volvulus.
- EMH = extramedullary hematopoiesis.
- FDP = fibrin degradation product.
- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- RBC = red blood cell.
- SLE = systemic lupus erythematosus.

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(CONTINUED)

TETANUS

- Constipation possible.

PREVENTION/AVOIDANCE

- Vaccinate—tetanus toxoid; not typically used in dogs and cats.
- Prevent skin wound trauma—clear runs and yards of wire, glass, etc.
- Wound management—early and thorough irrigation; debridement and drainage, especially in tetanus-prone wounds.

EXPECTED COURSE AND PROGNOSIS

- Younger dogs with tetanus may be more likely to develop severe clinical signs.
- The prognosis for survival in dogs with tetanus is good if abnormalities in heart rate or blood pressure values do not develop.
- Prognosis—depends on number of factors; poorer prognosis has been associated with

more toxin bound to nerves, wounds closer to the head, shorter interval between injury and first tetanic spasm, and development of aspiration pneumonia.

- Course of recovery—slow; requires rehabilitation to regain full use of limbs; most recover in 1 week; some have a course of 3–4 weeks; unattended disease can be fatal if it progresses to generalized disease (vs. localized tetanus).

**MISCELLANEOUS****ZOONOTIC POTENTIAL**

None, but tetanus spores ubiquitous in environment.

ABBREVIATIONS

- AST = aspartate aminotransferase.

INTERNET RESOURCES

<http://www.cdc.gov/vaccines/pubs/pinkbook/tetanus.html>

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T

THIRD EYELID PROTRUSION



BASICS

DEFINITION

Abnormal protrusion (elevation) of the third eyelid.

PATHOPHYSIOLOGY

- Dogs—movement of the third eyelid is passive.
- Cats—partial sympathetic nervous control of the third eyelid.
- May be primary (conformational) or secondary (exophthalmos, enophthalmos, sympathetic denervation, painful eye).

SYSTEMS AFFECTED

- Nervous—autonomic nervous system.
- Ophthalmic—third eyelid(s); orbit; globe.

SIGNALMENT

See Causes.

SIGNS

- Primary—often none; occasionally conjunctivitis and tearing.
- Secondary—associated with the underlying condition.
- Unilateral or bilateral—depending on cause.

CAUSES

Unilateral

Blepharospasm

- Painful ocular condition—corneal ulcer; glaucoma; uveitis; foreign body.
- Active retraction of the globe results in secondary third eyelid elevation.

Exophthalmos

- Increase in orbital volume—pushes the eye and third eyelid forward.
- Abscess or cellulitis—generally young patients; acute onset; painful on palpation.
- Neoplasm—generally older patients; gradual onset; frequently not painful.
- Salivary gland inflammation/mucocele—variable age; may be secondary to trauma; frequently not painful (see Orbital Diseases (Exophthalmos, Enophthalmos, Strabismus)).

Enophthalmos

- Globe—recedes into the orbit, causing third eyelid to appear elevated.
- Unilateral—may be caused by trauma, orbital fat atrophy, neoplasia, and inflammation.
- Horner's syndrome—clinical signs develop after sympathetic denervation; elevated third eyelid; enophthalmos; ptosis (drooping upper eyelid); miosis (see Horner's Syndrome).

Microphthalmos or Phthisis Bulbi

- Small globes—cause the third eyelid to appear elevated.
- Microphthalmos—congenital; idiopathic or may be inherited in specific breeds (many

reported); other intraocular abnormalities may be present. May result from toxin ingestion (griseofulvin in pregnant cats).

- Phthisis bulbi—acquired; severe damage to the globe (uveitis, glaucoma, or trauma); ciliary body fails to produce aqueous humor; diminished; small, fibrotic globe.
- Other
- Neoplasia of the third eyelid—slow growing; usually older patients. Most common: adenocarcinoma of the gland of the third eyelid; hemangioma/hemangiosarcoma, melanoma and squamous cell carcinoma and others may involve the eyelid.
- Cherry eye—see Prolapsed Gland of the Third Eyelid (Cherry Eye).
- Everted or scrolled cartilage of the third eyelid—primarily large and giant breeds; the T-shaped cartilage of the third eyelid is rolled away from the surface of the eye instead of conforming to the corneal surface.
- Symblepharon—post-inflammatory adhesions between the third eyelid and cornea or conjunctiva. Common in cats who had ocular surface inflammation before the eyelids opened.
- Foreign body.
- Previous injury.
- Facial nerve paralysis—patient will retract the globe and “flash” the third eyelid.

Bilateral

Exophthalmos

- Space-occupying lesions of both orbits.
- Usually caused by immune-mediated inflammatory lesions (e.g., eosinophilic myositis, extraocular muscle polymyositis).

Conformational

- Breed-specific—primarily large-breed dogs.
- Deep orbits and prominent third eyelids.
- Not pathologic.
- No treatment needed.

Plasmoma

- Immune-mediated thickening and hyperemia of the leading edge of the third eyelid due to infiltration of plasma cells and lymphocytes; follicle formation; depigmentation.
- Primarily in German shepherd dogs; other breeds reported.
- May be associated with chronic superficial keratitis (pannus).

Other

- Blepharospasm (active retraction of globe).
- Enophthalmos—caused by dehydration, bilateral orbital fat atrophy secondary to severe cachexia, and chronic masticatory muscle myositis.
- Haw's syndrome (cats)—idiopathic bilateral elevation of the third eyelids; primarily young cats with history of diarrhea; ophthalmic examination otherwise normal; self-limiting; usually resolves in 3–4 weeks without treatment.
- Dysautonomia (Key-Gaskell syndrome)—bilateral elevated third eyelids; dilated

nonresponsive pupils; keratoconjunctivitis sicca (KCS); dry mucosal surfaces; anorexia; lethargy; regurgitation; megaesophagus; bradycardia; megacolon; distended bladder (see Dysautonomia (Key-Gaskell Syndrome)).

- Tranquillizers—many (e.g., acepromazine) cause bilateral third eyelid elevation.
- Fatigue—transient third eyelid elevation, especially in dogs prone to ectropion.
- Cannabis intoxication.
- Tetanus—eyelids retract; third eyelid prolapse; enophthalmos; secondary to hypertonicity of extraocular muscles (see Tetanus).

Rabies—reported ocular signs include dilated pupils; anisocoria; third eyelid prolapse; uveitis (see Rabies).

RISK FACTORS

Depends on cause.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Most common causes of acute onset of unilateral condition—ocular pain (e.g., corneal ulcer; uveitis); orbital inflammation (e.g., orbital abscess, cellulitis).
- Middle-aged or older patient with unilateral, nonpainful condition—third eyelid or orbital neoplasm likely.
- All patients—must rule out a small eye (microphthalmos or phthisis bulbi) and Horner's syndrome.
- Likely causes of bilateral condition—systemic illness (e.g., dehydration, cachexia, dysautonomia); associated with conformational abnormalities.
- Prolapsed gland of the third eyelid—medial aspect of the third eyelid swollen; the third eyelid itself usually normal.
- Lightly pigmented third eyelid margin—normal conformation; may be falsely identified as an elevated third eyelid.

CBC/BIOCHEMISTRY/URINALYSIS

- Leukocytosis and a left shift—with orbital inflammatory processes.
- Blood work—generally normal despite differing causes.

OTHER LABORATORY TESTS

Dysautonomia—confirmed by measuring urine and plasma catecholamine concentrations and pharmacologic testing of the autonomic nervous system.

IMAGING

- Thoracic radiography—all patients with Horner's syndrome to rule out intrathoracic cause of sympathetic denervation, evaluate for metastatic disease.
- Orbital ultrasound—recommended to help localize suspected orbital mass and define its nature (e.g., solid or cystic).

THIRD EYELID PROTRUSION

(CONTINUED)

- CT or MRI—further define suspected or known orbital mass.
- Skull radiographs—rarely show signs of orbital disease unless lesion is very large and destructive.

DIAGNOSTIC PROCEDURES

- Thorough ophthalmic examination utilizing a source of magnification.
- All patients with unilateral condition—examine both surfaces of the third eyelid and the conjunctival cul-de-sac carefully for a foreign body or symblepharon.
- Pharmacologic testing—localize lesion with Horner's syndrome (see Horner's Syndrome).
- Exploratory surgery and biopsy—may be only means to make a definitive diagnosis for a suspected orbital or third eyelid mass.

Cytology

- For suspected mass lesions:
 - Unguided fine-needle aspiration—only if the mass is anterior to the equator of the eye.
 - Ultrasound-guided fine-needle aspiration—for masses posterior to the eye; help avoid delicate retrobulbar structures.
- Third eyelid scrapings—German shepherd dogs with suspected plasmoma reveal plasma cells and lymphocytes.



TREATMENT

- Depends on cause.
- Painful condition—remove the cause of the irritation (e.g., foreign body); treat the primary ocular condition.
- Orbital cellulitis and abscess—orbital drainage and systemic antibiotics.
- Orbital neoplasms—usually require wide surgical excision via an orbital exenteration; may require adjunct therapeutic modalities if excision is incomplete.
- Microphthalmic eyes—usually none required; enucleation if painful or subject to recurrent conjunctivitis.
- Blind traumatized eyes—enucleate if painful and to prevent formation of intraocular sarcomas (cats).
- Horner's syndrome—treat cause, if known (~50% of dogs and cats); otherwise may resolve without treatment in 4–12 weeks.
- Surgical removal of the entire third eyelid—indicated for third eyelid neoplasia; may require adjunct therapeutic modalities if the surgical margins are not free of neoplasm.

- Radiotherapy around the eye—may result in severe keratitis, dry eye, and cataracts; discuss enucleation with the client before initiating treatment if eye will be in the radiation field.
- Orbital exenteration—may be warranted if the mass extends into the orbit.
- Plasmoma—usually controlled with topical medications; not cured; life-long therapy needed; topical corticosteroids (0.1% dexamethasone or 1% prednisolone acetate q6h, reduced to q24h when appears resolved); topical 1% cyclosporine q12h also effective.
- Haw's syndrome—usually self-limiting without treatment.
- See Dysautonomia (Key-Gaskell Syndrome), tetanus, or rabies.



MEDICATIONS

DRUG(S) OF CHOICE

See Treatment.

CONTRAINdications

Topical corticosteroids—never use in patients with corneal ulceration.

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUG(S)

N/A



FOLLOW-UP

PATIENT MONITORING

Malignant neoplasia—thoracic radiographs and full physical exam q3–6 months to monitor for metastatic disease.

POSSIBLE COMPLICATIONS

- Neoplasm—extension to or involvement of adjacent orbital structures (e.g., eye, orbit, orbital sinuses, and cranial cavity) possible; metastasis to distant sites (usually thorax or liver) possible (approximately 90% are malignant).
- Vision loss—from the lesion itself, from elevation, or from treatment (e.g., radiotherapy and exenteration).



MISCELLANEOUS

ASSOCIATED CONDITIONS

N/A

AGE-RELATED FACTORS

- Middle-aged to older patients—at risk for neoplastic diseases of the third eyelid and orbit.
- Young patients—at risk for congenital abnormalities; affected by inflammatory conditions of the third eyelid more frequently than older animals.

ZOONOTIC POTENTIAL

N/A

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

- Elevated third eyelid.
- Haw's syndrome (cats).

SEE ALSO

- Dysautonomia (Key-Gaskell Syndrome).
- Ectropion.
- Entropion.
- Horner's Syndrome.
- Orbital Diseases (Exophthalmos, Enophthalmos, Strabismus).
- Prolapsed Gland of the Third Eyelid (Cherry Eye).
- Rabies.
- Tetanus.

ABBREVIATIONS

- KCS = keratoconjunctivitis sicca.

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Brian C. Gilger.

TICK BITE PARALYSIS



BASICS

DEFINITION

Flaccid, lower motor neuron tetraparesis to tetraplegia caused by salivary neurotoxins from certain species of female tick.

PATHOPHYSIOLOGY

- Presynaptic disorder—tick injects salivary neurotoxin that interferes with the depolarization/acetylcholine release from the presynaptic nerve terminal of the neuromuscular junction; this effect is probably associated with an interruption of the calcium flux across axonal membranes.
- Australian *Ixodes holocyclus* tick—neurotoxin (holocyclotoxin) effects are more pronounced at higher temperatures; one adult tick is sufficient to cause neurologic signs, but infestation with *I. holocyclus* larvae or nymphs can also induce signs; holocyclotoxin also interferes with acetylcholine release at the autonomic nerve terminals.
- Signs—5–9 days after initial tick attachment.
- Not all infested animals develop tick paralysis; not all adult female ticks produce the toxin.

SYSTEMS AFFECTED

- T**
- Nervous—peripheral nervous system and neuromuscular junction most affected; cranial nerves can become involved, including the vagus and facial nerves with the North American ticks and, in addition, the trigeminal nerves and sympathetic nervous system with the Australian *Ixodes* tick.
 - Respiratory—may see paralysis of the intercostal muscles and diaphragm; caudal brainstem respiratory center may be affected (rare with North American ticks; more common with Australian *Ixodes* ticks).

GENETICS

No genetic basis.

INCIDENCE/PREVALENCE

- North America—somewhat seasonal (more prevalent in the summer months); in the warmer areas (southern United States) may become a year-round problem.
- Australia—distinctly seasonal, up to 75% of cases occur during southern hemisphere spring season (September–November).
- Overall incidence—low in the United States; higher in Australia.

GEOGRAPHIC DISTRIBUTION

- United States—*Dermacentor variabilis*: wide distribution over the eastern two-thirds of the country, California, and Oregon; *D. andersoni*: from the Cascades to the Rocky Mountains; *Amblyomma americanum*: from Texas and Missouri to the Atlantic Coast; *A. maculatum*: Atlantic and Gulf of Mexico seaboards.

- Australia—*I. holocyclus*: coastal areas of the east; *I. cornuatus*, southern Australia (Tasmania).

- Other—cases with apparent tick paralysis have been described in South Africa (*Rhipicentor nuttalli*), southern Italy (*Rhipicephalus sanguineus*), and Iran (*Ornithodoros laborensis*).

SIGNALMENT

Species

- Australia—dogs and cats.
- United States—dogs; cats appear to be resistant.

Breed Predilections

None

Mean Age and Range

Any age.

Predominant Sex

N/A

SIGNS

Historical Findings

- Patient exposed to ticks (wooded area) approximately 1 week before onset of signs.
- Onset—gradual; starts with weakness in the pelvic limbs, progresses to the thoracic limbs within 12–72 hours.

Neurologic Examination Findings

North American Ticks

- Neurologic signs—rapidly ascending, flaccid generalized lower motor neuron tetraparesis to tetraplegia.
- Patient becomes extremely weak to recumbent in 1–3 days, with hyporeflexia to areflexia and hypotonia to atonia.
- Pain sensation preserved, no hyperesthesia.
- Cranial nerve dysfunction—uncommon; may note facial weakness and reduced jaw tone; sometimes dysphonia and dysphagia early in the course; megaesophagus uncommon.
- Urination and defecation usually normal.
- No cardiovascular effects.
- Respiratory paralysis—uncommon in the United States; may occur if ticks are not removed; death may occur in 1–5 days.

Australian Ticks

- Neurologic signs—much more severe and rapidly progressive; ascending motor weakness can progress to tetraplegia within a few hours.
- Sialosis, depressed gag reflex, dysphonia, megaesophagus, vomiting/regurgitation.
- Sympathetic nervous system—mydriatic and poorly responsive pupils (common in cats); hypertension; tachyarrhythmias; pulmonary edema.
- Urinary bladder dysfunction may be present.
- Caudal medullary respiratory center involvement—progressive reduction in respiratory rate and increased respiratory effort.

- Respiratory muscle paralysis—much more prevalent; dogs and cats progress to dyspnea, cyanosis, and respiratory paralysis within 1–2 days if not treated.

CAUSES

United States

- D. variabilis*—common wood tick.
- D. andersoni*—Rocky Mountain wood tick.
- A. americanum*—lone star tick.
- A. maculatum*—Gulf Coast tick.

Australia

- I. holocyclus*—far more potent neurotoxin than that of the North American species.
- I. cornuatus*—southern paralysis tick, occasionally causes paralysis in southern Australia.

RISK FACTORS

- Environments that harbor ticks.
- Australia—higher risk during spring, and in areas with higher rainfall, containing tree cover and areas of water; higher risk of death if dog <6 months old or a toy breed.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Botulism.
- Acute polyneuropathy.
- Acute polyradiculoneuritis (coonhound paralysis).
- Distal denervating disease.
- Fulminant myasthenia gravis.
- Generalized (diffuse) or multifocal myopathy.
- Intoxications (coral snake, black widow spider, lasalocid, blue and green algae).

CBC/BIOCHEMISTRY/URINALYSIS

Normal

OTHER LABORATORY TESTS

Arterial blood gases—severely affected patients may show hypoventilation and respiratory acidosis (low Pao_2 , high $Paco_2$, low pH).

IMAGING

Thoracic radiography (*Ixodes* ticks)—megaesophagus, aspiration pneumonia, pulmonary edema.

DIAGNOSTIC PROCEDURES

- History of exposure to ticks.
- Thoroughly search for a tick—head, neck, body and limbs, ear canals, mouth, rectum, vagina, prepuce, and in between the digits and footpads; clipping the entire fur may be needed; immediately remove tick.
- In some cases the offending tick may have dropped, a negative finding does not exclude tick paralysis.
- Electrodiagnostics—electromyogram; normal insertional activity without spontaneous myofiber activity; lack of motor unit action.

TICKS AND TICK CONTROL



BASICS

DEFINITION

- Arachnids, arthropod ectoparasites feed on the blood of their hosts.
- Most ticks are not host specific; divided into argasid (soft) and ixodid (hard) ticks.
- Argasid are more primitive, more commonly parasitize birds; one of importance in dogs and cats is spinous ear tick (*Otobius megnini*).
- Ixodid ticks are more specialized and highly parasitic, both sexes are bloodsuckers; *Rhipicephalus sanguineus* and *Dermacentor variabilis* are common in dogs and cats.

PATOPHYSIOLOGY

- Blood-loss anemia—from heavy infestations.
- Damage to the integument—local irritation and infection may occur; tick adaptations suppress host response and allow feeding for up to 1 week.
- Salivary secretions—neurotoxins; other pharmacologically active compounds cause impaired hemostasis and immune suppression at the tick-feeding site.
- Pathogens—acquired when ticks feed on infected reservoir hosts (often rodents and small feral mammals); transmitted while feeding on dogs and cats.

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Tick Biology

- Hard ticks—four life stages: egg, larva, nymph, and adult; larvae and nymphs feed to repletion before detaching and molting; after detachment, females lay thousands of eggs and die; various tick stages may survive over winter, tolerate long starvation, low humidity, as well as water deprivation. Completion of life cycle requires three hosts; some species pass all stages on the same mammal.
- Transovarial transmission—organisms disseminate to the ticks' ovaries; infected eggs hatch and produce infected larvae.
- Trans-stadial transmission—immature ticks become infected while feeding on reservoir hosts and maintain infection through the molt from one life stage to the next, transmitting organisms to the new host when next stage feeds.
- Ticks generally acquire hosts by a passive ambush process; when a suitable host brushes against vegetation harboring questing ticks, they transfer to the host.
- *Amblyomma americanum* can be an active hunter and traverse distances of up to 18 m to attack a suitable host.
- Symbiotic relationship—*Ixodes scapularis* infected with *Anaplasma phagocytophylum* express an antifreeze glycoprotein gene that enhances survival of the tick in cold weather.

SYSTEMS AFFECTED

- Skin/exocrine.
- Hemic/lymphatic/immune.
- Musculoskeletal.
- Nervous.

GEOGRAPHIC DISTRIBUTION

- Strong geographic specificities exist for some tick species and their associated pathogens, producing geographic prevalence of associated diseases.
- Ranges of ticks are expanding, therefore the geographic incidence of tick parasitism and infections vectored by them are expanding.
- Emergence of new tick-borne infections and coinfection (due to coinfecting vector ticks or parasitism of hosts by ticks of more than one species).
 - *I. scapularis* and *I. pacificus*—midwest, northeast, southeast, and south-central United States and west coast, respectively.
 - *R. sanguineus*—throughout the continental United States; *R. sanguineus* is unique among hard ticks; it can survive and establish its life cycle inside dwellings and kennels at (low) household humidity (common name “kennel tick”).
 - *D. variabilis*—eastern seaboard and west coast of United States.
 - *A. americanum*—found throughout the midwest, south-central, southeast, and parts of the northeast United States with strong range expansion.
 - *Amblyomma maculatum*—gulf coast states of United States with range expansion.

SIGNALMENT

Species

- Dog and cat.
- Cats are efficient at removing ticks; tick attachment and tick-vectored diseases including Lyme disease, anaplasmosis, and cytauxzoonosis have been diagnosed in domestic felines.

SIGNS

- Attached ticks or tick-feeding cavities may be seen on the skin.
- Irritation secondary to bite.
- Petechia secondary to infectious organisms (*Rickettsia*, *Anaplasma platys*).
- Blood-loss anemia (direct effect); thrombocytopenia, anemia, inclusion bodies in neutrophils, monocytes, red blood cells secondary to transmitted infectious organisms.
- Limb/joint abnormalities secondary to infectious organisms (*Borrelia burgdorferi* and other organisms implicated in oligo- and polyarthritis).
- Cardiac—Lyme carditis (*B. burgdorferi*), manifests typically as atrioventricular block; rare and poorly documented in dogs.
- Renal—unique, generally fatal protein-losing nephropathy in dogs infected with *B. burgdorferi* linked to immune complexes associated with antigen and antibody from infection.
- Rocky Mountain Spotted Fever—vague or non-specific symptoms of fever, lethargy, joint pain, gastrointestinal symptoms, focal hemorrhages (*Rickettsia rickettsii*).

- Paralysis—neurotoxins secreted from tick salivary glands produce ascending weakness and paralysis.

- Pyogranulomatous myositis, periosteal reaction, neutrophilia, antigenic stimulation, and amyloid deposition in viscera in *Hepatozoon americanum* infection in which the dog serves as the intermediate and reservoir host following tick ingestion.
- Weight loss, anemia, lethargy, fever, neutrophilia, hyperglobulinemia and hypoalbuminemia in *Hepatozoon canis* infection. Infection occurs by digesting the tick (*A. americanum*), which is the definitive host.

CAUSES

Ticks—attracted to hosts by warmth, presence of carbon dioxide, physical contact, and host-associated odors.

RISK FACTORS

- Domestic animals—can be in close contact with ticks due to invasion of ticks into suburban environments and expansion of suburban environment into surrounding forests, prairies, and coastline areas.
- Travel—increases risk for exposure.
- Risk is expanding as new cycles for maintenance of infectious organisms are emerging (and being discovered).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

N/A

OTHER LABORATORY TESTS

- Vector-borne disease (VBD) panels provide clinicians the ability to test blood for multiple agents by using serology and/or PCR.
- IDEXX Snap 4DXPlus Test—in-office rapid screening test for multiple VBD; detects antibodies (C₆ ELISA) against *B. burgdorferi*, *E. canis*, *E. ewingii*, *A. phagocytophilum*, *A. platys*, and *Dirofilaria immitis* antigens in canine serum, plasma, or whole blood.
- ABAXIS VetScan FLEX4 Rapid T—detects antibodies against *A. phagocytophilum*, *A. platys*, *B. burgdorferi*, *E. canis*, *E. chaffeensis*, *E. ewingii*, and *Dirofilaria immitis* antigens in canine whole blood, serum or plasma.
- Tests are sensitive and specific; *B. burgdorferi* test does not crossreact with vaccine-induced antibodies.



TREATMENT

APPROPRIATE HEALTH CARE

- Outpatient after removal of ticks.
- Removal—as soon as possible to limit time available for pathogen or neurotoxin transmission; grasp ticks close to the skin with fine-pointed tweezers and gently pull free.

(CONTINUED)

TICKS AND TICK CONTROL**NURSING CARE**

Wash feeding cavity with soap and water; generally sufficient to prevent local inflammation or secondary infection.

CLIENT EDUCATION

Application of hot matches, petrolatum jelly, or other materials not only fails to cause tick detachment but allows for longer periods of attachment and feeding.

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

See Prevention/Avoidance.

**FOLLOW-UP****PREVENTION/AVOIDANCE**

- Perimeter control and avoiding environments that harbor ticks.
- Frequent tick checks and tick removal.
- Year-round tick prevention.
- Tick control does not always equal control of tick-borne diseases: Products should quickly kill or prevent attachment and feeding by the tick.
- Tick-borne pathogens—may be transmitted very rapidly (viruses) or require several hours (*R. rickettsii*), less than 1 day (*A. phagocytophilum*), 1–2 days (*B. burgdorferi*), or 2–3 days (*Ehrlichia* species and *B. canis*).
- Ingestion of infected ticks makes tick control problematic for prevention of infection with *Hepatozoon* species.

Insecticides and Acaricides

- Acaricides meant only for dogs must not be applied to cats.
- Acaricidal collars—amitraz, deltamethrine, and flumethrin (Preventic, Seresto, and Scalibor, respectively).
- Spot-on treatments—fipronil, permethrin, flumethrin, etofenprox.
- Oral treatments—isoxazolines: fluralaner, afoxolaner, lotilaner, and sarolaner. Fluralaner is also available as a spot-on for dogs and cats. Sarolaner combined with selamectin is available as a spot-on for cats.

- Disease transmission interruption studies have been published for products containing fipronil, amitraz, isoxazolines, permethrin, and synthetic pyrethroids; rapid killing and clinical repellence are essential to prevent or interrupt tick feeding.

POSSIBLE COMPLICATIONS

Tick-borne diseases or tick paralysis.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

- Canine babesiosis—*B. canis*.
- Rocky Mountain spotted fever—*R. rickettsia*.
- Canine monocytic ehrlichiosis—*E. canis* or *E. chaffeensis*.
- Cyclic thrombocytopenia—*A. platys*.
- Granulocytic anaplasmosis—*A. phagocytophilum* and *E. ewingii*.
- Lyme disease—*B. burgdorferi*.
- American canine hepatozoonosis—caused by protozoa *H. americanum*, following ingestion of an infected tick.
- Canine hepatozoonosis—caused by *H. canis* following ingestion of an infected tick.
- Tick paralysis—caused by a neurotoxin; affects acetylcholine synthesis and/or liberation at the neuromuscular junction of the host animal; ascending flaccid paralysis initially affects the pelvic limbs 5–9 days after tick attachment.

VACCINES

Currently for Lyme disease there are three types for dogs: (1) whole-cell, killed bacterin: LymeVax, Duramune Lyme, and Nobivac Lyme, (2) outer surface protein A (OspA): Recombitek Lyme, and (3) chimeric recombinant (OspA and 7 types of OspC): Vanguard crLyme. Efficacy studies which duplicate natural exposure are lacking.

ZOONOTIC POTENTIAL

- Ticks may parasitize wildlife, domestic animals, or humans at different stages in their developmental cycles; infections acquired in early life stages may be transmitted when ticks feed again in the next stage.
- Humans, if parasitized, may be exposed to organisms in infected ticks. *B. burgdorferi*,

A. phagocytophilum, *R. rickettsia*, and *E. chaffeensis* are also human pathogens.

SYNOMYMS

Acarasis

SEE ALSO

- Babesiosis.
- Ehrlichiosis and Anaplasmosis.
- Lyme Borreliosis.
- Rocky Mountain Spotted Fever.

ABBREVIATIONS

- IFA = immunofluorescent antibody assay.
- VBD = vector-borne disease.

INTERNET RESOURCES

<https://www.cdc.gov/ncecid/dvbd/index.html>

Suggested Reading

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Acknowledgment The author and editors acknowledge the prior contribution of Steven A. Levy.



**Client Education Handout
available online**

T

TOXOPLASMOSIS



BASICS

DEFINITION

Toxoplasma gondii—obligate intracellular coccidian protozoan parasite that infects nearly all mammals. Felids are the definitive hosts and all other warm-blooded animals serve as intermediate hosts.

PATHOPHYSIOLOGY

- Three main modes of transmission: (1) congenital, (2) ingestion of bradyzoites encysted in tissue of intermediate hosts, or (3) ingestion of sporulated oocysts within feces of felids.
- Most cats infected via ingestion of intermediate hosts; release bradyzoites in gastrointestinal tract that invade enteropithelium; ultimately undergo sexual reproduction and oocyte formation; oocysts require 1–5 days to sporulate and become infectious after being passed in feces.
- Acute disseminated infection—organisms spread via blood or lymph; tachyzoites rapidly divide within extraintestinal tissues; causes focal necrosis, granulomatous inflammation; can be fatal.
- Following acute infection, slowly dividing bradyzoites encyst in host tissue, usually not clinically apparent unless immunosuppression or concomitant illness allows organism to reactivate to tachyzoite stage.
- Infection acquired during pregnancy—possible placatitis and transplacental transmission of tachyzoites to fetus; can induce abortion or clinical disease (kittens).

SYSTEMS AFFECTED

- Multisystemic.
- Ophthalmic—80% of affected cats have uveitis.

INCIDENCE/PREVALENCE

- ~30% of cats and up to 50% of people serologically positive for *T. gondii*.
- Most animals asymptomatic.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

Species

Cats more commonly symptomatic than dogs.

Mean Age and Range

Mean age 4 years; range 2 weeks–16 years.

Predominant Sex

More common in male cats.

SIGNS

General Comments

- Determined by site and extent of organ damage.
- Acute—at time of initial infection, rapid clinical course.

- Chronic—reactivation of encysted infection due to immunosuppression, slower clinical course.

Historical Findings

- Lethargy, depression, anorexia.
- Weight loss.
- Fever.
- Ocular discharge, photophobia, miotic pupils (cats).
- Respiratory distress.
- Neurologic—ataxia, seizures, tremors, paresis/paralysis, or cranial nerve deficits.
- Digestive tract—vomiting, diarrhea, abdominal pain, and/or jaundice.
- Stillborn kittens.

Physical Examination Findings

Cats

- Transplacentally infected kittens may be stillborn or die before weaning; surviving kittens—anorexia, lethargy, high fever.
- Signs reflect necrosis/inflammation of lungs (dyspnea, increased respiratory noises), liver (icterus, abdominal enlargement from ascites), and CNS (encephalopathy).
- Postnatal exposure.
- Respiratory and gastrointestinal abnormalities most common—anorexia, lethargy, high fever, dyspnea, weight loss, icterus, vomiting, diarrhea.
- Ocular abnormalities common—uveitis (aqueous flare, hyphema, mydriasis), iritis, detached retina, iridocyclitis, and/or keratic precipitates.
- 10% of patients show neurologic abnormalities—blindness, stupor, incoordination, circling, torticollis, anisocoria, or seizures.

Dogs

- Puppies—generalized infection; fever, weight loss, anorexia, tonsillitis, dyspnea, diarrhea, vomiting.
- Adults—localized infections associated with neural and muscular systems.
- Neurologic manifestations variable; result of diffuse neurologic inflammation—seizures, tremors, ataxia, paresis, paralysis, muscle weakness.
- Ocular inflammation—rare.
- Cardiac involvement—usually subclinical.

CAUSES

T. gondii

RISK FACTORS

- Ingestion of intermediate hosts, environment contaminated with cat feces.
- Immunosuppression—may predispose to infection or reactivation: feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), hemotropic mycoplasma, canine distemper, glucocorticoids, chemotherapy, postrenal transplant.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Cats

- Anterior uveitis—FIP, FeLV, FIV, other infectious, immune-mediated, trauma; lens-induced, corneal ulceration, lymphoma.
- Dyspnea—asthma, cardiogenic, pneumonia, neoplasia, heartworm disease, pleural space disease, diaphragmatic hernia, trauma.
- Meningoencephalitis—viral, fungal, parasitic, bacterial, idiopathic (feline polioencephalomyelitis).

Dogs

- Neurologic abnormalities—infectious, inflammatory, toxic, metabolic.

CBC/BIOCHEMISTRY/URINALYSIS

CBC (Cats)

- Normocytic normochromic anemia.
- Leukopenia—50% of patients with severe disease; primarily lymphopenia.
- Neutropenia with degenerative left shift.
- Leukocytosis during recovery.

Biochemistry

- Alanine aminotransferase and aspartate aminotransferase—increased enzyme activities.
- Hypoalbuminemia.
- Hyperbilirubinemia (25% of cats).

Urinalysis (Cats)

- Mild proteinuria.
- Bilirubinuria.

OTHER LABORATORY TESTS

Serology

- IgM—serologic titer of choice for diagnosis of active infection; elevated 2 weeks post infection (usually with onset of clinical signs) and persists for up to 3 months:
 - Prolonged titer—reactivation or delay in antibody class shift to IgG (due to immunosuppression).
- IgG—titers rise 2–4 weeks post infection, persist >1 year; single high titer not diagnostic for active infection; 4-fold increase over a 3-week period suggests active infection.
- Serum antigen—positive 1–4 weeks post infection; remains positive during active or chronic infections (not helpful to determine infection type).
- PCR—to verify presence of *T. gondii* in biologic specimens:
 - Prudent choice in suspect cases since many protozoa are morphologically similar and difficult to distinguish histopathologically.

(CONTINUED)

TOXOPLASMOSIS

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IMAGING

Radiographs—mixed pattern of patchy alveolar and interstitial pulmonary infiltrates; pleural and abdominal effusions and hepatomegaly may be present.

DIAGNOSTIC PROCEDURES

- Bronchoalveolar lavage, pulmonary fine-needle aspirate (cats with respiratory disease)—organism can be identified cytologically.
- Effusion cytology—organism rarely detected during acute infection.
- Cerebrospinal fluid (patients with encephalopathy)—high leukocyte count (both mononuclear cells and neutrophils) and protein.
- Fecal—active fecal oocyte shedding occurs for 1–3 weeks after infection in the cat and usually not during clinical disease; not recommended for determining whether or not an individual cat is infected with *T. gondii*. Oocysts may be detected on routine examination in asymptomatic cats but are morphologically indistinguishable from *Hammondia* spp. and *Besnoitia*.

PATHOLOGIC FINDINGS

- Potentially no gross lesions.
- Necrotic foci—up to 1 cm; most often in liver, pancreas, mesenteric lymph nodes, lungs; necrosis of brain (1 cm areas of discoloration).
- Ulcers and granulomas—in stomach and small intestine.



TREATMENT

APPROPRIATE HEALTH CARE

- Usually outpatient.
- Inpatient—severe disease; patient cannot maintain adequate nutrition or hydration.
- Confine—patients with neurologic signs.

NURSING CARE

Dehydration—IV fluids.

CLIENT EDUCATION

- Cats—prognosis guarded in patients needing therapy; response to therapy is inconsistent.
- Poorer prognosis for neonates and immunocompromised animals.



MEDICATIONS

DRUG(S) OF CHOICE

- Clindamycin 12.5–25 mg/kg PO, IV, IM q12h; continue at least 2 weeks after clinical resolution.
- 1% prednisone drops—q8h for uveitis.

PRECAUTIONS

Clindamycin—anorexia, vomiting, and diarrhea (dose-dependent).

ALTERNATIVE DRUG(S)

- Sulfadiazine 30 mg/kg PO q12h in combination with pyrimethamine 0.5 mg/kg PO q12h for 2 weeks; can cause depression, anemia, leukopenia, and thrombocytopenia, especially in cats.
- Folinic acid 5 mg PO q24h or brewer's yeast 100 mg/kg PO q24h—correct bone marrow suppression caused by above therapy.



FOLLOW-UP

PATIENT MONITORING

- Examine 2 days after treatment initiation for resolution of clinical signs; uveitis should resolve within 1 week.
- Neuromuscular deficits take longer to resolve, should see partial resolution within 2 weeks (some deficits may be permanent).
- Examine 2 weeks after resolution of clinical signs to determine if treatment may be discontinued.

PREVENTION/AVOIDANCE

Cats

- Diet—prevent ingestion of raw meat, bones, viscera, or unpasteurized milk (especially goat's milk), or mechanical vectors (flies, cockroaches). Only well-cooked meat should be fed.
- Behavior—prevent free-roaming to hunt prey (birds, rodents) or to enter buildings where food-producing animals are housed.

EXPECTED COURSE AND PROGNOSIS

- Prognosis—guarded; varied response to drug treatment.
- Acute—prompt and aggressive therapy often successful.
- Residual deficits (especially neurologic) cannot be predicted until course of therapy is completed.
- Ocular disease—usually responds to appropriate therapy.
- Severe muscular or neurologic disease—usually chronic debility.



MISCELLANEOUS

ASSOCIATED CONDITIONS

- Young dogs—distemper.
- Cats—renal transplant recipients, FeLV, FIP, FIV; FIV infection does not affect clinical outcome or the ability of the animal to mount a protective immune response to subsequent reinfection.

AGE-RELATED FACTORS

Disease worse in neonates.

ZOONOTIC POTENTIAL

- Of most concern is infection of pregnant women or immunocompromised individuals. Pregnant women should avoid contact with cats excreting oocysts in feces, contact with soil and cat litter, and should not handle or eat raw meat (to kill organism, cook to ≥66°C/150°F):

- Young cats are most likely to be shedding oocysts.

- *Important:* oocysts need to be sporulated to be infectious. Unsporulated oocysts are shed in the feces and require at least 24 hours to sporulate; daily cleaning of litter box should reduce risk of exposure to infectious form.

- Cats—healthy animals with a positive antibody titer pose little danger to humans; animal with no antibody titer at greater risk of becoming infected, shedding oocysts in the feces, and constituting a risk to humans.
- Avoid contact with oocysts or tissue cysts—do not feed raw meat; wash hands and surfaces (cutting boards) after preparing raw meat; boil drinking water if source is unreliable; keep sandboxes covered to prevent cats from defecating in them; wear gloves when gardening; wash hands and vegetables before eating; empty cat litter boxes daily; disinfect litter boxes with boiling water; control stray cat population.
- *T. gondii* causes abortion in sheep; prevent cats from ingesting placenta or aborted fetuses and keep cats from defecating in sheep feed to break the life cycle.

PREGNANCY/FERTILITY/BREEDING

- Parasitemia during pregnancy—spread of organism to fetus; probably does not happen unless first-time infection of dam occurs during pregnancy (as with humans).
- Placental transmission rare.

ABBREVIATIONS

- FeLV = feline leukemia virus.
- FIP = feline infectious peritonitis.
- FIV = feline immunodeficiency virus.

Suggested Reading

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Authors Matt Brewer and Katy A. Martin
Consulting Editor Amie Koenig



Client Education Handout
available online

UROLITHIASIS, STRUVITE—CATS



BASICS

DEFINITION

Struvite uroliths and urethral plugs have physical and etiopathogenic differences; these terms should not be used as synonyms. Struvite uroliths are polycrystalline concretions composed primarily of magnesium ammonium phosphate (MAP) and small quantities of matrix. Struvite urethral plugs are composed of large quantities of matrix mixed with crystals (especially MAP), while others are composed primarily of organic matrix, sloughed tissue, blood, and/or inflammatory reactants.

PATOPHYSIOLOGY

- See Urolithiasis, Struvite—Dogs.
- Most urethral plugs contain large quantities of matrix in addition to minerals, especially struvite. Risk factors associated with formation of MAP crystals contained in urethral plugs are similar to those associated with formation of struvite uroliths. Prevention or control of these risk factors should minimize the recurrence of the struvite component of urethral plugs.

SYSTEMS AFFECTED

Renal/urologic—upper and lower urinary tract.

INCIDENCE/PREVALENCE

- From 1981 to 2002, the prevalence of struvite uroliths has decreased and while that of calcium oxalate (CaOx) uroliths has increased. In 2015, struvite comprised 49% and CaOx comprised 36% of feline uroliths.
- Currently, struvite makes up ~50% of all types of uroliths in the lower urinary tract. Of these, 95% are sterile.
- Struvite has been detected in approximately 8% of feline nephroliths.
- Struvite has remained the most common (~90%) mineral in matrix-crystalline urethral plugs.

SIGNALMENT

Species

Cat (see Urolithiasis, Struvite—Dogs).

Mean Age and Range

- Mean age at time of diagnosis is 7 years (range, <1–22 years).
- Sterile struvite uroliths do not affect immature cats; infection-induced struvite may occur in immature (<1 year) and senior cats (>10 years).

Predominant Sex

- Struvite uroliths are more common in female cats (55%) than in males.
- Struvite urethral plugs primarily affect males.

SIGNS

General Comments

- Affected cats may be asymptomatic.

- Depend on location, size, number, and cause of uroliths.

Historical Findings

- Typical signs of urocystoliths include pollakiuria, dysuria, periuria, hematuria, and sometimes voiding of small, smooth uroliths.
- Signs of renal dysfunction (polyuria and polydipsia) are found in some cats with nephroliths.
- Signs of outflow obstruction (e.g., dysuria, large painful urinary bladder, and postrenal azotemia) are found with struvite urethral plugs.

Physical Examination Findings

- A thickened, firm, contracted bladder wall may be appreciated.
- Palpation is insensitive and unreliable for detection of urocystoliths.
- Urethral plugs or urethroliths may be detected by examination of the distal penis.
- Outflow obstruction results in an enlarged urinary bladder and signs of postrenal azotemia.

CAUSES

See Pathophysiology.

RISK FACTORS

- Sterile struvite uroliths—mineral composition, energy content, and moisture content of diets; urine-alkalinizing metabolites in diets; quantity of diet consumed; *ad libitum* vs. meal-feeding schedules; formation of concentrated urine; and retention of urine.
- Infection-induced struvite urolithiasis—urinary tract infection (UTI) with urease-producing bacteria, abnormalities in local host defenses that allow bacterial UTIs, and the quantity of urea excreted in urine.
- The small diameter of the male distal urethra predisposes to obstruction with plugs and urethroliths.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uroliths mimic other causes of pollakiuria, dysuria, periuria, hematuria, and/or outflow obstruction.
- Differentiate struvite uroliths and urethral plugs from other types of uroliths by signalment, urinalysis, urine culture, radiography, ultrasonography, cystoscopy, and quantitative analysis of uroliths or plugs.

CBC/BIOCHEMISTRY/URINALYSIS

- Complete outflow obstruction may cause postrenal azotemia.
- MAP crystals typically appear as colorless, orthorhombic (having three unequal axes intersecting at right angles), coffin-like prisms. They often have 3–8 sides.

OTHER LABORATORY TESTS

- Pretreatment urine cultures (preferably obtained by cystocentesis) can detect primary infections with urease-producing microbes

causing infection-induced struvite uroliths and differentiate them from infections acquired as a sequelae to urolithiasis.

- Quantitative mineral analysis should be performed on all uroliths and plugs.
- Bacterial culture of inner portions of uroliths retrieved from patients with urease-positive UTI may be of value.

IMAGING

Radiography

- Struvite uroliths—radiodense, single or multiple, rough or smooth, round or faceted, sometimes disc-shaped; some struvite urethral plugs may be detected by survey radiography.
- The size and number of uroliths are not a reliable index of probable efficacy of dissolution therapy.
- Contrast urethrocystography helps identify the site of urethral obstruction and strictures.

Ultrasonography

- Detects location and approximate size and number of uroliths. Tends to overestimate stone size and underestimate stone number.
- Does not indicate degree of radiodensity or shape of uroliths.

DIAGNOSTIC PROCEDURES

Cystoscopy reveals location, number, size, and shape of urethroliths and urocystoliths.

PATHOLOGIC FINDINGS

Urethral plugs may contain red blood cells, white cells, transitional epithelial cells, bacteria, and/or viruses in addition to matrix and minerals.



TREATMENT

APPROPRIATE HEALTH CARE

- Retrograde urohydropropulsion to eliminate urethral stones; lavage to remove urethral plugs.
- Voiding urohydropropulsion to eliminate small bladder and urethral stones.
- Medical dissolution of struvite uroliths is an outpatient strategy.

DIET

- Medical dissolution is the standard of practice for elimination of struvite uroliths.
- Treatment with a dedicated struvite calculolytic diet (e.g., Hill's Prescription Diet Feline s/d) results in dissolution within 2–4 weeks of therapy.
- Treatment with urinary therapeutic foods designed for struvite dissolution and CaOx prevention are effective but may require longer treatment times.
- Infection-induced struvite urocystoliths may be dissolved by feeding a calculolytic diet and an appropriate antimicrobial.
- Continue diet therapy for 1 month after radiographic evidence of urolith dissolution.

UROLITHIASIS, STRUVITE—CATS

(CONTINUED)

- Struvite crystalluria may be minimized by feeding magnesium-restricted urine-acidifying diets.
- Canned foods help to reduce urine concentration of calculogenic metabolites and promote increased frequency of voiding.

CLIENT EDUCATION

- If dietary management is used, limit access to other foods and treats.
- Short-term (weeks to months) treatment with a calculolytic diet and antibiotics as needed is effective in dissolving infection-induced struvite uroliths.
- Owners of cats with infection-induced struvite urocystoliths must comply with dosage schedule of antibiotics.
- Avoid feeding calculolytic diets to immature cats.

SURGICAL CONSIDERATIONS

- Ureteroliths cannot be dissolved. For persistent ureteroliths associated with morbidity, consider subcutaneous ureteral bypass, ureteral stents, or traditional surgery.
- Urethroliths cannot be medically dissolved. Consider voiding urohydropropulsion to remove urethroliths or urethral plugs. Alternatively, move urethroliths into the bladder by retrograde urohydropropulsion.
- Immovable urethroliths, recurrent urethral plugs, or strictures of the distal urethra may require perineal urethrostomy.
- Consider laser lithotripsy for urocystoliths and/or urethroliths.
- Consider surgical correction if uroliths are obstructing urine outflow and/or if correctable abnormalities predisposing to recurrent UTI are identified by radiography or other means.
- Radiographs should be obtained immediately following surgery to verify that all uroliths were removed.



MEDICATIONS

DRUG(S) OF CHOICE

- Dissolution of infection-induced urocystoliths requires appropriate antibiotics, chosen on the basis of bacterial culture and antimicrobial susceptibility tests. Give antibiotics at therapeutic dosages until the UTI is eradicated and there is no radiographic evidence of uroliths.
- Buprenorphine may be used to alleviate discomfort (15 µg/kg via buccal

transmucosal administration q8–12h). Tolteridine may be considered as an anticholinergic and antispasmodic to minimize hyperactivity of the bladder detrusor muscle and urge incontinence (0.05 mg/kg PO q12h).

CONTRAINdications

Do not give urine acidifiers to azotemic patients or immature cats.

PRECAUTIONS

Azotemic patients are at increased risk for adverse drug events.



FOLLOW-UP

PATIENT MONITORING

Check rate of urolith dissolution monthly by urinalysis, urine culture, survey or contrast radiography, or ultrasonography.

PREVENTION/AVOIDANCE

- Recurrent sterile struvite uroliths may be prevented by using acidifying, magnesium-restricted diets or urine acidifiers. Do not administer urine acidifiers with acidifying diets.
- For patients whose urine has been acidified, carefully monitor them for CaOx crystalluria. Change management protocol if persistent CaOx crystalluria develops.
- In patients at risk for both struvite and CaOx crystalluria, focus on preventing CaOx uroliths. Struvite uroliths can be medically dissolved; CaOx uroliths cannot be dissolved.
- Infection-induced struvite urolithiasis can be prevented by eradicating and controlling UTIs. Use of magnesium-restricted, acidifying diets is not required if the urease-positive microbes can be eradicated.

POSSIBLE COMPLICATIONS

- Urocystoliths may pass into and obstruct the urethra, especially if the patient is persistently dysuric. Urethral obstruction may be managed by retrograde urohydropropulsion.
- An indwelling transurethral catheter increases the risk for iatrogenic bacterial UTI and urethral stricture.

EXPECTED COURSE AND PROGNOSIS

Mean times for dissolution of sterile urocystoliths ranged from 13 to 36 days. Mean times for dissolution of infection-

induced struvite urocystoliths ranged from 21 to 44 days. Most struvite uroliths located in the urinary bladder can be safely dissolved with a low risk of adverse effects, including urethral obstruction.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Any disease that predisposes to bacterial UTI.

AGE-RELATED FACTORS

Infection-induced struvite is the most common urolith in immature cats. Sterile struvite is rare in immature cats.

SYNOMYS

Feline lower urinary tract disease.

SEE ALSO

- Crystalluria.
- Lower Urinary Tract Infection, Bacterial.
- Lower Urinary Tract Infection, Fungal.
- Nephrolithiasis.
- Urolithiasis, Struvite—Dogs.

ABBREVIATIONS

- CaOx = calcium oxalate.
- MAP = magnesium ammonium phosphate.
- UTI = urinary tract infection.

Suggested Reading

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Feline urethral plugs: Etiology and pathophysiology. Vet Clin North Am Small Anim Pract 1996; 26:233–254.

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Consulting Editor J.D. Foster

Acknowledgment The author and editors acknowledge the prior contribution of Carl A. Osborne, Jody P. Lulich, and Eugene E. Nwaokorie.



Client Education Handout
available online

UROLITHIASIS, STRUVITE—DOGS



BASICS

DEFINITION

Formation of polycrystalline concretions (i.e., uroliths, calculi, or stones) composed of magnesium ammonium phosphate hexahydrate (MAP, struvite) in the urinary tract.

PATHOPHYSIOLOGY

Infection-Induced Struvite

- Urine must be supersaturated with MAP for struvite uroliths to form. MAP supersaturation of urine is often associated with urinary tract infections (UTIs) with urease-producing microbes.
- UTIs caused by urease-producing microbes (*Staphylococcus*, *Proteus*, and *Ureaplasma*) and urine containing sufficient urea favors formation of uroliths containing struvite, carbonate apatite, and calcium apatite.
- Consumption of dietary protein exceeding the daily requirement results in formation of urea from catabolism of amino acids.
- Metabolic and anatomic abnormalities may indirectly induce struvite uroliths by predisposing to UTIs.

Sterile Struvite

- In dogs, this type of struvite is uncommon.
- Dietary or metabolic factors may be involved in the genesis of sterile struvite uroliths in dogs.
- Microbial urease is not involved in formation of sterile struvite uroliths.

SYSTEMS AFFECTED

Renal/urologic.

GENETICS

- The high incidence of struvite uroliths in some breeds such as miniature schnauzers suggests a familial tendency. Susceptible miniature schnauzers may inherit an abnormality of local host defenses of the urinary tract that increases their susceptibility to UTI.
- Sterile struvite uroliths were found in a family of English cocker spaniels.

INCIDENCE/PREVALENCE

Struvite uroliths account for approximately 40% of stones affecting the canine lower urinary tract and 23% of stones affecting the upper urinary tract.

GEOGRAPHIC DISTRIBUTION

Ubiquitous

SIGNALMENT

Species

Dog

Breed Predilections

- Miniature schnauzer, shih tzu, bichon frise, miniature poodle, cocker spaniel, and Lhasa apso.
- Any breed may be affected.

Mean Age and Range

- Mean age, 6 years (range <1 to >19 years).

- Most uroliths in immature (<12 months old) dogs are infection-induced struvite.

Predominant Sex

More common in females (~85%) than males (~15%), which may be related to the greater propensity for females to develop bacterial UTI.

SIGNS

General Comments

- Some dogs are asymptomatic.
- Signs depend on location, size, and number of uroliths and virulence of bacteria.

Historical Findings

- Typical signs of urocystoliths include pollakiuria, dysuria, and hematuria; sometimes small, smooth uroliths are voided.
- Typical signs of urethroliths include pollakiuria and dysuria; sometimes small, smooth uroliths are voided, and some medium size uroliths are associated with urethral obstruction.
- Nephroliths may be associated with manifestations of renal insufficiency. Obstruction to urine outflow with bacterial UTI may result in generalized pyelonephritis and septicemia.

Physical Examination Findings

- Uroliths may be palpated in the urinary bladder and urethra (by rectal exam).
- Urethral obstruction may cause enlargement of the urinary bladder.
- Ureteral obstruction may cause enlargement and pain of the associated kidney.
- Complete urine outflow obstruction combined with bacterial infection may cause ascending UTI and signs of renal failure and septicemia.

CAUSES

- Urinary tract disorders that predispose to infections with urease-producing bacteria, fungal pathogens, or ureaplasma in patients whose urine contains a large quantity of urea.
- Specific causes of sterile struvite uroliths are unknown.

RISK FACTORS

- Exogenous or endogenous exposure to high concentrations of glucocorticoids predispose to bacteriuria.
- Abnormal retention of urine.
- Alkaline urine decreases the solubility of struvite.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Uroliths mimic other causes of pollakiuria, dysuria, hematuria, and/or outflow obstruction.
- Differentiate from other types of uroliths by signalment, rectal exam, urinalysis, urine culture, radiography, and quantitative analysis of uroliths.

CBC/BIOCHEMISTRY/URINALYSIS

- Complete outflow obstruction can cause postrenal azotemia and hyperphosphatemia.
- MAP crystals typically appear as colorless, orthorhombic, coffin-like prisms. They may have 3–6 or more sides and often have oblique ends.

OTHER LABORATORY TESTS

- Quantitative bacterial culture of urine, preferably collected by cystocentesis.
- Bacterial culture of inner portions of infection-induced struvite uroliths.
- Quantitative mineral analysis of urolith.

IMAGING

- Struvite uroliths are radiodense and may be detected by survey radiography.
- Ultrasonography can detect uroliths, but provides no information about their density, shape, or size.
- Determine precise location, size, and number of uroliths; the size and number are not a reliable index of probable efficacy of dissolution therapy.



TREATMENT

APPROPRIATE HEALTH CARE

- Medical dissolution with antimicrobials and therapeutic food is preferred treatment for non-obstructing struvite uroliths.
- Ureteral stenting facilitates medical dissolution of obstructing nephroureteroliths.
- Appropriate antimicrobial administration is the cornerstone of treatment for infection-induced struvite dissolution and prevention.
- Voiding urohydropropulsion, laser lithotripsy, percutaneous cystolithotomy, and/or surgery require short periods of hospitalization.

DIET

- Infection-induced and sterile struvite urocystoliths and nephroliths may be dissolved by feeding a calculolytic food (Hill's Prescription Diet Canine c/d, s/d, Royal Canin® and others).
- Continue calculolytic diet therapy for 1 month beyond survey radiographic evidence of urolith dissolution.
- Avoid use of the protein restricted diet in patients with protein-calorie malnutrition. Some calculolytic diets are designed for short-term (weeks to months) dissolution therapy, rather than long-term (months to years) prophylactic therapy. Monitor the patient for evidence of protein malnutrition. Consider dissolution diets meeting maintenance nutritional requirements in immature dogs. Avoid high sodium foods in dogs with cardiac valvular disease or heart failure.

CLIENT EDUCATION

- If dietary management is used, limit access to other foods and treats.

UROLITHIASIS, STRUVITE—DOGS

(CONTINUED)

- Short-term (2–3 months) treatment with a calculolytic food and administration of antibiotics is effective in dissolving struvite uroliths.
- Comply with dosage schedule for antibiotic and diet therapy.

SURGICAL CONSIDERATIONS

- Ureteroliths and urethroliths may be difficult to medically dissolve because they are minimally immersed in urine.
- Consider ureteral stenting or shock-wave lithotripsy for persistent ureteroliths associated with morbidity. Ureteral stenting may allow for renal decompression and allow time for stone dissolution.
- Consider voiding urohydropropulsion if urethroliths are likely to pass through the urethra. Alternatively, consider laser lithotripsy or move urethroliths into the bladder by retrograde urohydropropulsion.
- Consider surgical correction if uroliths are obstructing urine outflow and minimally invasive procedures are ineffective or not available. Immovable urethroliths may require urethrotomy or urethrostomy.



MEDICATIONS

DRUG(S) OF CHOICE

- U**
- Dietary dissolution of infection-induced urocystoliths or nephroliths requires oral administration of appropriate antibiotics, chosen on the basis of quantitative bacterial culture and antimicrobial susceptibility tests. Give antibiotics until there is no radiographic evidence of uroliths and there is eradication of UTI.
 - In most cases, antimicrobics need to be administered for the entire dissolution period. Shorter duration may be successful if they sterilize the urolith (e.g., small uroliths).

PRECAUTIONS

- Diet-induced polyuria will reduce the concentration of antimicrobial drugs in urine; consider this fact when calculating antimicrobial dosages.



FOLLOW-UP

PATIENT MONITORING

Monitor rate of urolith dissolution at 4 to 6 week intervals by urinalysis, urine culture,

and imaging (ultrasonography, and/or survey or contrast radiography).

PREVENTION/AVOIDANCE

- Infection-induced struvite urolithiasis may be prevented by eradicating and controlling infections by urease-producing bacteria.
- Recurrent sterile struvite uroliths may be prevented by use of acidifying, magnesium-restricted diets (Hill's Prescription Diet Canine c/d and others) or urine acidifiers.
- Monitor patients whose urine has been acidified for calcium oxalate crystalluria. Change management protocol if persistent calcium oxalate crystalluria develops.
- In patients at risk for both struvite and other urolith types, focus dietary prevention of metabolic uroliths (e.g., calcium oxalate, urate, cystine)—and UTI prevention for struvite uroliths.

POSSIBLE COMPLICATIONS

- Benefits and risks are associated with feeding low protein-high fat struvitolytic diets. Potential contraindications include those with (1) abnormal fluid accumulation, (2) chronic kidney disease, and (3) predispositions to pancreatitis (especially miniature schnauzers with hyperlipidemia).
- Urocystoliths may pass into and obstruct the urethra. Urethral obstruction can be managed by retrograde urohydropropulsion or lithotripsy.
- Dysuria may be minimized by antimicrobial treatment of bacterial UTIs and oral administration of anticholinergic drugs.
- Diet-associated polyuria will result in voiding increased urine volume. This may be associated with varying degrees of urinary incontinence in neutered female dogs with a predisposition to incontinence. Allow frequent opportunity to urinate to minimize inappropriate housesoiling.

EXPECTED COURSE AND PROGNOSIS

- The mean time for dissolution of all infection-induced urocystoliths was 3 months (range 2 weeks–7 months), whereas nephroliths took 6 months (range 2–10 months). The mean dissolution time of sterile struvite urocystoliths was 6 weeks (range 4–12 weeks).
- When feeding Hills Prescription Diet s/d, compliance with dietary recommendations is verified by a reduced concentration of urea in serum (approximately 10 mg/dL) and a low urine specific gravity (1.004–1.014).
- If uroliths increase or fail to decrease in size after approximately 6–8 weeks of appropriate management, alternative methods should be considered. Difficulty in inducing complete

dissolution of uroliths should prompt consideration that (1) the wrong mineral component was identified, (2) the nucleus of the uroliths has a different mineral composition than other portions of the urolith, and (3) the owner is not complying with therapeutic recommendations. With the addition of high sodium dissolution foods lacking protein reduction, the proportion of calcium phosphate carbonate associated with infection-induced struvite has increased. Struvite uroliths with high percentages of calcium phosphate carbonate appear less amenable to medical dissolution.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Any disease that predisposes to bacterial UTI.

AGE-RELATED FACTORS

Infection-induced struvite is the most common form of urolith in immature dogs. The uroliths develop as a result of microbial UTI.

PREGNANCY/FERTILITY/BREEDING

- The calculolytic foods are not designed to sustain pregnancy.

SYNONYMS

- Phosphate calculi.
- Infection stone.
- Urease stone.
- Triple-phosphate stone.

ABBREVIATIONS

- MAP = magnesium ammonium phosphate.
- UTI = urinary tract infection.

Suggested Reading

Osborne CA, Lulich JP, Bartges JW, et al. Canine and feline urolithiasis: relationship of etiopathogenesis to treatment and prevention. In: Osborne CA, Finco DR, eds., *Canine and Feline Nephrology and Urology*. Baltimore, MD: Williams & Wilkins, 1995, pp. 798–888.

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Consulting Editor J.D. Foster

Acknowledgment The author and editors acknowledge the prior contribution of Carl A. Osborne and Eugene E. Nwaokorie.



Client Education Handout
available online

VAGINAL DISCHARGE



BASICS

DEFINITION

Any substance emanating through the vulvar labia.

PATHOPHYSIOLOGY

- Dependent on underlying cause of vaginal discharge.
- Discharge may originate from uterus, vagina, vestibule, clitoris, clitoral sinus, perivulvar dermis, or urinary tract.

SYSTEMS AFFECTED

- Reproductive.
- Renal.
- Skin.
- Urinary.

INCIDENCE/PREVALENCE

- Unknown as there are many causes.
- Considered a common reason for seeking veterinary care.

SIGNALMENT

- Healthy bitch <6–12 months of age (prepubertal)—juvenile (puppy) vaginitis and congenital anomalies more common.
- Nonpregnant bitch that has undergone at least one estrous cycle—normal estrus, persistent estrus (cystic ovarian disease or granulosa cell tumor), pyometra, neoplasia
- Bitch bred in the last 30–70 days—normal parturition (50–70 days) or abortion (<50 days).
- Bitch that has recently whelped—normal lochia or postpartum metritis more common, subinvolution of placental sites.
- Ovariectomized bitch—vaginal stricture or estrogen-responsive urinary incontinence more common; neoplasia.

SIGNS

Historical Findings

- Discharge from the vulva.
- Licking, scooting, and spotting.
- Attracting male dogs.
- Parturition—with postpartum discharge.
- Recent estrus—with pyometra.
- Hemorrhagic discharge >8 weeks postpartum—subinvolution of placental sites.
- Vomiting, anorexia—may be seen with metritis and pyometra.

Physical Examination Findings

Vaginal discharge that may be serosanguinous, purulent, lochial, hemorrhagic, mucoid, or urinous.

CAUSES

Normal Physiologic Conditions

- Proestrus.
- Estrus.
- Diestrus.
- Late pregnancy.

- Parturition.
- Normal lochia.

Pathologic Conditions

See specific chapters for further information.

- Cystic ovarian disease (persistent estrus).
- Brucella canis* infection.
- Metritis.
- Pyometra.
- Retained placenta or fetuses.
- Subinvolution of placental sites (hemorrhagic discharge postpartum ≥8 weeks).
- Neoplasia—uterus, vagina, urinary tract (including transmissible venereal tumor), ovary (granulosa cell tumor/persistent estrus).
- Vaginitis.
- Estrogen-responsive urinary incontinence.
- Coagulopathy.
- Congenital defects of the distal genital tract—intersex conditions, imperfect embryologic fusion of the Müllerian ducts (vagina), joining of the genital folds (vestibule) and genital swellings (vulvar lips), ectopic ureters.
- Trauma.
- Foreign body.

RISK FACTORS

- Prophylactic antibiotics—may alter normal vaginal flora and predispose to secondary infection.
- Exogenous estrogen—predispose to pyometra in the intact bitch.
- Exogenous androgens—may cause clitoral hypertrophy.
- Exogenous or endogenous progesterone—predispose to pyometra or stump pyometra.
- Obesity—excess skin folds around vulva.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Healthy intact bitch <6–12 months of age—juvenile vaginitis (prepubertal), normal estrous cycle, urogenital trauma or neoplasia, foreign body, coagulopathy, ectopic ureter(s), congenital abnormalities of the perineum or distal genital tract, intersex conditions, urinary tract disease.
- Nonpregnant bitch that has undergone at least one estrous cycle—normal estrus, pyometra, split heat, foreign body, urogenital trauma, neoplasia, coagulopathy, cystic ovarian disease (follicular cysts).
- Bitch bred in the last 30–70 days—abortion, pyometra, normal parturition (>57 days from breeding), fetal/embryonic death, split heat, *Brucella canis* infection.
- Bitch that has recently whelped—lochia (normal up to 6–8 weeks postpartum), subinvolution of placental sites (hemorrhagic discharge ≥8 weeks postpartum), postpartum metritis, vaginal trauma, retained placenta or fetus.

- Ovariectomized bitch—vaginal stricture, foreign body, neoplasia, polyps, stump pyometra due to exogenous or endogenous progesterone, exogenous estrogens (exposure to owner's hormone replacement therapy), perivulvar dermatitis, ovarian remnant syndrome, estrogen-responsive urinary incontinence.

CBC/BIOCHEMISTRY/URINALYSIS

- Regenerative anemia—may be normal in pregnancy or during estrus.
- Urinalysis—may indicate urinary tract infection.

OTHER LABORATORY TESTS

- Progesterone—determine if bitch is in luteal phase, which increases likelihood of pyometra. Progesterone, 17-hydroxyprogesterone may be secreted in animals with adrenal cortex disease.
- Adrenocorticotrophic hormone (ACTH) stimulation test—to diagnose adrenocortical disease.
- Brucella canis* serology—screen with rapid slide agglutination test; agar gel immunodiffusion test confirmatory.
- Bacterial culture of whole blood or lymph node aspirate for *B. canis*.
- PCR for *B. canis* available, best to use on abortive discharge (Kansas State Veterinary Diagnostic Laboratory).

IMAGING

Radiography

- Detect enlarged uterus or ovary, pregnancy.
- Evidence of fetal death—presence of gas around fetus or misalignment and/or collapse of fetal skeleton.

Ultrasonography

- Determine contents of uterus; free fluid in the uterus is characteristic of pyometra, hydrometra, and mucometra.
- Pregnancy diagnosis and embryonic/fetal wellbeing—heartbeat may be seen as early as the 20th day of diestrus, heart rate <180 bpm indicates fetal stress.
- Masses—neoplasia, granulomas, cystic ovarian disease, granulosa cell tumor, or foreign body; saline distention of the vagina may help visualization.

Contrast Radiography—Vaginogram/Urethrogram/Cystogram/Excretory Urography

- Identify abnormal conformation or structure (i.e., neoplasia or foreign body) within the vagina.
- Rule out vestibulovaginal strictures, rectovaginal and urethrovaginal fistulas.
- Rule out differentials and help localize the problem.
- Pronounced folds (rugae) of vagina during estrus will cause filling defects (normal).

VAGINAL DISCHARGE

(CONTINUED)

DIAGNOSTIC PROCEDURES

Vaginal Cytology

- Determine nature of discharge—Inflammatory, hemorrhagic, purulent.
- Evaluate epithelial cells—Superficial (cornified) cells present under the influence of estrogen.
- Always performed in order to interpret vaginal cultures (inflammation should accompany infection).

Vaginal Culture and Sensitivity

- Performed prior to other diagnostic procedures.
- Use guarded swab to sample cranial vagina.
- The vagina is not a sterile environment and culture of normal bitches results in growth of normal vaginal flora; use of vaginal cytology and other diagnostic tools is essential for interpretation of culture results.
- Most common organisms in the microbiome (commensals and potential pathogens) are *Escherichia coli*, *Streptococcus* spp., *Pasteurella* spp., and *Staphylococcus* spp.
- Other organisms which can be commensals include *Mycoplasma* spp., *Enterobacter* spp., *Pseudomonas* spp., *Klebsiella* spp.
- Normal microbiome consists of numerous opportunistic pathogens, e.g., *E. coli* and *Mycoplasma* spp.

Vaginoscopy

- Rigid cystourethroscope or ureteroscope, pediatric gastroscope or proctoscope, or flexible endoscope used to visualize vagina.
- Identify source of vaginal discharge—uterine, vaginal, vestibular, or urethra.
- Visualize anomalies, persistent hymen, neoplasia, foreign body, trauma, abscess, and evaluate the vaginal and vestibular mucosa.
- Removal of foreign body or biopsy of vaginal mass.

Other

- Digital examination of vestibule, vaginovestibular junction, and distal vagina.
- Biopsy and histopathology of mass lesions.
- Cystocentesis—urine culture and sensitivity.
- Coagulation profile, platelet count.



TREATMENT

- Based on diagnosis.
- No treatment for normal causes of vaginal discharge.

SURGICAL CONSIDERATIONS

- Ovariectomy or ovariohysterectomy (OHE) is treatment of choice for neoplastic conditions.

- Cystic ovarian disease can be medically managed or ovariectomy/OHE performed.
- Removal of foreign body or surgical excision of mass(es).
- Surgical excision or radiation therapy are options for transmissible venereal tumor (TVT).



MEDICATIONS

DRUG(S) OF CHOICE

- Antibiotic—choice based on guarded cranial vaginal culture and sensitivity.
- Dopamine agonist—may be used in addition to PGF 2α for luteolysis via suppression of the luteotropic hormone prolactin—bromocriptine 10 μ g/kg PO or cabergoline 5 μ g/kg PO q8–24h until serum progesterone level <2.0 ng/mL.
- Supportive care including IV fluids as indicated.

CONTRAINDICATIONS

Certain antibiotics may be contraindicated during pregnancy and nursing.

PRECAUTIONS

Dopamine agonists—side effects include vomiting and nausea; can be controlled with antiemetics.

ALTERNATIVE DRUG(S)

Aglepristone (Alizin') 10 mg/kg SC, 2 doses given 24 hours apart—progesterone receptor antagonist that may be used alone or concurrently with prostaglandin therapy for treatment of pyometra (currently not widely available in the United States without special authorization).



FOLLOW-UP

PATIENT MONITORING

Subinvolution of Placental Sites

Monitor hematocrit or packed cell volume (PCV)—may have significant blood loss.

PREVENTION/AVOIDANCE

- Puppy vaginitis—delay elective OHE until after first estrous cycle in cases of juvenile vaginitis; may avoid chronic vaginitis.
- Addition of probiotics to daily diet.
- Avoid exogenous steroids (estrogens, progestins, androgens).

POSSIBLE COMPLICATIONS

Endotoxemia and septicemia may occur with pyometra or metritis.



MISCELLANEOUS

ASSOCIATED CONDITIONS

Pyometra and cystic endometrial hyperplasia.

AGE-RELATED FACTORS

- Increased risk for pyometra after each estrous cycle.
- Neoplasia more common in older bitches.

ZOONOTIC POTENTIAL

- Brucella canis*—fluids and fetal tissue during abortion are highly contaminated with organisms.
- Immunocompromised people are at highest risk. Animal caretakers and pathologists are at risk due to high exposure.

PREGNANCY/FERTILITY/BREEDING

- Neoplasia—poor prognosis for future fertility.
- TVT—sexually transmitted disease; breeding should be avoided.
- Brucella canis*—sexually transmitted disease and grave prognosis for resolution of disease and normal fertility; should not be used for breeding.

SEE ALSO

- Abortion, Spontaneous (Early Pregnancy Loss)—Cats.
- Abortion, Spontaneous (Early Pregnancy Loss)—Dogs.
- Brucellosis.
- Ovarian Remnant Syndrome.
- Pyometra.
- Retained Placenta.
- Sexual Development Disorders.
- Subinvolution of Placental Sites.
- Transmissible Venereal Tumor.
- Vaginal Malformations and Acquired Lesions.
- Vaginitis.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- OHE = ovariohysterectomy.
- PCV = packed cell volume.
- TVT = transmissible venereal tumor.

Suggested Reading

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Consulting Editor Erin E. Runcan



Client Education Handout
available online

VENTRICULAR FIBRILLATION



BASICS

DEFINITION

- A ventricular rhythm of disorganized electrical activity resulting in nonproductive ventricular muscle quivering (i.e., fibrillation).
- Also known as V-fib or VF and is considered the most severe cardiac rhythm disturbance.

PATHOPHYSIOLOGY

Loss of organized ventricular activity results in acute and profound drop in cardiac output, systemic blood pressure, and organ perfusion, eventually leading to death.

SYSTEMS AFFECTED

- Cardiovascular. • All organ systems affected by loss of perfusion.

GENETICS

- Not recognized in veterinary patients.
- However, there are known ventricular arrhythmias with modes of inheritance in the dog.

INCIDENCE/PREVALENCE

Unknown

SIGNALMENT

Species

Dog and cat.

Breed Predilections

None

Mean Age and Range

Unknown, but probably more common in geriatric animals.

SIGNS

Historical Findings

- Severe systemic illness. • Severe cardiac disease. • Previously documented cardiac arrhythmias.

Physical Examination Findings

- Collapse. • Loss of consciousness (i.e., syncope). • Cardiac arrest. • Death.

CAUSES

Cardiac

- Cardiac surgery/interventional procedure.
- Cardiomyopathy. • Myocardial injury.
- Myocarditis. • Subaortic/aortic stenosis.

Extracardiac

- Anoxia. • Autonomic imbalances, especially high sympathetic tone or administration of catecholamines.
- Circulatory shock. • Drug reactions—e.g., anesthetic agents, especially halothane and ultrashort-acting barbiturates, digoxin.
- Electrical shock. • Electrolyte and acid-base imbalances. • Hypothermia.

RISK FACTORS

Any severe systemic illness or cardiac disease.



DIAGNOSIS

ECG Features (Figures 1 and 2)

- Rapid, chaotic, irregular rhythm with bizarre waves or oscillations. • Oscillations may be large (coarse fibrillation) or small (fine fibrillation). • Absent P waves. • Absent QRS complexes.

DIFFERENTIAL DIAGNOSES

- Check for pulse. • Rule out ECG artifact.
- Reapply ECG clips and ensure good skin contact and adequate gel (or alcohol) applied to leads. • If there is possibility of using defibrillator to shock patient, do *not* use alcohol as it is a flammable substance.

CBC/BIOCHEMISTRY/URINALYSIS

The abnormalities generally relate to the underlying metabolic problem that causes ventricular fibrillation.

OTHER LABORATORY TESTS

Cardiac troponin I may be elevated in case of severe arrhythmia, cardiac ischemia, or myocarditis.

IMAGING

- Can utilize point of care ultrasound to visualize heart chamber activity. • Avoid alcohol and utilize gel whenever possible (see above).

PATHOLOGIC FINDINGS

Vary depending on histopathologic findings on post-mortem examination.



TREATMENT

APPROPRIATE HEALTH CARE

- Rapidly fatal rhythm requiring immediate, aggressive treatment. • Outcome is often death without use of electrical cardioversion (defibrillation).

Direct Current Defibrillation

- Immediate defibrillation is recommended when the duration of cardiopulmonary arrest caused by ventricular fibrillation is 4 minutes or less. • Otherwise, a 2-minute cycle of chest compressions before defibrillation is recommended. • The dose of energy for initial defibrillation is 2–4 J/kg (biphasic defibrillator) or 4–6 J/kg (monophasic defibrillator). • If an initial shock is not successful, CPR is resumed for 2 minutes before defibrillation is attempted again. • A 50% escalation in the energy delivered may be considered for subsequent defibrillation attempts.

Precordial Thump

- To be used if no access to an electrical defibrillator. • Apply a sharp blow with the ulnar aspect of a closed fist to the chest wall over the heart. • Rarely successful in conversion to sinus rhythm. • This technique is *not* recommended for other rhythms as a thump can also cause more malignant arrhythmias.

NURSING CARE

Treat any identified conditions such as hypothermia, electrolyte disturbances, and acid–base disorders.

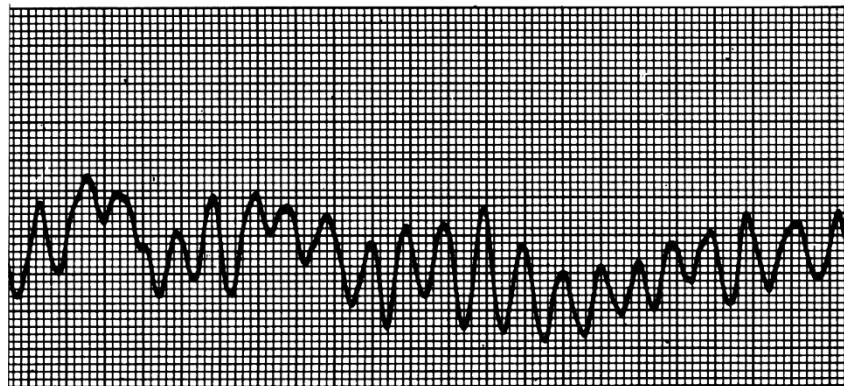


Figure 1.

Coarse ventricular fibrillation. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

VENTRICULAR FIBRILLATION

(CONTINUED)

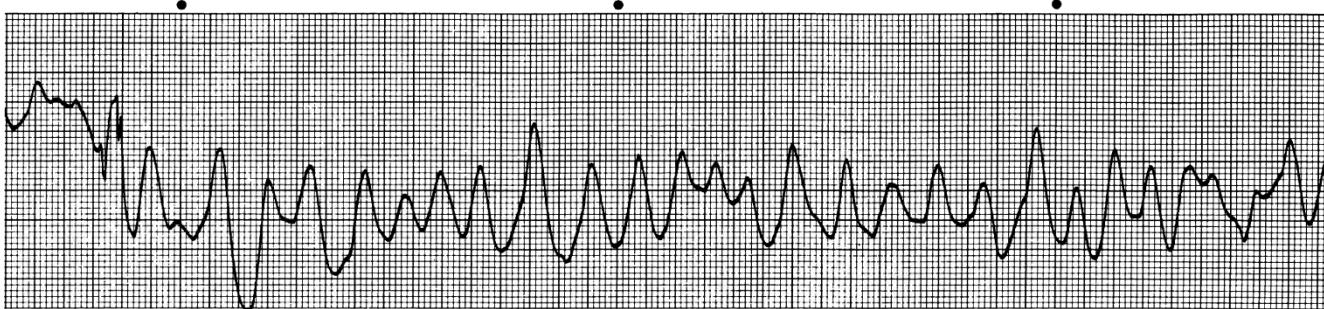


Figure 2.

Ventricular flutter–fibrillation in a cat with severe myocardial damage from an 11-story fall. The complexes are very wide, bizarre, tall, and rapid. (Source: From Tilley LP. Essentials of Canine and Feline Electrocardiography, 3rd ed. Baltimore: Williams & Wilkins, 1992. Reprinted with permission of Wolters Kluwer.)

CLIENT EDUCATION

If the patient is converted back to a sinus rhythm, warn the owner that the patient is at high risk for recurrence of the arrhythmia in the immediate post-resuscitation period.

SURGICAL CONSIDERATIONS

N/A



MEDICATIONS

DRUG(S) OF CHOICE

- Institute cardiopulmonary cerebral resuscitation. • Epinephrine—low dose (0.01 mg/kg) of epinephrine is recommended as high-dose therapy has not been associated with increased survival. A shortcut to calculate low-dose epinephrine volume for administration is 0.1 mL/10 kg. The dose may be repeated at 3- to 5-minute intervals.
- Vasopressin—there is evidence that this drug may be equivalent to or even superior to epinephrine in some situations. The dose of vasopressin is 0.8 units/kg (dogs and cats), and the dose may be repeated at 3- to 5-minute intervals.
- Once the animal is successfully converted, administer IV lidocaine or amiodarone to lower the risk of refibrillation or development of ventricular tachycardia.
- Lidocaine 2 mg/kg (dogs, IV, IO, IT); a shortcut to calculate the dose for the 2% (20 mg/mL) solution is 1 mL/10 kg.
- Amiodarone (Nexterone®) 2–5 mg/kg (dogs, IV). Do NOT use amiodarone with polysorbate 80; this has been shown to cause anaphylaxis in dogs. Hypotension is a common occurrence during amiodarone administration.

PRECAUTIONS

- Lidocaine raises the fibrillation threshold but makes defibrillation more difficult.
- Lidocaine and amiodarone have the potential to be proarrhythmic.
- There is currently no evidence for improved outcome with use of these medications in patients with VF.

ALTERNATIVE DRUG(S)

- Magnesium (chloride or sulfate) is commonly administered (0.3 mEq/kg IV) for antiarrhythmic treatment. Magnesium is not known to have any proarrhythmic effect. There is no supportive evidence for its use in VF. • Chemical conversion can be attempted if no access to electrical defibrillator. Administer 1 mEq potassium/kg and 6 mg/kg acetylcholine IC. This approach is rarely successful.



FOLLOW-UP

PATIENT MONITORING

- CBC, biochemistry profile, urinalysis, arterial blood gases with acid–base analysis.
- If primary cardiac disease is suspected—echocardiogram, cardiac troponin, and thoracic radiographs. • Continuous ECG monitoring.

PREVENTION/AVOIDANCE

Careful monitoring of critically ill patients to prevent and correct acid–base disturbances, hypotension, and hypoxemia.

POSSIBLE COMPLICATIONS

- Recurrence of VF.
- Death.
- Disseminated intravascular coagulation.
- Multiorgan failure.

EXPECTED COURSE AND PROGNOSIS

Most patients die because of either the arrhythmia or the underlying disease.



MISCELLANEOUS

AGE-RELATED FACTORS

May be more likely in patients of advanced age.

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

Cardiopulmonary Arrest.

ABBREVIATIONS

- IC = intracardiac.
- IT = intratracheal.
- VF = ventricular fibrillation.

Suggested Reading

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Consulting Editor Michael Aherne

VENTRICULAR TACHYCARDIA



BASICS

DEFINITION

Ventricular tachycardia (VT) may occur in structurally normal hearts (hereditary arrhythmias) or may be a manifestation of myocardial abnormalities associated with cardiomyopathy, significant valvular disease, myocarditis, infiltrative disease or electrolyte abnormalities. To date, no available medical therapy is known to prevent sudden death (SD) in animals afflicted with VT.

PATOPHYSIOLOGY

Severity of VT depends both on the hemodynamic consequences (hypotension) and on the electrical instability of a rhythm, i.e. its potential to degenerate into ventricular fibrillation (VF), resulting in SD. In Dobermanns, SD due to VT–VF occurs in about 30–50% of cases. In boxers with arrhythmogenic right ventricular cardiomyopathy (ARVC), 33% are syncopal due to VT and 30% have SD due VT–VF. Similarly, 13% of English bulldogs with inherited ARVC experience SD. Underlying mechanisms of VT include increased automaticity, reentry, and triggered activity.

ECG Features (Figure 1)

- QRS complexes—typically wide and bizarre.
- Three or more ventricular premature contractions in a row.
- May be intermittent (paroxysmal) or sustained; heart rate usually >150 bpm with a regular or irregular rhythm.
- P waves, if visible, are dissociated from the QRS complexes.
- Breed-specific ECG changes—VT in boxers is characteristically positive in the ventrocaudal leads (leads II, III, and aVF), thus manifests a “left bundle branch block pattern.” VT in Doberman pinschers and German shepherd dogs has both polymorphic and monomorphic characteristics.

SYSTEMS AFFECTED

Cardiovascular system, with secondary effects on other systems due to poor perfusion.

GENETICS

• In boxers, ARVC is inherited as autosomal dominant trait with adult onset of disease. Some boxers have a mutation in the striatin gene, but the disease is manifested with incomplete penetrance (i.e., even if a boxer has the genetic mutation, it may not lead to the development of arrhythmias in that dog) and it is likely that there is more than one mutation in boxers that may lead to the disease in some lines. Striatin is a desmosomal protein (scaffolding protein) located in the intercalated disc region of the cardiomyocyte and colocalizes with desmosomal proteins such as plakophilin-2 and other known proteins that

are mutated in human ARVC. DNA test results can indicate if a dog is heterozygous or homozygous for the genetic striatin deletion. Homozygous dogs are more likely to show disease and should not be used for breeding.

- English bulldogs also appear to harbor a form of inherited ARVC manifest with VT and SD in 13% of dogs. Genetic mode of inheritance is undetermined. There is 2.9:1 male to female ratio of affectedness. Unlike boxers with ARVC, the majority of English bulldogs appear to present with signs of CHF at the time of arrhythmia detection.
- Dilated cardiomyopathy with VT in Doberman pinschers is inherited as an autosomal dominant trait with adult onset of disease. In Dobermanns there are two genetic mutations associated with dilated cardiomyopathy (DCM) and VT identified in the pyruvate dehydrogenase kinase 4 (PDK4) gene (*PDK4/NCSU/DCM1*) and the titin gene (*NCSU DCM2*). Dogs with both mutations are at the highest risk of getting DCM, although dogs with a mutation in either gene can develop the disease as well.
- Inherited VT and SD, considered primarily an “electrical disorder” (since no underlying structural heart disease is identified), is found in young German shepherd dogs and English springer spaniels. They have been shown to have inherited channelopathies, resulting in repolarization abnormalities. In springer spaniels a mutation in the *KCNQ1* gene, responsible for a repolarizing K channel, was found to exhibit QT interval prolongation on ECG and SD. In German shepherd dogs, the mode of inheritance is polygenic due to an abnormality in a major gene with modifiers.
- Young Rhodesian ridgebacks have been found to be affected with severe ventricular arrhythmias and SD. It is inherited in an autosomal recessive mode and linked to a genetic mutation, likely associated with mitochondrial alterations.

INCIDENCE/PREVALENCE

Common in dogs; uncommon in cats.

GEOGRAPHIC DISTRIBUTION

None

SIGNALMENT

Species

Dog and cat.

Breed Predilections

Commonly seen in large-breed dogs with cardiomyopathy, especially boxers and Doberman pinschers, also in German shepherd dogs and Rhodesian ridgebacks.

Mean Age and Range

- All age groups, if not breed-specific VT.
- Boxers with ARVC usually present at 4–6 years of age; frequency and severity of the arrhythmia usually increase over time.
- Doberman pinschers with occult cardiomyopathy typically develop ventricular

arrhythmias beginning at 3–6 years of age, but it also can occur much later in life; frequency and severity usually increase over time.

- German shepherd dogs develop ventricular arrhythmias at 12–16 weeks of age and the frequency and severity of the arrhythmias increase until 24–30 weeks of age. After 8 months of age the arrhythmia severity stabilizes or starts to decrease.
- The Rhodesian ridgeback's most severe arrhythmias are found between 6 and 30 months of age, after which many dogs appear to outgrow the problem.
- Bulldogs with ARVC have a mean age of 9.2 years at time of presentation for arrhythmias.

SIGNS

Historical Findings

- Syncope.
- Weakness.
- Exercise intolerance.
- SD.
- May be asymptomatic.

Physical Examination Findings

- May be normal if arrhythmia is paroxysmal and absent during examination.
- Paroxysmal or sustained tachycardia may be auscultated.
- Femoral pulses may have variable pulse intensity or be weak during runs of VT.
- Signs of CHF or a murmur may be present, depending on cause of arrhythmia.

CAUSES

- Cardiomyopathy.
- Inherited channelopathies.
- Congenital defects (especially subaortic stenosis).
- Chronic degenerative valve disease.
- Traumatic or infectious myocarditis.
- Cardiac neoplasia.
- Gastric dilation and volvulus.
- Splenic neoplasia/hemorrhage.
- Hyperthyroidism (cats).
- Digitalis toxicity.
- Pancreatitis.
- VT can also be found in dogs affected with noncardiac disease states including electrolyte abnormalities (potassium), or systemic diseases where imbalance of cardiac autonomic modulation may elicit VT. The VT occurring secondary to those circumstances may occur at heart rates similar to the sinus rate (in this scenario the rhythm is termed “accelerated idioventricular rhythm” rather than VT since the heart rate is normal), thus considered less malignant, and are often self-limiting with correction or resolution of the underlying cause.

RISK FACTORS

- Hypokalemia, hyperkalemia.
- Hypomagnesemia.
- Acid–base disturbances.
- Hypoxemia.
- Neoplasia (e.g., cardiac or splenic hemangiosarcoma).
- Anemia.

VENTRICULAR TACHYCARDIA

(CONTINUED)

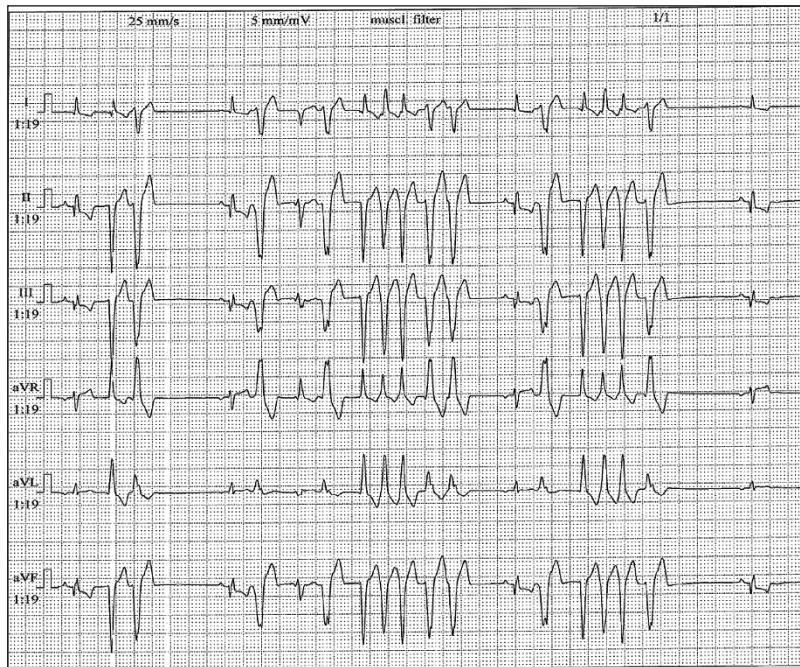


Figure 1.

Ventricular tachycardia. 6-lead ECG demonstrating the wide and bizarre QRS complexes that occur in runs of up to 6 beats in a Doberman pinscher with DCM. Ventricular tachycardia should be treated as soon as possible. Acid-base and electrolyte abnormalities should always be corrected.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

Supraventricular tachycardia with bundle branch block. If P waves can be identified, look for association between P waves and QRS complexes. If there is a consistent PR interval, then the rhythm is supraventricular with bundle branch block. If there is no association between P waves and QRS complexes, the rhythm is probably VT. If P waves cannot be identified due to a fast rate (P buried in preceding T wave), lidocaine administration may result in slowing of the VT rate and P waves may be identified if present. Termination of a tachyarrhythmia after administration of lidocaine supports diagnosis of VT. If no effect with lidocaine, esmolol administration may result in slowing of a supraventricular tachycardia with bundle branch block, so that P waves associated with QRS complexes can be identified.

CBC/BIOCHEMISTRY/URINALYSIS

- Hypokalemia and hypomagnesemia predispose to VT and blunt response to class I antiarrhythmic drugs (e.g., lidocaine, procainamide, mexiletine, and quinidine).
- High amylase and lipase if arrhythmia is secondary to pancreatitis.

- Inflammatory changes may occur on CBC such as increased neutrophil count if arrhythmia secondary to myocarditis.

OTHER LABORATORY TESTS

- Increased cardiac troponin I (cTnI) with myocarditis.
- High T₄ (cats) if arrhythmia is secondary to hyperthyroidism.
- Lyme or tick titers in myocarditis.
- Genetic testing is available at NC State (<https://cvm.ncsu.edu/genetics/>) for arrhythmias originating due to boxer ARVC, Doberman DCM and Rhodesian ridgeback inherited arrhythmias.
- Increased trypsin-like immunoreactivity and pancreatic lipase immunoreactivity if suspect pancreatitis is a cause for the VT.

IMAGING

Echocardiography may reveal underlying structural heart disease.

DIAGNOSTIC PROCEDURES

ECG and long-term ambulatory (Holter) or event recording of the ECG—for detection of intermittent VT in patients with unexplained syncope or weakness.

PATHOLOGIC FINDINGS

Vary with underlying cause.



TREATMENT

APPROPRIATE HEALTH CARE

- Most patients with intermittent VT can safely be evaluated for underlying diseases (echocardiogram, lab work) and it is ideal to establish a true baseline of the arrhythmia quantity and quality by a 24-hour Holter prior to initiating therapy.
- If unstable (laterally recumbent, weak, or frequent syncope), immediate IV treatment in a hospital setting with continuous ECG monitoring may be required. Once the arrhythmia is controlled and patient is hemodynamically stable, oral medication should be instituted. A follow-up 24-hour Holter is required to evaluate efficacy and possible pro-arrhythmic effects of antiarrhythmic therapy.

NURSING CARE

Varies with underlying cause.

ACTIVITY

Boxers tend to have an increased incidence of VT during excitement, so in some cases owners should know what specific situations to avoid. In humans with ARVC, exercise has been shown to exacerbate arrhythmia incidence and risk of SD.

(CONTINUED)

VENTRICULAR TACHYCARDIA**DIET**

Dogs with diet-associated (boutique, exotic-ingredient, or grain-free [BEG] diets) DCM may have an increased incidence of VT and risk of SD.

CLIENT EDUCATION

Alert the owner to the potential for SD.

SURGICAL CONSIDERATIONS

- When possible, determine the cause of the arrhythmia and treat it prior to inducing general anesthesia.
- Assess if VT is correctable with a test dose of lidocaine; if it is, treat as necessary with lidocaine, either using IV boluses or CRI.
- Premedication with acepromazine 0.02–0.05 mg/kg raises the threshold for VF.
- Avoid proarrhythmic drugs such as alpha-2 agonists (xylazine, medetomidine) and thiopental.
- Mask induction is not recommended in inadequately sedated patients with ventricular arrhythmias because increased sympathetic tone during mask induction will aggravate the arrhythmia.
- Continuous ECG monitoring during anesthesia.

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

Correct any hypokalemia or hypomagnesemia, if possible, prior to instituting medical therapy.

Dogs*Acute Life-Threatening VT*

- Administer lidocaine slowly in 2 mg/kg IV boluses (up to 8 mg/kg total) to convert to sinus rhythm; follow with lidocaine CRI, 30–80 µg/kg/min.
- If lidocaine fails—administer procainamide 5–15 mg/kg slow IV bolus (may cause vomiting or hypotension due to negative inotropic effect), followed by 25–50 µg/kg/min IV CRI.
- In cases of refractory VT, lidocaine and procainamide CRIs can be combined.
- If no response to lidocaine or procainamide, amiodarone (*Nexterone*) can be administered as a 2 mg/kg IV bolus infused over 10 minutes, followed by a CRI of 0.8 mg/kg/h for 6 hours, then decrease to 0.4 mg/kg/h or alternatively try slow IV boluses of esmolol (a short-acting beta-blocker) at 0.05–0.1 mg/kg q5min to a cumulative dose of 0.5 mg/kg, or as a 50–200 µg/kg/min CRI.
- If there is inadequate response to the various IV therapies, then PO medication may be administered. Sotalol 1.5–2.5 mg/kg PO q12h may convert dangerous VT within 1–3 hours in such situations, even when the usual IV medications failed. It can be administered in a “loading protocol”

(1.5–2.5 mg/kg PO q4h or q6h), for the first 2 doses, depending on the severity of the VT and myocardial function.

Chronic VT in a Stable Patient

- Sotalol 1–2.5 mg/kg PO q12h.
- Mexiletine monotherapy is not very effective, but combination of mexiletine 4–8 mg/kg PO q8h with a beta-blocker such as atenolol 0.25–1 mg/kg PO q12h or sotalol 1–2.5 mg/kg PO q12h may be more effective for refractory VT, especially in boxers.
- Amiodarone may be used for refractory VT in dogs with poor myocardial function (loading dosage of 5–15 mg/kg PO q12h for 2–14 days, maintenance dosage of 6–15 mg/kg PO q24h). Requires regular monitoring due to the risk for serious side effects in dogs (hepatotoxicity, neutropenia, thyroid dysfunction). Signs of toxicity include anorexia, vomiting, lethargy, and hepatic enzyme elevation. Amiodarone hepatopathy is reversible after reduction of dosage or discontinuation of the drug. Overt clinical signs of toxicity generally resolve within a few days of stopping amiodarone. Monitoring of serial serum chemistries is recommended, since increases in liver enzyme activities usually precede the onset of clinical signs of amiodarone toxicity. Liver enzymes should be measured after 7 days of drug loading and once monthly during maintenance therapy.
- Amiodarone can be combined with atenolol 0.5–1.0 mg/kg twice a day to enhance antiarrhythmic effects.
- In German shepherd dogs the combination of mexiletine and sotalol is the most effective therapy for VT. Sotalol monotherapy should be avoided due to its proarrhythmic effects in this breed.

Cats

- Use lidocaine cautiously and only for sustained VT; neurotoxicity (seizures) is common in cats. Use one-tenth of the dosage used for dogs.
- For oral maintenance therapy of severe VT in cats use sotalol 10 mg/cat q12h or atenolol 6.25–12.5 mg PO q12h.

CONTRAINDICATIONS

Avoid atropine, catecholamines (e.g., epinephrine, dopamine) until arrhythmia is controlled.

PRECAUTIONS

- Use beta-blockers cautiously in animals with CHF. Monitoring by echocardiogram is recommended to check for worsening of myocardial function due to beta blockade.
- Sotalol, when used as a sole agent, and other drugs that prolong action potential duration may worsen VT in German shepherd dogs with inherited ventricular arrhythmias.

POSSIBLE INTERACTIONS

Quinidine and amiodarone raise digoxin levels.

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

- Holter monitoring is preferred for assessment of severity of the arrhythmia and efficacy of antiarrhythmic therapy; the goal of antiarrhythmic therapy is to reduce the frequency of ventricular ectopy by >85%.
- Serial ECG and telemetry can be used alternatively—but not as meaningful as Holter monitoring because ventricular premature complexes and paroxysmal VT can occur sporadically throughout the day.

PREVENTION/AVOIDANCE

- Correct predisposing factors such as hypokalemia, hypomagnesemia, myocardial hypoxia, and digoxin toxicity.
- In boxers, limit significant stress or excitement as the increase in sympathetic tone may exacerbate the arrhythmia.

POSSIBLE COMPLICATIONS

- Syncope.
- SD.

EXPECTED COURSE AND PROGNOSIS

- If cause is metabolic—condition may resolve with a good prognosis.
- If condition is associated with cardiac disease—prognosis is guarded because the underlying heart disease is likely chronic and progressive and therefore the arrhythmias may also worsen over time; presence of significant VT increases the risk of SD.
- If VT associated with hemangiosarcoma (cardiac or splenic)—the long-term outcome is grave due to the poor prognosis of the underlying disease.
- Approximately 50% of German shepherd dogs with more than 10 runs of VT/24 hours die suddenly.
- Doberman pinschers with VT and DCM may die suddenly during their first syncopal episode.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

If German shepherd dogs reach the age of 18 months, the probability of SD decreases, similarly in Rhodesian ridgebacks, after 30 months of age.

ZOONOTIC POTENTIAL

None

PREGNANCY/FERTILITY/BREEDING

N/A

SEE ALSO

- Cardiomyopathy, Arrhythmogenic Right Ventricular.

VENTRICULAR TACHYCARDIA

(CONTINUED)

- Cardiomyopathy, Dilated—Dogs.
- Chagas Disease (American Trypanosomiasis).
- Digoxin Toxicity.
- Myocarditis.
- Ventricular Arrhythmias and Sudden Death in German Shepherds.
- Ventricular Premature Complexes.

ABBREVIATIONS

- ARVC = arrhythmogenic right ventricular cardiomyopathy.

- CHF = congestive heart failure.
- cTnI = cardiac troponin I.
- DCM = dilated cardiomyopathy.
- PDK4 = pyruvate dehydrogenase kinase 4.
- SD = sudden death.
- T₄ = thyroxine.
- VF = ventricular fibrillation.
- VT = ventricular tachycardia.

Suggested Reading

Cunningham SM, Sweeney JT, MacGregor J, et al. Clinical features of English bulldogs

with presumed arrhythmogenic right ventricular cardiomyopathy: 31 cases (2001–2013). *J Am Anim Hosp Assoc* 2018, 54(2):95–102.

Authors Marc S. Kraus and Anna R.M. Gelzer

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Client Education Handout
available online

VOMITING, CHRONIC



BASICS

DEFINITION

Persistent vomiting lasting longer than 5–7 days or vomiting that occurs intermittently several days/week. This condition is usually nonresponsive to symptomatic treatment.

PATHOPHYSIOLOGY

- Vomiting occurs when the vomiting center, located within the medulla oblongata, is activated by the humoral or neural pathway.
- There are four main components to the vomiting reflex: (1) visceral receptors within the gastrointestinal (GI) tract; (2) vagal and sympathetic afferent neurons; (3) chemoreceptor trigger zone (CRTZ); and (4) vomiting center.
- The humoral pathway is mediated via activation of the CRTZ and is affected by bloodborne triggers such as uremic toxins, drug toxicity, and endotoxemia.
- The neural pathway is mediated via activation of the vomiting center and is affected by disorders associated with obstruction, distension, or inflammation of the GI tract.
- All causes of vomiting (including the vestibular apparatus and cerebrum) are ultimately mediated via the vomiting center.

SYSTEMS AFFECTED

- Endocrine/metabolic—dehydration, electrolyte and acid-base imbalances.
- Cardiovascular—hypovolemia; electrolyte or acid-base imbalances can cause arrhythmias.
- GI—esophagitis and subsequent esophageal stricture.
- Respiratory—aspiration pneumonia.
- Nervous—altered mentation.

SIGNALMENT

- Dog and cat.
- Young animals are more likely to ingest foreign bodies; linear foreign bodies are more common in cats.
- Confirmed or suspected breed predispositions—brachycephalic breeds are prone to pyloric outflow obstruction secondary to mucosal hypertrophy; basenji, German shepherd dog, and shar-pei are prone to inflammatory bowel disease (IBD); Rottweiler are prone to eosinophilic IBD; Airedale terrier prone to pancreatic carcinoma; beagle, Bedlington terrier, cocker spaniel, Doberman pinscher, Labrador retriever, Skye terrier, and standard poodle are prone to chronic hepatitis. Yorkshire terrier predisposed to intestinal lymphangiectasia.

SIGNS

Historical Findings

- Hematemesis, decreased appetite or anorexia, and melena, may suggest gastric disease.

- Diarrhea and profound weight loss may suggest intestinal disease.
- Signs such as weakness, polyuria, or jaundice may relate to other underlying metabolic diseases.

Physical Examination Findings

- Weight loss and poor hair coat may indicate chronic malnutrition.
- Abdominal palpation may reveal abdominal distention, pain, thickened bowel loops, lymphadenopathy, or mass effects.
- Tacky mucous membranes and prolonged skin tenting if dehydration is present; pale membranes if patient is anemic.
- Oral examination may reveal uremic ulcerations or sublingual string foreign bodies.
- Rectal examination may detect diarrhea, hematochezia, or melena.

CAUSES

Esophageal Disease

- Hiatal hernia (more commonly associated with regurgitation).
- Gastroesophageal reflux (more commonly associated with regurgitation).

Infectious Disease

- *Helicobacter*-related gastritis.
- Histoplasmosis.
- Pythiosis.
- Small intestinal bacterial overgrowth.
- Gastric or intestinal parasites.

Metabolic Diseases

- Renal disease.
- Hepatobiliary disease.
- Hypoadrenocorticism.
- Chronic pancreatitis.
- Diabetic ketoacidosis (DKA).
- Electrolyte abnormalities—hypo-/hyperkalemia, hyponatremia, hypercalcemia.

Inflammatory Bowel Disease

- Lymphocytic, plasmacytic, eosinophilic, or granulomatous.
- Gastritis, enteritis, or colitis.

Obstructive GI Disease

- Foreign body.
- Chronic hypertrophic pyloric gastropathy.
- Intussusception.

Neoplastic Disease

- GI lymphoma, adenocarcinoma, fibrosarcoma, GI stromal cell tumor.
- Pancreatic adenocarcinoma.
- Gastrin-secreting tumor (gastrinoma).
- Mast cell tumor.

Neurologic

- Cerebral edema.
- CNS tumors.
- Encephalitis/meningoencephalitis.
- Vestibular disease.

Motility Disorders

- Postgastric dilatation.
- Postsurgical—gastric, duodenal.

- Electrolyte imbalances.
- Ileus.

Miscellaneous

- Drugs (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], glucocorticoids, chemotherapy, antibiotics, antifungals).
- Food sensitivity.
- Toxicity.

Additional Causes

- Parasitic (cats)—dirofilariasis, *Ollulanus tricuspis*.
- Inflammatory—cholecystitis, cholangiohepatitis.
- Metabolic—hyperthyroidism.
- Functional—constipation/obstipation.

RISK FACTORS

Breed-associated disease (see Signalment).



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Vomiting must first be differentiated from regurgitation.
- Regurgitation is a passive process and occurs without an abdominal component, thus localizing disease to the esophagus.
- Vomiting is a centrally mediated reflex often preceded by prodromal signs of restlessness, nausea, salivation, and repeated swallowing.

CBC/BIOCHEMISTRY/URINALYSIS

- Chronic GI bleeding can cause a non-regenerative anemia, often with characteristics of iron deficiency (microcytosis, hypochromasia, thrombocytosis).
- Non-regenerative anemia may also occur secondary to chronic metabolic or inflammatory diseases.
- Inflammatory conditions may cause neutrophilic leukocytosis and monocytosis.
- Eosinophilia can occur from eosinophilic IBD, hypoadrenocorticism, and GI parasitism.
- Thrombocytopenia has been reported with IBD.
- Dehydration increases the packed cell volume and total protein.
- Electrolyte and acid-base imbalances reflect severity of losses and can help to localize disease.
- Hypochloremic metabolic alkalosis, often with hypokalemia, suggests gastric outflow obstruction.
- Hyperkalemia suggests hypoadrenocorticism or oliguric/anuric renal failure; occasionally, enteritis caused by trichuriasis or bacterial infection (salmonellosis) mimics hypoadrenocorticism.
- Metabolic acidosis is common in patients with dehydration, renal failure, DKA, and severe gastroenteritis with diarrhea.

(CONTINUED)

- Increased liver enzyme activity, hypoalbuminemia, hyperbilirubinemia, hypoglycemia, or low urea nitrogen concentration suggest hepatic disease.
- Persistent hyperglycemia and glucosuria is consistent with diabetes mellitus.
- Hyperglobulinemia may indicate chronic inflammation or infection.
- Hypoproteinemia, hypocholesterolemia, lymphopenia, and hypomagnesemia occur secondary to a protein-losing enteropathy caused by infiltrative intestinal diseases such as lymphocytic plasmacytic gastroenteritis, neoplasia, histoplasmosis, or intestinal lymphangiectasia.
- Urinalysis is used to rule out renal failure and DKA.
- Aciduria in the hypokalemic, hypochloremic, alkalic patient suggests gastric outflow obstruction.

OTHER LABORATORY TESTS

- Resting cortisol to screen for hypoadrenocorticism. A resting cortisol $<2 \mu\text{g}/\text{dL}$ should be followed with an ACTH stimulation test.
- Pancreatic lipase immunoreactivity assay may help confirm pancreatitis together with supportive history, physical exam findings, and ultrasound.
- Serum cobalamin and folate as indicators of intestinal absorption.
- Pre- and postprandial bile acids to screen for hepatobiliary dysfunction.
- Fecal testing for GI parasitism.

IMAGING

- Survey radiographs of the abdomen help identify foreign bodies, GI distension with fluid or gas, and displacement, malposition, shape, and/or size changes of abdominal organs.
- Survey radiographs of the thorax are used to evaluate for pulmonary metastases, gross esophageal abnormalities, or infectious disease.
- A barium upper GI series can be used to identify foreign bodies, GI wall masses or infiltrative disease, mucosal ulceration, delayed gastric emptying, and motility disorders; however, the procedure is relatively insensitive for detection of mucosal ulceration.
- Abdominal ultrasonography to identify abnormalities of the liver, gallbladder, kidneys, pancreas, GI tract, and mesenteric lymph nodes.
- CT and MRI further evaluate for abnormalities of abdominal organs.

DIAGNOSTIC PROCEDURES

- Gastroduodenoscopy—allows direct inspection of the gastric and intestinal lumen to identify gross mucosal lesions and foreign bodies and provides a minimally invasive method of biopsy to evaluate for microscopic disease. Limitations of endoscopy include the working length of the endoscope (unable to

access the jejunum in large-breed dogs) and depth of the biopsies.

- Laparoscopy or exploratory laparotomy is used for more extensive diagnostic and therapeutic procedures.



TREATMENT

APPROPRIATE HEALTH CARE

Specific treatment should be aimed at eliminating the underlying cause in conjunction with supportive therapy. Care may be inpatient or outpatient depending on the case.

NURSING CARE

- If vomiting is intractable, stop oral intake of food and water for 12–24 hours or until the vomiting episodes are better controlled with antiemetics.
- Use crystalloid fluid therapy to replace deficits and to provide for maintenance and ongoing losses.
- Supplement potassium if hypokalemia is present; 20 mEq of KCl/L of fluid can be safely added for replacement and maintenance; use higher concentrations if severe hypokalemia is present.

DIET

- Debilitated patients and those in poor nutritional condition may need supplemental parenteral or enteral nutrition.
- Dietary therapy for patients with suspected food allergy or with IBD should use an elimination diet containing a single, novel protein source or a hydrolyzed diet.

CLIENT EDUCATION

Dependent on underlying disease.

SURGICAL CONSIDERATIONS

Use surgical treatment if uncontrolled hemorrhage, obstruction, or perforation is suspected.



MEDICATIONS

DRUG(S) OF CHOICE

- Antisecretory drugs such as H₂-receptor blockers (e.g., famotidine, ranitidine) or proton pump inhibitors such as omeprazole (more potent)—famotidine 0.5–1 mg/kg PO, IV, or SC q12h; ranitidine 1–2 mg/kg PO, IV q12h; omeprazole 0.7–1.5 mg/kg PO q12h.
- Protectants such as sucralfate 0.25–1 g/dog PO q6–12h or 0.25 g/cat PO q6–12h to accelerate gastric mucosal healing; can be used with antisecretory drugs for patients with evidence of upper GI bleeding (e.g., hematemesis or melena).
- Antibiotics—indicated for treatment of *Helicobacter*-associated gastritis, small intestinal

VOMITING, CHRONIC

bacterial overgrowth (SIBO), and as an adjunct to corticosteroids in the treatment of IBD.

- Metronidazole—may be used at 10 mg/kg PO q12h in conjunction with corticosteroids to treat IBD, although evidence of direct benefit of this approach is currently lacking.

Antibiotic-responsive enteropathy (tylosin-responsive enteropathy)—tylosin is the drug of choice administered at 10–40 mg/kg q12h for 8–12 weeks. Alternative option is metronidazole 10 mg/kg q12h for 8–12 weeks, although tylosin may be superior for this disorder.

- Use corticosteroids in conjunction with dietary changes to treat biopsy-confirmed IBD; azathioprine, chlorambucil, or cyclosporine can also be used in patients with poor response to corticosteroids alone or to decrease the dosage of steroids required to control symptoms. Avoid the use of more than two immunomodulatory drugs given concurrently.

Prokinetic drugs (e.g., metoclopramide, cisapride, or erythromycin) are used to treat delayed gastric emptying not associated with obstructive disease. Metoclopramide 0.2–0.5 mg/kg IV, IM, PO q6–8h; more effective as a CRI of 1–2 mg/kg q24h in hospitalized patients.

- Pyrantel pamoate is effective for *Physaloptera*; fenbendazole is effective for *Ollulanus*.

Iron supplementation for animals with chronic GI bleeding that develop microcytic hypochromic anemia.

- Surgery and/or chemotherapy for neoplasia, depending on the tumor type and location.

Paraneoplastic hypersecretion of gastric acid, as occurs with mastocytosis and gastrin-secreting pancreatic tumors, is best treated with antisecretory drugs (e.g., omeprazole).

- Reserve antiemetics for patients with persistent vomiting unresponsive to treatment of the underlying disease. Maropitant 1 mg/kg SC q24h, 2 mg/kg PO q24h. Chlorpromazine 0.5 mg/kg SC, IM q6–8h. Ondansetron 0.2–0.5 mg/kg SC, IV q8–12h, 0.5–1.0 mg/kg PO q12h.

Vomiting caused by chemotherapy is best treated with ondansetron 0.5–1 mg/kg IV, PO given 30 minutes before chemotherapy.

CONTRAINDICATIONS

N/A

PRECAUTIONS

- Do not give α -adrenergic blockers such as chlorpromazine to dehydrated patients as they can cause hypotension.

Use antiemetics with caution, as they can mask the underlying problem.

- Metoclopramide can cause lethargy, restlessness, agitation, and other behavioral changes, particularly in cats.

Corticosteroids are immunosuppressive and are a risk factor for development of GI

VOMITING, CHRONIC

(CONTINUED)

ulceration; use caution when treating IBD with corticosteroids at high dosages or for long periods.

- Azathioprine and chlorambucil are myelotoxic; monitor CBCs for neutropenia and thrombocytopenia every 2 weeks for the first month of treatment and monthly thereafter.
- Cyclosporine can exacerbate vomiting and diarrhea when used at high dosages; use with caution in patients with renal disease.
- Do not use anticholinergics as antiemetics, as they can exacerbate vomiting by causing gastric atony and gastric retention.
- Metoclopramide and cisapride are contraindicated in patients with GI obstruction.

POSSIBLE INTERACTIONS

Ranitidine interferes with hepatic metabolism of theophylline, phenytoin, and warfarin, and should not be used concurrently with these drugs. Avoid use of cimetidine because it is a weak H₂-receptor antagonist and is a potent inhibitor of the cytochrome P450 enzyme pathway.

ALTERNATIVE DRUG(S)

N/A

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

- Frequency of vomiting.
- Body weight; body condition score.

V

PREVENTION/AVOIDANCE

N/A

POSSIBLE COMPLICATIONS

- Esophagitis.
- Aspiration pneumonia.

EXPECTED COURSE AND PROGNOSIS

Varies with underlying disease.

**MISCELLANEOUS****ASSOCIATED CONDITIONS**

N/A

AGE-RELATED FACTORS

N/A

ZOONOTIC POTENTIAL

Dependent on underlying cause.

PREGNANCY/FERTILITY/BREEDING

N/A

SYNONYMS

N/A

SEE ALSO

- Bilious Vomiting Syndrome.
- Constipation and Obstipation.
- Food Reactions (Gastrointestinal), Adverse.
- Gastric Motility Disorders.
- Gastritis, Chronic.
- Gastroduodenal Ulceration/Erosion.
- Gastroenteritis, Eosinophilic.
- Hypertrophic Pyloric Gastropathy, Chronic.

- Ileus.
- Inflammatory Bowel Disease.
- Intussusception.
- Pancreatitis—Cats.
- Pancreatitis—Dogs.

ABBREVIATIONS

- ACTH = adrenocorticotrophic hormone.
- CRTZ = chemoreceptor trigger zone.
- DKA = diabetic ketoacidosis.
- GI = gastrointestinal.
- IBD = inflammatory bowel disease.
- NSAID = nonsteroidal anti-inflammatory drug.
- SIBO = small intestinal bacterial overgrowth.

Suggested Reading

Guilford WG, Center SA, Williams DA, Meyer DJ. Chronic gastric diseases. In: Strombeck's Small Animal Gastroenterology, 3rd ed. Philadelphia, PA: Saunders, 1996, pp. 275–302.

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**Client Education Handout
available online**

WHIPWORMS (TRICHURIASIS)



BASICS

OVERVIEW

- The whipworm, *Trichuris*, infects the cecum of dogs (*T. vulpis*) and cats (*T. campanula* and *T. serrata*); feline trichuriasis is extremely rare in continental United States.
- Life cycle is direct; infection is acquired by ingestion of larvated eggs; infective eggs can persist in environment for months to years.
- Infection can be asymptomatic or cause bloody diarrhea and large bowel inflammation.
- Clinical signs can occur before patency, i.e., before eggs are shed in feces; prepatent period is approximately 70–90 days.
- No extraintestinal migration occurs.

SIGNALMENT

- Dogs and cats.
- No age, breed, or sex predilections.

SIGNS

- Range from asymptomatic to severe.
- Intermittent large bowel diarrhea often containing mucus and fresh blood (hematochezia).
- Bloody diarrhea with dehydration, anemia, and weight loss in severe cases.
- Signs can occur before eggs detectable in feces.
- Acute to chronic debilitation.

CAUSES & RISK FACTORS

- Ingestion of infective (larvated) eggs from fecally contaminated environment.
- Eggs accumulate in environment and remain infective for months to years, especially in soil in moist, shady areas.
- Return of dog to an environment contaminated with infective eggs after anthelmintic treatment will result in reinfection.



DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

- Bacterial (spirochaetal) infections of cecum.
- Hookworm infection—identify eggs in feces; signs include anemia, pale mucous membranes, melena rather than hematochezia.
- Inflammatory bowel disease.
- Gastrointestinal ulcers.
- Dietary indiscretion.
- Capillarid infections (*Pearsonema*, *Eucoleus*)—eggs similar in appearance but smaller with roughened surface; infect urinary or respiratory tracts, respectively, rather than gastrointestinal tract; usually asymptomatic.
- Secondary pseudo-hypoadrenocorticism in severe trichuriasis with metabolic acidosis, hyponatremia, hyperkalemia, and dehydration; adrenocorticotropic hormone (ACTH) stimulation response is normal in cases of trichuriasis.

CBC/BIOCHEMISTRY/URINALYSIS

Usually normal; hyponatremia, hyperkalemia, and metabolic acidosis can occur in severe cases.

OTHER LABORATORY TESTS

ACTH stimulation test in severe cases with electrolyte disturbances to differentiate trichuriasis from hypoadrenocorticism.

IMAGING

N/A

DIAGNOSTIC PROCEDURES

- Centrifugal flotation of feces in sugar solution (specific gravity >1.2) preferred method.
- Differentiate *Trichuris* eggs (brown, ovoid or lemon-shaped with prominent bipolar plugs, smooth shell, single cell within egg, ~90 × 45 µm) from similar capillarid eggs (smaller, roughened shell surface).
- ELISA for whipworm antigen in feces—commercial test detects antigen produced by male and female adult and immature worms, can detect prepatent infection; combine with microscopy as above.



TREATMENT

- Outpatient treatment with anthelmintic for most cases.
- Severe cases with dehydration and electrolyte disturbances require inpatient fluid therapy in addition to anthelmintic.



MEDICATIONS

DRUG(S) OF CHOICE

- Fenbendazole—50 mg/kg PO q24h for 3 days; repeat monthly 3 times; extra-label in cats.
- Febantel/praziquantel/pyrantel pamoate—label dose PO in dogs.
- Milbemycin oxime—0.5 mg/kg PO q30 days in dogs.
- Moxidectin/imidacloprid—label dose in dogs.



FOLLOW-UP

PATIENT MONITORING

Repeat fecal examination for trichurid eggs and/or retreat with anthelmintic at 3 weeks and at 3 months following initial treatment or once a month for 3 months to detect and eliminate recently matured adults.

PREVENTION/AVOIDANCE

- Prompt removal and disposal of feces to prevent environmental contamination with infective eggs.

- Anthelmintic treatment of infected dogs to prevent shedding of eggs and contamination of environment.

EXPECTED COURSE AND PROGNOSIS

Good prognosis following treatment and implementation of preventive measures.



MISCELLANEOUS

ZOONOTIC POTENTIAL

Relatively rare cases of human infection with *T. vulpis* have been diagnosed based on morphologic differences between eggs of the human whipworm, *T. trichiura*, and those of *T. vulpis*.

ABBREVIATIONS

- ACTH = adrenocorticotropic hormone.

INTERNET RESOURCES

<http://www.capcvet.org>

Suggested Reading

Adolph C, Barnett S, Beall M, et al.

Diagnostic strategies to reveal covert infections with intestinal helminths in dogs. Vet Parasitol 2017, 247(0):108–112.

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