

Neurology

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OUTLINE

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Neurologic diseases in cats present a unique challenge to the feline practitioner because of the inherent difficulties of examining feline patients. Cats are not prone to the same diseases as dogs, and often clinical signs in cats may be atypical, further complicating the veterinarian's ability to develop a neuroanatomic diagnosis. The neurologic exam may be markedly altered in cats as a result of their high sympathetic overdrive and their physiologic responses to stress; therefore, in many instances, unless the patient is extremely obtunded or unusually compliant, a complete examination may not be possible. Because the examiner may have difficulty even eliciting the most basic reflexes and postural responses in an apprehensive cat, minimal restraint, a quiet environment, and extreme patience are imperative. Although a complete neurologic assessment may not always be possible in a fractious cat, a thorough history, physical examination, and observation of the cat in most cases will allow the practitioner to develop a neuroanatomic diagnosis. On the basis of this diagnosis, the veterinarian can generate a reasonable list of differentials and determine appropriate ancillary testing. Detailed descriptions of individual disorders and abnormalities on the neurologic exam are discussed in the following sections. For a detailed description of the neurologic exam, the reader is referred to *Veterinary Neuroanatomy and Clinical Neurology*, by Dr. A. DeLahunta and Dr. R. Glass (Box 27-1).

INTRACRANIAL DISEASES

Seizure Disorders

Seizure disorders in cats present a significant diagnostic challenge and may result from primary intracranial

disease or extracranial disease. Seizures can be classified as focal, partial, or generalized.³⁴ A *focal* seizure is one in which there is spontaneous discharge of neurons of the prosencephalon in the absence of clinical signs and that may be present in the interictal period but is detectable only with use of an electroencephalogram (EEG). A *partial* seizure is a focal seizure that may be observed clinically and consists of varying degrees of motor or sensory abnormalities in the absence of loss of consciousness. A *simple partial* seizure results in abnormal motor activity such as twitching, tremors, limb flexion, ptalism, facial twitching, and mydriasis with no alteration in sensorium. A *complex partial* seizure may resemble the simple partial seizure, but changes in the mental status are evident, including maniacal running, staring into space, aggression, and self-inflicted trauma.³⁴ *Generalized seizures* (grand mal) are more easily recognized by pet owners and result in loss of consciousness, recumbency, tonic-clonic muscle activity in the limbs, chewing movements, ptalism, mydriasis, and loss of stool and urine.³⁴ The seizure type does not necessarily reflect underlying etiology,¹¹⁴ although seizure pattern in cats is reportedly different from that of dogs, with complex partial seizures being more common than generalized seizures.¹⁰⁹ Cluster seizures are defined as more than two seizures in a 24-hour period, whereas status epilepticus (SE) is a seizure lasting more than 5 minutes or multiple seizures between which there is no recovery.³⁴ Structural brain disease has been identified as the most common cause of seizures in cats and includes meningoencephalitis, feline ischemic encephalopathy, neoplasia, trauma, abscess, and vascular disorders.^{4,109} However, *idiopathic epilepsy* (defined as recurrent seizures in the absence of an underlying cause) is an important and often

BOX 27-1**Additional Resources**

DeLahunta A, Glass R: *Veterinary neuroanatomy and clinical neurology*, St Louis, 2009, Saunders.

Brain tumors in dogs and cats, North Carolina State College of Veterinary Medicine:
http://cvm.ncsu.edu/vth/clinical_services/neuro/brain_tumor.html

Comparative neuromuscular laboratory, University of California, San Diego:
<http://vetneuromuscular.ucsd.edu/>

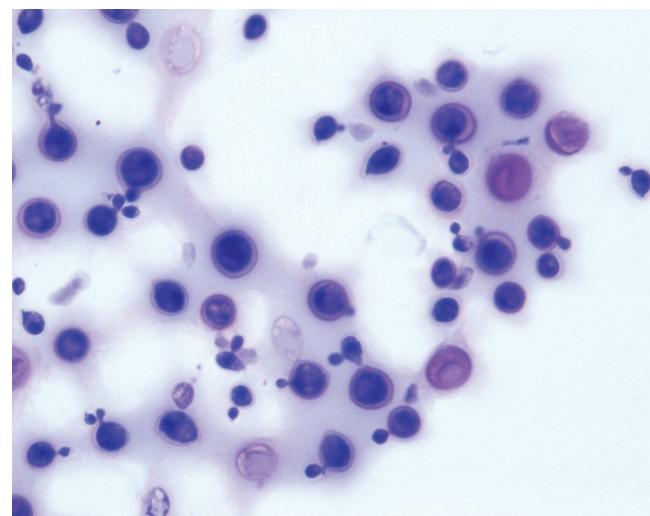


FIGURE 27-1 Cryptococcus organisms found in cerebrospinal fluid. (Wright's stain.) (From Cowell RL, Tyler RD, Meinkoth JH et al, editors: *Diagnostic cytology and hematology of the dog and cat*, ed 3, St Louis, 2008, Mosby Elsevier.)

overlooked cause of seizures in cats, accounting for 25% of cases in one report of 91 cats.¹¹⁴ Cats with idiopathic epilepsy tended to be younger than those with structural brain disease, with a mean age of 3.5 years in two publications.^{114,126} Feline hippocampal necrosis should also be considered in the differential diagnosis for a seizuring cat. It is characterized by acute onset seizures and behavioral changes in young to middle-aged cats with poor response to conventional anticonvulsant therapy and progressively worsening signs.⁴⁰ Histopathologic findings include severe, diffuse, bilateral necrosis of neurons in the hippocampus and piriform lobes.⁴⁰ Prognosis is guarded.

Diagnosis

Evaluation of affected cats requires a thorough history and neurologic exam, as well as consideration of the breed, age, and vaccine history of the patient. A thorough description of the seizure as well as duration, frequency, and the presence or absence of interictal abnormalities are vital to formulate a diagnostic plan. An initial minimum database should include a complete blood count, chemistry panel, blood pressure measurement, urinalysis, and testing for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV). Thoracic radiographs, abdominal ultrasonography, echocardiography, bile acid assessment, and thyroid testing may all be part of the workup, depending on the results of the physical examination, history, and preliminary testing. If a metabolic or systemic cause is ruled out through the preliminary workup, advanced imaging and cerebrospinal fluid (CSF) analysis is indicated. Magnetic resonance imaging (MRI) is the most reliable imaging modality for the diagnosis of structural diseases of the brain on account of its superior anatomic detail.^{4,34}

CSF analysis is an invaluable resource in the diagnosis of many primary encephalopathies, but findings are rarely specific and results must be interpreted in light of clinical and MRI findings. CSF analysis infrequently provides a definitive diagnosis, unless infectious agents such as *Cryptococcus* (Figure 27-1) or neoplastic cells are identified. In one report, despite extensive evaluation, a

definitive diagnosis could not be made after CSF analysis in 37% of cats.¹⁷

Processing of CSF is typically done by a clinical pathologist and may include evaluation of the following parameters: color, turbidity, specific gravity, protein concentration, red blood cell count, nucleated cell count and differential analysis, and glucose concentration. In cases of specific infectious diseases, culture and sensitivity, gram stain, infectious disease titers, or polymerase chain reaction (PCR) assays may be indicated. Cytologic analysis should be performed using a hemocytometer after concentration of the sample because of the typically low number of cells present in CSF, even in the face of inflammatory disease.

Collection techniques require a thorough understanding of neuroanatomy as well as application of the proper technique.¹⁷ In most cats the cerebellomedullary cistern is the site of choice, although lumbar collection may be preferable in cats with a thoracolumbar myelopathy.

A 22-g, 1.5-inch spinal needle with a stylet is appropriate for most cats. General anesthesia is induced, and the desired site of collection is clipped and aseptically prepped. For collection from the cerebellomedullary cistern, the cat is placed in right lateral recumbency for a right-handed clinician with the neck flexed. The wings of the atlas and occipital protuberance are palpated and an imaginary line drawn between the wings of the atlas and the point where this line transects midline. The spinal needle is inserted slowly, with frequent removal of the stylet to evaluate CSF flow. When the subarachnoid space is entered, the CSF (at least 1 mL) can be allowed to passively drip into a sterile glass tube.¹⁷

Collection from the lumbar cistern can be performed with the patient in sternal or right or left lateral recumbency. In cats fluid is typically collected from the L6-7

TABLE 27-1 Drugs Used for Control of Seizures in Cats

Drug	Dose	Adverse effects	Comments
Phenobarbital	2.5 mg/kg, PO, every 12 hours	Thrombocytopenia, facial pruritus, neutropenia, swelling of the feet, hepatotoxicity	Monitor drug levels 10 days after starting therapy or change in dose; monitor drug levels, CBC, chemistries, bile acids every 4 months
Zonisamide	5 mg/kg, PO, once daily	Anorexia, vomiting, diarrhea, somnolence, ataxia	Recommended for cats refractory to phenobarbital
Levetiracetam	20 mg/kg, PO, every 8 hours	Not reported	No hepatic metabolism
Potassium bromide		Eosinophilic pneumonitis	Not recommended
Diazepam		Hepatic necrosis	Not recommended

PO, By mouth; CBC, complete blood count.

intervertebral space. With the patient positioned such that the spine is flexed, L7 is palpated and the spinal needle inserted perpendicularly along the cranial border of the dorsal spinous process of L7. A twitch of the tail or limb can be felt once the needle is advanced into the canal. It is best to attempt to collect from the dorsal subarachnoid space instead of passing the needle through the nervous structures to the floor of the canal. Once CSF flow is evident, fluid can be collected passively into a glass tube or extracted with a 3-mL syringe and T-connector.

Although CSF collection is usually a safe and rapid diagnostic procedure, it may be contraindicated in some instances. For example, cats with known or suspected increased intracranial pressure may be at high risk of brain herniation, either of the cerebrum under the tentorium cerebelli or of the brain stem and cerebellum through the foramen magnum. Many patients with neurologic disease are poor anesthetic candidates, and clinicians should carefully consider the risk-to-benefit ratio, as well as take special precautions in anesthetizing these cases. Ketamine is considered relatively unsafe in patients with disorders of the brain because of its potential to increase intracranial pressure, whereas propofol is relatively safe as an induction agent. An adequate plane of anesthesia is vital to prevent movement of the patient during the spinal tap. Intubation and supplemental oxygen are indicated in most cases to maintain the airway and provide inhalant anesthesia if necessary.

Specific testing and descriptions for most primary diseases of the brain are described in further detail later in this chapter, in the section that deals with disorders of the brain.

Treatment

Treatment is directed at the underlying disease and pharmacologic management of the seizures (Table 27-1). Phenobarbital (PB) is the drug of choice for most feline seizure disorders because of its efficacy, relative safety, ease of administration, and bioavailability.^{34,133} A

starting dose of 2.5 mg/kg, administered orally every 12 hours, is recommended,¹³³ but serum PB concentrations vary greatly among individuals on the same dosage, which suggests that there are differences in elimination kinetics among populations of cats.²³ These differences emphasize the need for individual monitoring of cats receiving PB,²³ and researchers recommend more frequent monitoring of PB levels in cats compared with dogs.¹⁰⁸ Elimination of PB may be accelerated in cats receiving steroids and in kittens, which suggests a probable need for higher dosing in these individuals.¹⁰⁸ Toxicity is extremely unusual in cats receiving therapeutic doses but may include thrombocytopenia, facial pruritus, neutropenia, or swelling of the feet.¹⁰⁸ Hepatotoxicity is equally rare. The author suggests checking PB levels approximately 10 days after initiation of therapy or after a change in dose, as well as every 4 months along with a complete blood count, chemistry panel, and assessment of bile acids. Samples can be drawn at any time during the day.

Potassium bromide (KBr) is commonly used in dogs as an add on to PB or in patients with hepatic disease. Although relatively effective for seizure control (seizures were eradicated in 7 of 15 cats in one report), KBr has fallen out of favor for cats because of the high incidence of drug-induced eosinophilic pneumonitis associated with its use.¹³ Similarly, diazepam, once considered the second line of therapy for controlling seizures in cats, is not recommended owing to the risk of fatal hepatic necrosis associated with oral administration.¹⁸ Zonisamide, a newer anticonvulsant medication, has been used by the author in cats refractory to PB with promising results. Toxicity is reportedly low, but approximately half the cats in one study developed adverse reactions such as anorexia, vomiting, diarrhea, somnolence, and ataxia.⁵² Further studies are needed regarding efficacy and pharmacokinetics of this drug, but anecdotally, a starting dose of 5 mg/kg, administered orally once daily, has proved effective in a number of cases.

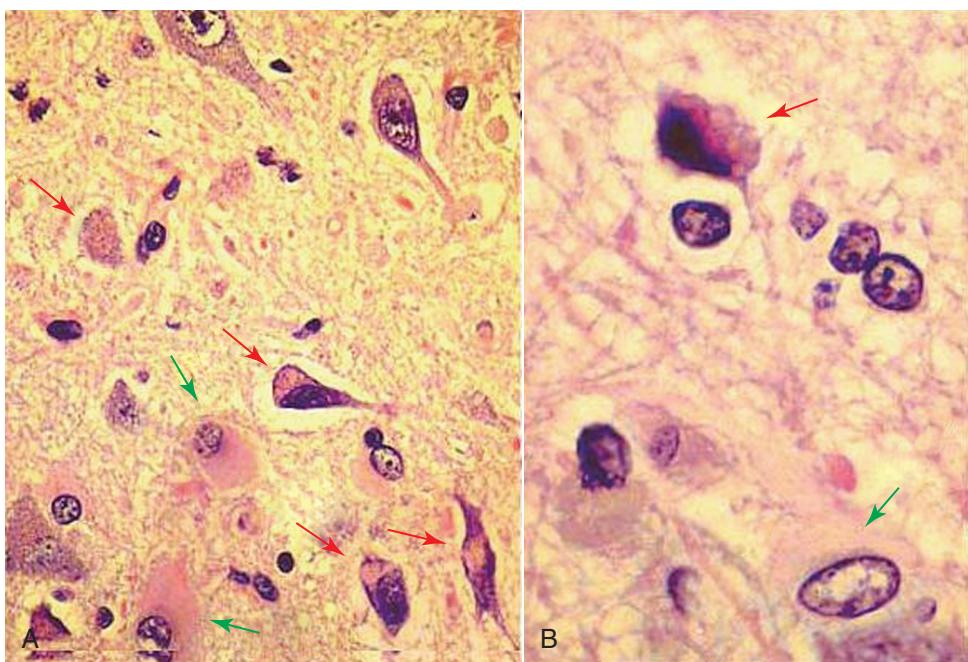


FIGURE 27-2 A, Storage vacuoles in neurons of an animal with Niemann–Pick disease. B, Cytoplasmic pallor of choroid plexus epithelium due to accumulation of storage material. (Reprinted with permission from DeLahunta A: Degenerative diseases of the central nervous system. In Summers BA, Cummings JF, DeLahunta A, editors: Veterinary neuropathology, St Louis, 1995, Mosby.)

Levetiracetam, another relatively new drug, has been shown to be an effective and safe drug when used as an adjunct to PB therapy in cats with idiopathic epilepsy.³ Adverse effects were not reported, and 7 of 10 cats treated experienced a greater than 50% reduction in seizure frequency and none of the cats experienced SE after beginning the drug.³ It is noteworthy that there appears to be no hepatic metabolism. The suggested starting dose is 20 mg/kg, administered orally every 8 hours.

Prognosis for seizure disorders depends on the underlying cause and is discussed for individual diseases in detail in the following section. It is important to note that severity of seizures does not predict prognosis,¹⁰⁸ and cats without other neurologic abnormalities may have excellent outcomes with aggressive management.^{4,108}

Degenerative Disorders

Lysosomal storage diseases are genetic disorders resulting in accumulation of large cytoplasmic inclusions containing undigested products of cellular metabolism (Figure 27-2).³⁰ Most are inherited as an autosomal recessive trait and result in a deficiency or malfunction of key enzymes within the lysosomal catabolic pathway.¹²⁵ Storage diseases are highly diverse and have been organized into subgroups (on the basis of the deranged metabolic pathway), including the glycoproteinoses, the oligosaccharidoses, the sphingolipidoses, the mucopolysaccharidoses (MPS), and the proteinoses.¹²⁵ Features common to the storage diseases include equal

distribution between males and females, a slowly progressive clinical course (with the cat being normal at birth and in the first few months of life), and in some cases a history of neonatal deaths within the litter.³⁰ The neurologic signs can be highly diverse depending on the specific disease; multiple organ systems and all levels of the nervous system may be affected. However, the predominant clinical signs usually begin with cerebellar or cerebellovestibular impairment.¹²⁵ In some disorders, such as Niemann–Pick disease type A or globoid cell leukodystrophy (GCL), signs of a peripheral neuropathy may predominate. Similarly, ceroid lipofuscinoses, reported rarely in Siamese cats, may present with primarily prosencephalic signs, including seizures and blindness.¹²⁵

Diagnosis

Diagnosis of a storage disease can be challenging, and an index of suspicion may be raised if an at-risk breed is involved or if there is a history of prior progeny of the same parents being similarly affected.³⁰ Results of routine hematologic and biochemical testing is usually normal in these patients, although careful examination of blood smears may alert the clinician to the presence of storage vacuoles within leukocytes.¹²⁵ Biopsy of lymphoid tissue, including the spleen, or liver may reveal evidence of vacuolation.¹²⁵ In some subgroups, such as MPS, connective tissue abnormalities are common and radiography may reveal skeletal abnormalities, particularly of the spine. Muscle biopsies may reveal pathologic changes, particularly with glycogen storage diseases,

and peripheral nerve biopsies are advocated in the diagnosis of GCL.¹²⁵ Urine metabolic screening is available (Josephine Deubler Genetic Disease Testing Laboratory, University of Pennsylvania) to identify the presence of urinary excretory products, with characteristic excretory profiles being described for specific diseases.¹²⁵ A definitive means of diagnosing a storage disease is through the use of lysosomal enzyme analysis, in which activity of select lysosomal enzymes in the affected cat are measured against an age-matched control. Affected animals typically have 0% to 5% of the normal activity of the enzyme in question, whereas carrier animals have approximately 50% of normal activity.¹²⁵ Molecular genetic testing will become increasingly available in the coming years as another means of diagnosing this group of disorders; currently, DNA testing is available only for MPS 6 in cats.¹²⁵

Anomalous and Congenital Disorders

Malformations of the brain are not uncommon in veterinary patients, with the majority resulting from hereditary causes and in utero exposure to toxins or infectious agents.³⁴ Infectious agents lead to both hypoplasia after destruction of progenitor cells and atrophy secondary to destruction of differentiated actively growing tissue.³⁴

Hydrocephalus

Hydrocephalus is one of the more commonly recognized congenital central nervous system (CNS) disorders in young cats, with clinical signs becoming apparent in kittens as young as 2 to 3 months of age.²² It is characterized by an increase in volume of CSF caused by compensatory or obstructive mechanisms leading to varying degrees of dilation of the ventricular system.³⁴ Enlargement of the cranium, small stature, an open fontanelle, calvarial distortion, divergent strabismus, abnormal behavior, ataxia, seizures, visual deficits, head pressing, and stupor may all be sequelae to hydrocephalus, depending on the severity of the pathologic changes in the brain.²² Advanced imaging is necessary to confirm the diagnosis and rule out other causes of intracranial disease. Typical findings on MRI (Figure 27-3) include varying degrees of ventricular dilation, reduction of periventricular white matter, expansion of the cranial cavity, and loss of cortical bone.

Treatment of congenital hydrocephalus may include medical management with the aim of reducing CSF volume and production through the use of diuretics and corticosteroids.²² Furosemide at a dose of 0.5 to 4.4 mg/kg PO, IV, IM, every 12 to 24 hours, may be used to decrease CSF production through inhibition of the sodium-potassium cotransport system.²² Acetazolamide (Diamox) may be used in a similar fashion at 10 mg/kg PO, every 8 hours; it acts to decrease CSF production through inhibition of carbonic anhydrase.²² Prednisone

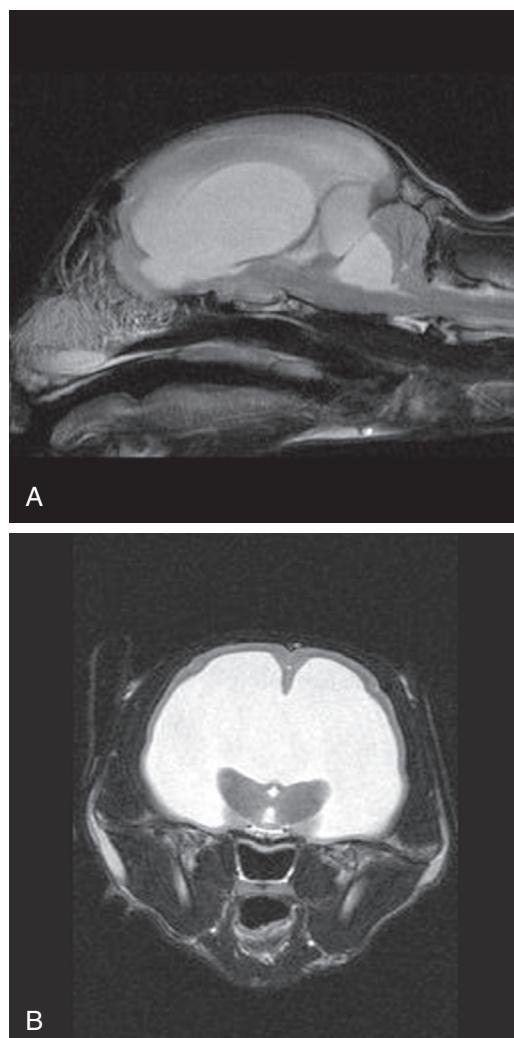


FIGURE 27-3 **A**, Sagittal T2-weighted image of a 1-year-old cat with blindness, seizures, and lethargy. Note the massive dilation of the lateral ventricles, in which fluid appears hyperintense (bright). **B**, Axial T2-weighted view of the same cat with hydrocephalus. Note the small and misshapen diencephalon.

may also be administered to reduce production of CSF, but medical management usually provides only temporary relief of clinical signs.²² Surgical intervention requires placement of a ventriculoperitoneal or ventriculoatrial shunt, with prognosis dependent on the severity of the underlying disease.²²

Cerebellar Hypoplasia

Cerebellar hypoplasia is a well-recognized syndrome in cats resulting from in utero or perinatal exposure to feline panleukopenia virus.³⁴ The virus has a predilection for rapidly dividing cells and targets the external germinal layer of the cerebellum. As such, hypoplasia of the granule layer and disorganization of the Purkinje cells results (Figure 27-4), leading to varying degrees of impairment.³⁴ Clinical signs become evident as soon as the animal is able to walk and include a base-wide

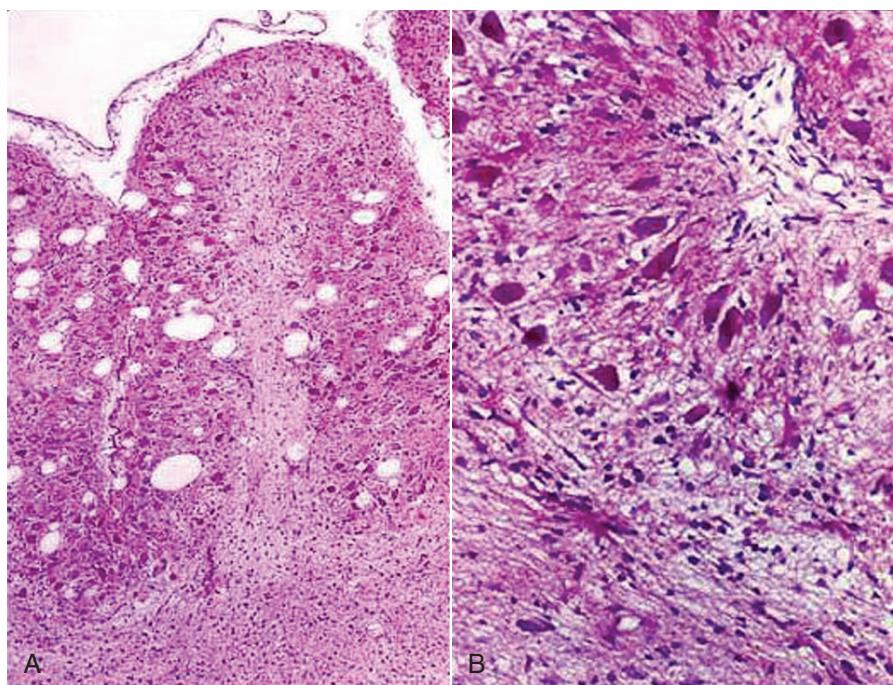


FIGURE 27-4 Cerebellar hypoplasia in a kitten. The Purkinje neurons are disorganized, and the granular layer is absent. (Reprinted with permission from DeLahunta A, Glass R: Veterinary neuroanatomy and clinical neurology, St Louis, 2009, Saunders.)

stance, coarse whole body tremors, intention tremors, cerebellar quality ataxia, and hypermetria. Neurologic deficits are symmetric and nonprogressive in nature.³⁴ Depending on severity of disease, an affected kitten can have a good quality of life, provided adequate measures are taken to prevent injury from falling and to keep it indoors. This disorder is best prevented by vaccinating queens before pregnancy.³⁴ Although similar clinical signs are seen in cats with cerebellar abiotrophy, the two disorders can be readily distinguished given that signs resulting from abiotrophy usually do not become apparent until several months to years of age and are progressive in nature.⁶

Miscellaneous Anomalies

Other congenital anomalies are less well recognized and occur sporadically from genetic, toxic, or infectious causes. Meningoencephalocele has been well recognized in Burmese kittens as part of an inherited craniofacial malformation and has also been associated with in utero exposure to griseofulvin.³⁴ Intracranial arachnoid cysts have been reported to arise in the quadrigeminal cistern in Persian cats, with clinical signs including obtundation and collapse.^{80,110} Lissencephaly with microencephaly in Korat cats has been reported and is associated with signs of abnormal behavior and self-mutilation.

Metabolic and Nutritional Encephalopathies

Numerous metabolic diseases result in neurologic signs in cats through effects on the metabolism of neurons in

the CNS.³⁴ Hypoglycemia is a well-recognized cause of seizures in pediatric patients and has also been reported infrequently in older cats with insulinoma or other insulin-secreting tumors.^{50,67} Additional causes include hepatic disease, sepsis, lysosomal storage diseases, inadvertent overdose of insulin, and hypoadrenocorticism.⁶⁷ Clinical signs associated with neuroglycopenia in addition to seizures may include lethargy, weakness, disorientation, ataxia, and visual deficits. Chronic hypoglycemia may cause irreversible nerve damage in cats,⁶⁷ and thus prompt treatment aimed at correcting the underlying problem is essential.

Hepatic encephalopathy is most often seen in young cats with portosystemic shunts (PSSs) and has also been recognized in other hepatic disorders (e.g., lipidosis, damage caused by hepatotoxic drugs). Toxic products that are released from the gut normally are detoxified by the liver, but in affected cats increased levels of ammonia, benzodiazepine-like substances, and other metabolites circulate to the brain.³⁴ Resultant clinical signs include seizures (often postprandial), circling, depression, ptymatism, blindness, head pressing, disorientation, and poor growth.¹⁴⁵ Gastrointestinal and urinary signs as well as poor growth often accompany neurologic deficits. A complete description of diagnosis and treatment of PSS and other hepatopathies can be found in Chapter 23.

Various endocrinopathies and electrolyte abnormalities have also been associated with intracranial signs. Diabetic ketoacidosis and diabetic hyperosmolar nonketotic syndrome may produce neurologic dysfunction leading to signs of lethargy, depression, anorexia, and

stupor.¹³⁸ Coma may result from dehydration of brain cells secondary to chronic hypovolemia, osmotic diuresis, and shifts in fluid balance between the intracellular and extracellular compartments.¹³⁸

Hyperthyroidism has been reported to cause restlessness, hyperexcitability, pacing, circling, anxiety, and mental confusion.⁶¹ Seizures may also be seen, either as a direct result of thyroid hormones decreasing the electric threshold of cerebral tissue or related to a vascular accident secondary to hypertension.

Naturally occurring hypoparathyroidism results in severe hypocalcemia and results in focal or generalized muscle tremors, seizures, ataxia, disorientation, stilted gait, lethargy, anorexia, and elevated nictitans. Other causes of hypocalcemia include renal disease, ethylene glycol toxicity, pancreatitis, eclampsia, phosphate-containing enemas, and iatrogenic causes related to thyroidectomy.⁴¹

Hypercalcemia can cause disturbances of the CNS such as depression and seizures and is most often associated with hypercalcemia of malignancy or renal failure, although there are rare reports of primary hyperparathyroidism in cats.⁴¹

Hypernatremia, defined as a serum sodium concentration above 165 mEq/L in cats, results in clinical signs of weakness, ataxia, seizures, and coma.⁸⁶ The severity of clinical signs is related directly to the acuteness of onset and degree of hypernatremia⁸⁶ and is attributed to rapid shifts of water from the intracellular to the extracellular space.⁴⁸ Rapid correction with inappropriate fluid therapy can lead to severe complications, including cerebral edema and death.⁴⁸

Thiamine-deficiency encephalopathy is well recognized in cats and is characterized by vestibular-quality ataxia, mydriasis, cervical ventroflexion, and seizures.³⁰ Affected cats often have a history of eating a raw-fish diet, which is rich in thiaminase.³⁰ The author has observed a number of cats with presumed thiamine deficiency in which clinical signs were preceded by prolonged anorexia, such as with hepatic lipidosis. Administration of thiamine (10 to 25 mg administered intramuscularly and followed by oral supplementation) will result in complete resolution of clinical signs. If the condition is left untreated, signs progress to prostration, opisthotonus and spasticity, coma, and death.³⁰ On post-mortem examination, petechial hemorrhages are found bilaterally in the brain stem, with degenerative lesions found in the caudal colliculi, lateral geniculate, vestibular, oculomotor, and habenular nuclei.³⁰

Neoplasia

Brain tumors occur in cats with an overall incidence of 3.5 cases per 100,000 cats and account for 2.2% of all tumors.⁷⁶ Primary brain tumors include meningioma, glioma (astrocytoma, oligodendroglioma),

ependymoma, choroid plexus tumor, and rare embryonal tumors (e.g., neuroblastoma, primitive neurectodermal tumors, medulloblastoma).¹³⁹ Secondary tumors include pituitary tumors, tumors that invade by direct extension into the brain (e.g., nasal tumors, otic tumors, ocular tumors), and metastatic tumors (e.g., mammary adenocarcinoma).⁷⁶ In a retrospective study of 160 cats with intracranial neoplasia,¹⁴¹ tumor prevalence was determined to be as follows: 58.1% meningioma, 14.4% lymphoma, 8.8% pituitary, 7.5% glioma, 5% neuroepithelial, 5.6% metastatic, and 3.8% direct extension. There is no reported breed predisposition in cats, and the median age for developing a brain tumor is 11 years.¹³⁹

Intracranial tumors infiltrate the parenchyma of the brain, leading to disruption of blood flow, cerebral edema, local necrosis, disruption of CSF flow leading to obstructive hydrocephalus, and increased intracranial pressure (which can result in herniation).⁹⁹ Primary intracranial tumors rarely metastasize, but in some cases they may spread to the lungs by drainage through the venous sinus plexuses in the cranial vault.⁹⁹ Clinical signs can include behavioral changes, circling, seizures, visual deficits, ataxia, and paresis;¹¹⁵ however, signs can be nonspecific, and in one report 21% of cats presented only for anorexia and lethargy.¹³⁶ Signs are often slowly progressive and asymmetric in nature; however, in some asymptomatic patients tumors may be found as incidental findings at necropsy.¹⁴¹

Meningiomas

Meningiomas are the most common primary brain tumor in cats and are mesenchymal in origin, arising from the arachnoid layer of the meninges. The majority of cases involve older patients^{34,93} with males slightly overrepresented at a ratio of 3:2.³³ Their topography is similar to that of dogs, with most being supratentorial and frequently involving the third ventricle.^{33,140} There is a tendency in cats for these tumors to be multiple, and in one report 19% of cats had more than one meningioma.¹⁴⁸ In another report three cats had two meningiomas, and another cat had four meningiomas.⁴³ The presence of multiple lesions may result in multifocal signs, confounding the clinical picture and differential diagnosis. However, despite multiple lesions, 75% of cats in one study presented with signs suggestive of a focal lesion.⁴³

Microscopically, most feline meningiomas are meningotheiomatosus or psammomatous, and many have cholesterol deposits.³³ Clinical signs depend on the location and rate of growth of the tumor but are usually insidious in onset because of their slow growth rate.¹¹⁵ The median duration of clinical signs before presentation was 1.25 months in a retrospective of 42 cats and included mentation changes (100%), visual deficits (93%), paresis (83%), and seizures (19%).⁴⁹



FIGURE 27-5 Computed tomography scan of a cat with confirmed meningioma. Note the hyperdense area of calcification ventrally and the hyperostosis in the overlying calvaria. (*Courtesy Dr. Kerry Bailey, Oradell Animal Hospital.*)

Definitive diagnosis ultimately requires histopathologic analysis, but advanced imaging (computed tomography [CT], MRI) can be highly suggestive of meningioma on account of the characteristic imaging features and anatomic location. CT is not as useful for detection of intracranial masses as MRI because of its poor soft tissue detail and lack of ability to identify lesions in the caudal fossa. However, in a study of canine brain tumors, CT correctly predicted histologic type in 86% of cases.¹⁰⁷ Meningiomas appear isodense to hyperdense, homogeneous, and brightly enhanced on CT, and calcification is easily recognized (Figure 27-5).¹¹⁵ Hyperostosis, frequently seen in the calvarium overlying feline meningiomas, is readily detected by CT scan and is reported to occur in approximately 73% of cases.

MRI is considered the superior modality for detecting these tumors and correctly identified meningioma on the basis of MRI features alone in 96% of cases in 33 cats.¹⁴⁰ Imaging features are variable but include an extraaxial location, distinct margins, mild peritumoral edema, mass effect, dural tail, and broad base (Figure 27-6).¹⁴⁰ In one report enlargement of the lateral ventricle was present in 64% of cases, and herniation under the tentorium or cerebellum was evident in 63% of cases.¹⁴⁰ Results of CSF analysis in cats with meningioma have not been reported, but in dogs they are nonspecific and unlikely to be of diagnostic benefit.

The mainstay of treatment for feline meningioma is surgical removal. Surgery is often successful owing to the superficial location over the cerebral convexities and frontal lobes, the lack of invasion of underlying parenchyma (unlike dogs), and the well-circumscribed nature of these generally benign tumors. Postoperative mortality rates have been reported to be as high as 19%,⁴⁹ but in the author's experience and that of other



FIGURE 27-6 Magnetic resonance imaging of a cat with a confirmed meningioma. Note the extraaxial location and mass effect typical for this tumor type. (*Courtesy Dr. Mark Troxel, In Town Veterinary Group.*)

experienced clinicians,¹¹⁵ the mortality rate is typically lower. The most common postoperative complication after meningioma excision is anemia, which occurs in as many as one third of cats.⁴⁹ Overall, median survival time (MST) in a study of 42 cats was 26 months, with a 1-year survival rate of 66% and a 2-year survival rate of 50%.⁴⁹ In the same report 30% of cats developed a recurrence of neurologic signs, with a median time of 30.75 months. In another report of 34 cats with surgically treated meningioma, MST was 685 days, with 20% of cats experiencing a recurrence of clinical signs (285 days). Data regarding treatment of feline meningioma with radiation or chemotherapy are lacking, probably because of the high success and long survival times after surgery.

Pituitary Tumors

Pituitary tumors are rarely diagnosed in cats and often exert their clinical effects through excessive secretion of growth hormone. Clinical signs include acromegaly, characterized by enlargement of the head, lameness, dyspnea resulting from cardiomegaly, protrusion of the mandible, respiratory stridor caused by hypertrophy of oropharyngeal soft tissues, and widening of the interdental space.¹²⁸ Severe insulin-resistant diabetes is often evident. However, neurologic signs (e.g., seizures, behavioral changes, blindness) may occur in the absence of an endocrinopathy.^{62,88} Middle-aged to older male cats are overrepresented.^{88,128}

Definitive diagnosis requires advanced imaging of the brain (CT or MRI) and usually reveals a mass lesion in the sella with dorsal expansion into the overlying diencephalon (Figure 27-7). The majority of macroadenomas are contrast enhancing and may have areas of necrosis, hemorrhage, or calcification.

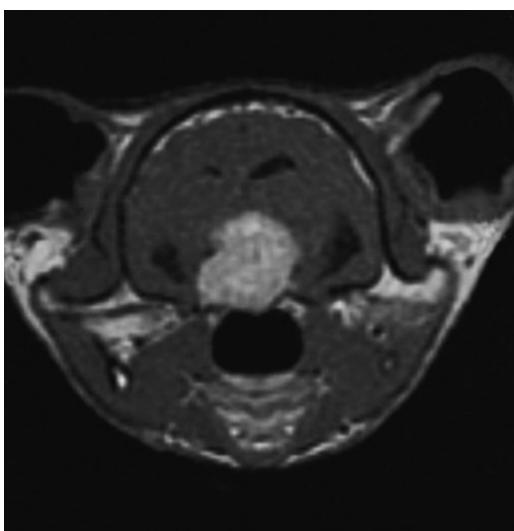


FIGURE 27-7 T1-weighted magnetic resonance imaging after contrast administration in a cat with a confirmed pituitary macroadenoma. Note the strong contrast uptake and obliteration of the diencephalon. (Reprinted with permission from DeLahunta A, Glass R. Veterinary neuroanatomy and clinical neurology, St Louis, 2009, Saunders.)

Medical management of these tumors is largely unrewarding, and more definitive treatment requires surgical intervention or radiation. In seven cats treated with transphenoidal hypophysectomy, surgery was well tolerated in most cases, with clinical signs resolving in five cats and two cats surviving 28 and 46 months after surgery.⁸⁹ However, surgeons competent in this procedure are lacking, and complications, including chronic oronasal fistula, can have a significant impact on quality of life.⁸⁹ Treatment with radiation therapy has been shown to ameliorate or resolve clinical signs and has been associated with prolonged survival times in numerous studies.^{62,88} Median survival time in a report of eight cats treated with radiation was 17.4 months (range, 8.4 to 63.1 months).⁶²

Lymphoma

Lymphoma of the brain can be primary or secondary or may be an aspect of multicentric disease.⁷⁶ It is seen uncommonly, accounting for only 14.4% of cases in a series of 160 cats with intracranial tumors.¹⁴¹ In a retrospective of 18 cats with CNS lymphoma, 14 had intracranial involvement and 10 presented with a chief complaint of seizures.⁹⁸ Most important, the prevalence of involvement of bone marrow and other organs was extremely high, suggesting that perhaps the most reliable means of diagnosing lymphoma in the CNS is through confirming its presence in other body systems.⁹⁸

There are no pathognomonic findings on MRI of cats with intracranial lymphoma, and in some cases imaging features are similar to those of meningioma.¹⁴⁰ CSF analysis may be highly useful, and malignant cells were seen

in the CSF of 5 of 11 cats in one report⁹⁸ and 6 of 17 in another.⁷²

Although lymphoma is considered chemotherapy sensitive, prognosis in affected cats is guarded, with a MST of approximately 21 days in patients treated with prednisone alone.¹⁴¹ Chemotherapy alone has not proved to substantially prolong survival times, but when combined with radiation, the MST was found to be 125 days (range 40 to 210 days).⁹⁸

Other Tumors

The incidence of other tumors of the brain in cats is not known, but they are seen only rarely in clinical practice. Of 160 cats with intracranial tumors, astrocytoma, oligodendrogloma, olfactory neuroblastoma, and ependymoma accounted for only 7.6% of cases. Because of the rarity of these tumors, there is a paucity of information regarding treatment and prognosis. However, gliomas typically appear to carry a grave prognosis, and in a cat with an astrocytoma treated with surgery and radiation, the survival time was only 179 days.¹⁴¹ Ependymomas carry a more favorable prognosis and seem to respond well to surgical intervention, with survival times as long as 2 years reported.^{124,141}

Inflammatory Disorders

Feline Infectious Peritonitis

Feline infectious peritonitis (FIP) is the most common and clinically significant inflammatory disorder in the CNS, accounting for 48% of cases of infectious neurologic diseases reported in cats.¹⁴ The causative agent, a highly pathogenic variant of feline enteric corona virus (FIPV), produces immune-mediated disease through infection of macrophages, with severity of signs determined by host susceptibility, host-specific immune response, and virus strain.⁴² The majority of cases are younger than 2 years of age and come from multicat households, with males and purebreds being overrepresented.^{35,42}

Neurologic signs can be seen with both the effusive ("wet") and the noneffusive ("dry") form of this disease, but the dry form appears more commonly to involve the CNS.³⁵ Signs referable to cerebellomedullary involvement are most common,³² but seizures may also be evident and have been reported in up to 25% of cats with histopathologically confirmed FIP.¹³⁵ Ataxia, spastic paresis, head tilt, nystagmus, hyperesthesia, proprioceptive deficits, blindness, and behavioral changes have all been reported.^{35,42} Non-neurologic signs frequently accompany the CNS signs and include uveitis, chorioretinitis, respiratory infections, mesenteric lymphadenopathy, dehydration, weight loss, lethargy, fever, and pica.⁴²

Antemortem diagnosis of FIP can be extremely challenging and requires a high index of suspicion, especially in those patients with no obvious systemic

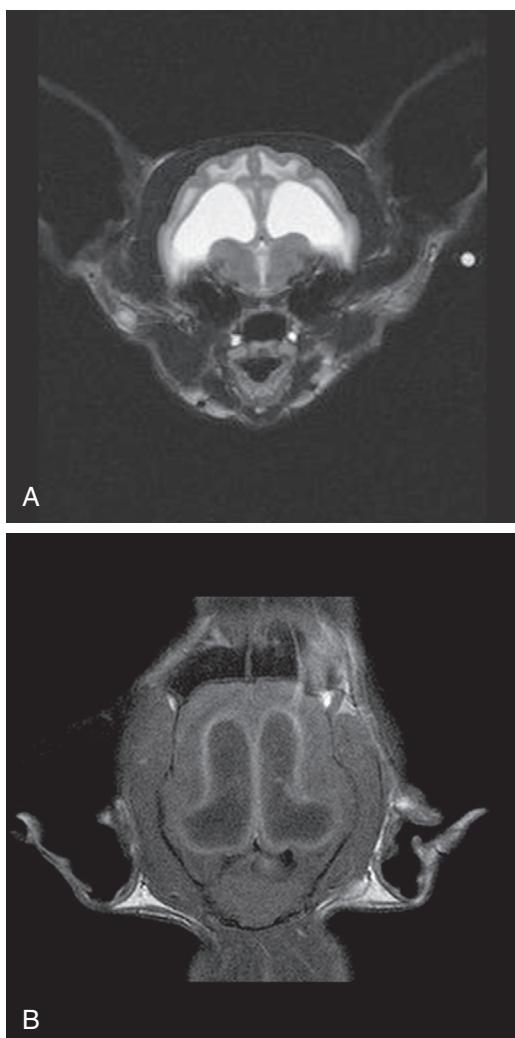


FIGURE 27-8 A, T2-axial magnetic resonance imaging of a cat with progressive ataxia and seizures. Polymerase chain reaction for feline infectious peritonitis virus was positive in the cerebrospinal fluid. Note the massive ventricular dilation and edema in the corona radiata. B, T1 postcontrast magnetic resonance imaging of same cat in A. Note the strong uptake of contrast in the ependymal lining of the lateral ventricles.

involvement (see Chapter 33). Complete blood count findings are nonspecific, but serum protein concentration is often elevated, specifically the alpha-2, beta, and gamma-globulins.³⁵ CSF analysis in cats with FIP is characterized by increased cellularity (which may be predominantly neutrophilic or mononuclear), as well as increased protein levels as high as 2 g/L. The presence of anti-coronavirus antibodies in either serum or CSF proves only that the cat has been exposed to a coronavirus and is not a means of definitively diagnosing FIP. In a prospective study of 67 cats, detection of anti-coronavirus antibodies in CSF had a sensitivity of 60% and a specificity of 90%.¹¹

MRI is a useful adjunctive tool in cases of suspected intracranial FIP, both to help confirm the diagnosis and rule out other causes of neurologic signs (Figure 27-8).

Typical findings include ventricular dilation, ependymitis, choroid plexitis, meningitis (most evident on the ventrocaudal surfaces of the brain), cervical syringomyelia, and periventricular inflammation.^{42,100} However, there are no pathognomonic imaging findings, and results must be considered in light of clinical and clinicopathologic findings. PCR can be performed on CSF and other fluids (e.g., abdominal effusion) or tissues, but its sensitivity is relatively low, and a negative test does not necessarily rule out FIP.⁴²

Postmortem examination of the brain often reveals gross lesions, including meningeal opacity around the medulla and choroid plexus of the fourth ventricle and coating of the choroid plexuses with a white tenacious exudate.³² Ependymal cells may be coated by fibrin and may lead to hydrocephalus rostral to the obstruction. Histologically, there is a severe pyogranulomatous leptomeningitis, choroiditis, ependymitis, and encephalomyelitis, with lesions predominantly surface oriented.³² Prognosis is extremely grim, and despite claims of effective treatments for FIP, it appears that the disease is uniformly fatal, even with supportive care and immunomodulatory therapies.

Toxoplasmosis

Toxoplasma gondii is a protozoal parasite for which the cat can serve as both the intermediate and definitive host.^{32,79} Infection occurs by direct ingestion of tissue cysts in meat or sporulated oocysts from cat feces, as well as transplacentally.³² After infection bradyzoite organisms will become encysted in various tissues, including muscle and CNS, but often the infection remains latent and the patient will be asymptomatic.³² Clinical disease occurs with a variety of immunocompromising factors, including steroid administration, concurrent infection with FIV or FeLV, stress, a large infective dose in very young animals, and neoplasia.^{32,79}

Clinical findings include fever, pneumonia, icterus, abdominal discomfort, dyspnea, pericardial effusion, ascites, pancreatitis, and mesenteric lymphadenopathy.^{79,134} Lesions in the CNS are uncommon, accounting for only 7 of 100 cats with histologically confirmed toxoplasmosis.^{36a} Clinical signs of CNS involvement are often multifocal and include seizures, blindness, ataxia, abnormal behavior, depression, anisocoria, head tilt, and nystagmus.^{36a,79}

Antemortem diagnosis can be challenging and use of an IgG-based test (e.g., enzyme-linked immunosorbent assay [ELISA], latex agglutination test) requires demonstration of a fourfold increase in IgG over 2 to 3 weeks.⁷⁹ CSF can be used to determine intrathecal antibody production, but results must be interpreted cautiously because *T. gondii*-specific IgG has been found in the CSF of normal cats.⁷⁹ PCR has also been used to detect *T. gondii* in CSF, and results were found to be positive in seven of seven cats with immunohistochemical or

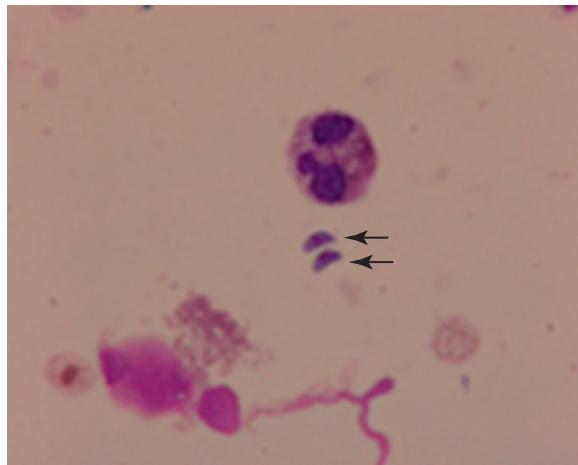


FIGURE 27-9 Cerebrospinal fluid of a cat infected with *Toxoplasma gondii* (arrows).

serologic evidence of toxoplasmosis.¹¹³ In rare cases organisms may be seen directly in CSF (Figure 27-9) or other biologic material, such as fluid obtained through bronchial lavage.

Histologically, nonsuppurative meningoencephalitis affecting gray and white matter is seen with occasional periventricular involvement.³² Necrosis may be severe, especially in congenital infections, and organisms may be visualized at the margins of lesions, within macrophages, and in tissue cysts.³² Treatment may yield a favorable response, and clindamycin (10 to 12 mg/kg, administered orally every 12 hours for 4 weeks) is considered the drug of choice.⁷⁹ Alternatively, trimethoprim sulfa (15 mg/kg, administered orally every 12 hours for 4 weeks) can be used.

Fungal Infections

Fungal infections are occasionally identified in the CNS in cats, with *Cryptococcus neoformans* being the most commonly reported. Because cats with cryptococcosis frequently are infected through inhalation of unencapsulated organisms, it is not unusual for the cat to have concurrent upper respiratory signs as well as swelling of the nose.⁷⁴ Clinical signs usually reflect a multifocal process, but forebrain signs may predominate because of the proposed route of entry. Ocular involvement often accompanies lesions in the CNS, with organisms being found between the choroid and the retina.³² There is no significant age or sex predilection, and both indoor and outdoor cats can become infected.

Definitive diagnosis can be obtained with the latex agglutination (LA) test for capsular antigen, a test that is both highly sensitive and specific. LA may also be performed on CSF and may be preferable in cats without obvious systemic involvement. The organism may also be directly visualized in CSF, nasal exudates, skin lesions, urine, and lymph node aspirates.⁷⁴ In cases in which the organism is not seen in CSF, it is generally still abnormal

and may yield neutrophilic, eosinophilic, mononuclear, or mixed pleocytosis with elevated protein.⁷⁴ MRI of affected cats is variable and may include a solitary granuloma, multifocal masses, meningeal inflammation, and enhancement of the ependyma and choroid plexuses.¹³⁰ Microscopic findings include the presence of numerous, tightly packed organisms filling the subarachnoid space and expanding the sulci with a mild nonsuppurative inflammatory response in the meninges and parenchyma (Figure 27-10).³²

The treatment of choice is currently fluconazole (25 to 50 mg orally every 12 hours) because of its ability to cross the blood-brain barrier, its relative safety margin, and its reported efficacy.⁷⁴ However, prognosis is considered extremely guarded in cats with CNS involvement and relapses are common. Other fungal infections, such as *Blastomyces dermatitidis*, *Histoplasma capsulatum*, and *Cladophialophora* spp., are sporadically reported in endemic areas and are typically associated with a grave prognosis.^{74,127}

Borna Disease

Borna disease virus (BDV) is the cause of a severe non-suppurative encephalomyelitis reported in many parts of the world, particularly Europe and Australia. It is most often seen in rural cats prone to hunting birds and rodents and is characterized by pelvic limb ataxia followed by mentation changes, visual deficits, photophobia, circling, and seizures.⁹ Clinical signs last from 1 to 4 weeks and usually result in progressive impairment and death, although in some cases recovery is possible. Cats that have recovered have permanent ataxia, behavioral changes, and polyphagia.⁹

Definitive diagnosis can be difficult, and other causes of multifocal CNS disturbances, such as FIP, must be ruled out. Fewer than half of affected cats test positive for BDV-specific antibodies, and PCR has not proved to be a reliable test in this species.⁹ The disease can be definitively diagnosed only through postmortem examination. Findings include inflammatory changes, mostly in gray matter, perivascular cuffing, neuronophagia, and detection of BDV antigen in the CNS parenchyma.⁹ Prognosis is grave, and there is no known treatment. Many other infectious encephalitides in cats have been reported uncommonly, including rabies, FIV, rickettsial disease, pseudorabies, and feline spongiform encephalopathy.

Toxic Disorders

Toxin ingestion should be considered in any cat presenting with acute neurologic signs, particularly in those cats with a history of indiscriminate ingestion of foreign materials or those that have had access to the outdoors with no supervision. Because many toxins can produce effects similar to naturally occurring diseases on the CNS, a thorough history, as well as a complete

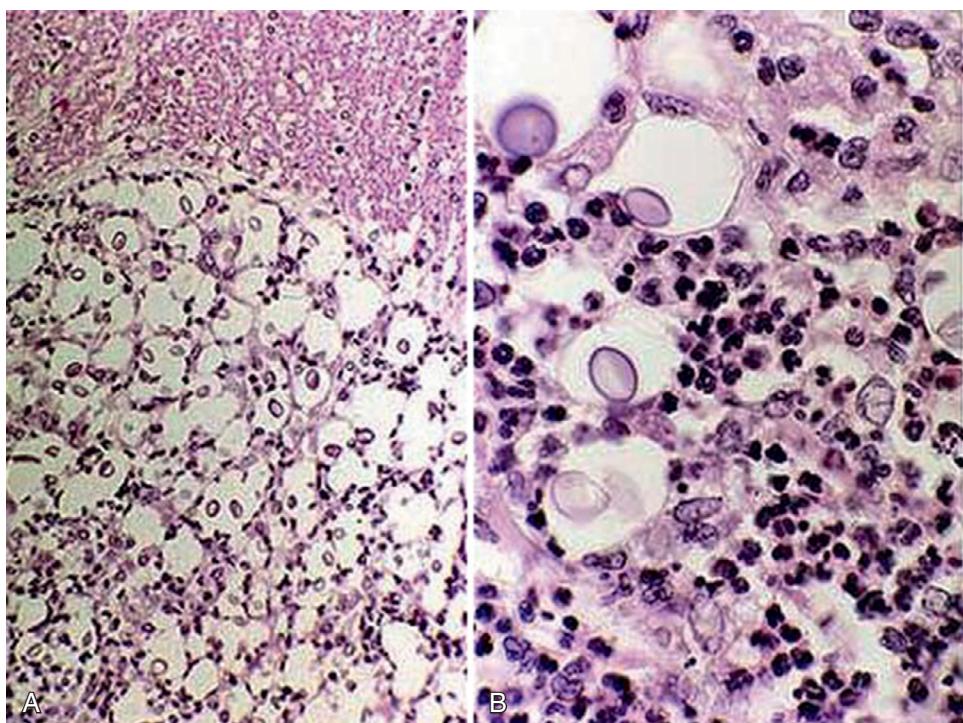


FIGURE 27-10 Hippocampus of a cat infected with *Cryptococcus neoformans* (H & E, $\times 140$). Cavities representing perivascular spaces distended with organisms are readily seen. (Reprinted with permission from DeLahunta A: Inflammatory diseases of the nervous system. In Summers BA, Cummings JF, DeLahunta A, editors: Veterinary neuropathology, St Louis, 1995, Mosby.)

neurologic examination, is essential. Although the list of potential neurotoxins is endless, this section addresses only the most common and clinically relevant ones seen by feline practitioners (see also Chapter 31).²⁵

Topical pesticides represent a significant source of toxicity in cats and usually result from inappropriate administration of flea and tick products. Clinical signs of permethrin toxicity include tremors and muscle fasciculations, twitching, hyperesthesia, seizures, ataxia, mydriasis, and central blindness. Severe clinical signs require intensive treatment, and left unchecked, death from aspiration pneumonia, respiratory arrest, or electrolyte abnormalities may result. However, the majority of cats will have a good outcome with no long-term complications.^{12,37} Organophosphate and carbamate insecticides act by inhibiting acetylcholinesterase, resulting in signs consistent with a "cholinergic crisis" marked by muscarinic, nicotinic, and mixed signs.³⁶ Tremors, depression, seizures, miosis, abnormal behavior, and cervical ventroflexion all have been reported in affected cats within minutes to hours after exposure.³⁶

A number of drugs have been reported to cause neurologic signs in cats, the most well described being metronidazole.^{16,112} Neurologic signs include disorientation, ataxia, central blindness, and seizures. All reported cases have been on doses greater than 30 mg/kg per day. Withdrawal of the medication and institution of supportive care result in rapid resolution of clinical signs within several days.^{16,112} Ivermectin is also reported to

cause seizures, as well as ataxia, blindness, mydriasis, coma, disorientation, and death.

Plant toxicities account for approximately 10% of reported exposures to poison control centers, with more than 50% of cases being less than 1 year of age.⁵⁸ These are often particularly challenging to the clinician because many pet owners do not know the names of the plants the cat may have ingested, and in some cases it is unclear whether the animal did in fact ingest the plant material. Tobacco, marijuana, and other hallucinogenic plants have all been reported to cause a multitude of signs, from depression to ataxia, seizures, and death.⁵⁸

Ingestion of lead continues to be an important toxicologic problem in cats, particularly in those living in homes constructed before 1977. Owners of cats with suspected lead poisoning should be questioned carefully to determine whether remodeling is taking place because the grooming habits of cats put them at risk for ingesting lead-containing particles.³⁶ Neurologic signs, including behavioral changes, seizures, blindness, and ataxia usually develop after acute, high-level lead exposure.³⁶ In cats gastrointestinal signs (e.g., vomiting, anorexia, abdominal pain, constipation, and megaesophagus) are more common than neurologic signs. The diagnosis of lead poisoning can be confirmed by measuring a blood lead level greater than 0.22 ppm.³⁶

Although numerous other toxins have the potential to affect the nervous system in cats, a complete discussion is beyond the scope of this chapter; the reader is

referred elsewhere for an excellent review of veterinary toxicology.¹⁰³

Vascular Encephalopathies

Cerebrovascular Accidents

Cerebrovascular accidents (CVAs) are becoming recognized in veterinary medicine with increasing frequency because of the greater availability of MRI. CVAs can be divided into two broad categories: ischemic stroke, in which a vessel is occluded by thrombus or vasospasm, and hemorrhagic stroke, which arises from rupture of blood vessels into CNS parenchyma or subarachnoid space.⁴⁵ The incidence of CVA in cats is unknown, insofar as the majority of reports in the veterinary literature are based on canine studies. Risk factors include hyperfibrinogenemia, polycythemia, coagulopathies, neoplasia (e.g., intravascular lymphoma), hypertension, multiple myeloma, cardiac disease, infectious diseases (e.g., FIP), renal disease, vasculitis, and others.^{45,53,55} Postanesthetic cerebellar ischemia has been reported in Persian cats after anesthesia with ketamine.¹¹⁶

Clinical signs reflect the location and extent of the affected area and are usually acute in onset and asymmetric, with minimal progression after the first 24 hours. The cerebellum is the most common site for vascular accidents to occur,^{19,34} but the cerebral hemispheres and thalamus are also frequently affected. A minimum database in any cat with suspected brain infarction should include a complete blood count, chemistry panel, FeLV and FIV testing, urinalysis, thyroid panel if applicable, coagulation profile if applicable, multiple blood pressure measurements, electrocardiogram, and possible thoracic radiographs and abdominal ultrasound. If cardiomyopathy is suspected, echocardiography should also be performed. Definitive diagnosis requires advanced imaging of the brain, with MRI considered the superior modality for detecting intracranial infarction (Figure 27-11). Findings may vary depending on the amount of time that has elapsed between the onset of the stroke and performance of imaging. Typical abnormalities noted on MRI include a focal, sharply demarcated lesion that is hyperintense on T2 and FLAIR images, hypointense on T1, with a discrete cutoff between normal and abnormal tissue. Mass effect or midline shifting is usually not seen, and there is minimal, if any, contrast enhancement.

There is no specific treatment for vascular accidents in most feline patients, and care must be taken to try to identify and correct an underlying cause. Acutely, supportive care, especially when signs are severe, is aimed at maintaining perfusion to the brain through judicious use of intravenous fluids and administration of oxygen. Mannitol (0.5 to 1 g/kg administered intravenously) may be indicated in the acute phase if cerebral edema is a concern, provided the cat is hemodynamically stable

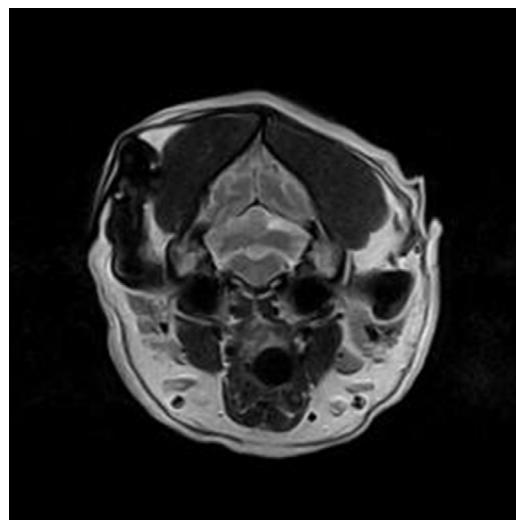


FIGURE 27-11 T2-axial magnetic resonance imaging of a brain infarct. Note the sharply delineated borders and wedge shape. (Courtesy Dr. Boaz Levitin, NYC Veterinary Specialists.)

and electrolytes are normal. Corticosteroids have not been shown to play a role in the treatment of stroke and in fact may exacerbate oxidative damage to the brain. Prognosis depends on a number of factors, including underlying cause, severity of clinical signs, and the extent of the lesion, but the majority of patients will improve over a period of days to weeks.

Feline Ischemic Encephalopathy

A unique vascular disorder of the CNS, feline ischemic encephalopathy is well described in cats and thought to be related to *Cuterebra* larvae myiasis.^{34,47} Affected cats typically have access to the outdoors and present in summer and early fall with unilateral prosencephalic signs, including progressive seizures, behavioral changes (often aggression), blindness, and depression. In some cases neurologic signs are preceded by signs of upper respiratory disease, including sneezing.⁴⁷ Abnormal rectal temperatures, either hyperthermia or hypothermia, were noted.⁴⁷

Neither routine hematology nor CSF analysis is specific for this disorder. MRI of the brain (Figure 27-12) may show parasitic track lesions, as well as cerebrocortical degeneration caused by toxin release by the parasite.³⁴ Grossly, marked atrophy of the affected cerebral hemisphere can be apparent (Figure 27-13). Vasospasm secondary to release of toxin produced by the parasite results in infarction in the region perfused by the middle cerebral artery or its branches.³⁴

Histologic findings include parasitic track lesions, superficial laminar cerebrocortical necrosis, cerebral infarction, subependymal rarefaction, and subpial astrogliosis.¹⁴⁶ Larvae are most commonly found in the olfactory bulbs and peduncles, optic nerves, and cribriform plate, suggesting entry from the nasal cavity.¹⁴⁶



FIGURE 27-12 T1 postcontrast magnetic resonance imaging (coronal) of a cat with feline ischemic encephalopathy. Contrast uptake associated with necrosis caused by the parasite is seen in the olfactory and prefrontal lobe on the right. (Reprinted with permission from DeLahunta A, Glass R: Veterinary neuroanatomy and clinical neurology, St Louis, 2009, Saunders.)



FIGURE 27-14 Kitten with left head tilt secondary to otitis media-interna. (Reprinted with permission from DeLahunta A, Glass R: Veterinary neuroanatomy and clinical neurology, St Louis, 2009, Saunders.)

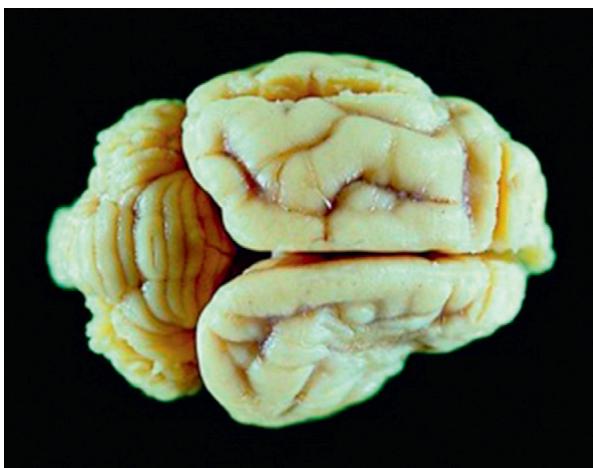


FIGURE 27-13 Gross specimen of a cat with feline ischemic encephalopathy. Atrophy is evident in the affected hemisphere (left) in the distribution of the middle cerebral artery. (Reprinted with permission from DeLahunta A, Glass R: Veterinary neuroanatomy and clinical neurology, St Louis, 2009, Saunders.)

Treatment options are extremely limited, and most cats are euthanized because of severe neurologic impairment and aggression.

PERIPHERAL VESTIBULAR DISEASES

The vestibular system is responsible for maintaining the position of the eyes, neck, trunk, and limbs relative to the position of the head in space.³⁴ Dysfunction of the vestibular system results in dramatic clinical presentations, including head tilt (Figure 27-14), nystagmus,

falling, vomiting, rolling, wide-based stance, loss of equilibrium, and vestibular-quality ataxia.³⁴ It is of key importance that the clinician recognizes whether the signs are due to peripheral or central disturbances of the vestibular system; this is primarily ascertained with a thorough neurologic examination and history (Table 27-2). The presence of a head tilt and vestibular-quality ataxia can be seen with either peripheral or central disease; however, paresis, spasticity, hypermetria, or postural deficits are suggestive of a central lesion. Likewise, horizontal or rotary nystagmus with the fast phase opposite the side of the lesion can be seen in both central and peripheral disease, but vertical nystagmus is typically seen with central disease. Nystagmus with a fast phase directed toward the side of the lesion or that changes with changing position of the head is consistent with a central lesion.³⁴ The presence of cranial nerve abnormalities (other than VII) is also more common with central lesions, whereas Horner's syndrome is more often seen with peripheral dysfunction. Bilateral peripheral vestibular disease is characterized by a crouched gait, wide head excursions, absent oculocephalic reflex, and a wide-based stance.³⁴ It should be noted that blue-eyed cats often have a resting pendular nystagmus because of the larger portions of axons of the optic nerve crossing in the chiasm compared with normal animals. This is of no clinical significance and occurs in the absence of other vestibular signs.³⁴

There are myriad causes of vestibular signs in cats, but this section covers only those affecting the peripheral vestibular system. Common causes of peripheral disease in cats include feline idiopathic peripheral vestibular disease, otitis media-interna (OMI), nasopharyngeal

TABLE 27-2 Clinical Signs Associated with Central Versus Peripheral Vestibular Disease

Central	Peripheral	Bilateral peripheral	Both central and vestibular
Paresis, spasticity, hypermetria, postural deficits, vertical nystagmus, nystagmus with a fast phase directed toward the side of the lesion or that changes with changing position of the head, cranial nerve abnormalities (other than VII)	Horner's syndrome Facial paralysis	Crouched gait, wide head excursions, absent oculocephalic reflex, wide-base stance	Head tilt, vestibular quality ataxia; horizontal or rotary nystagmus with the fast phase opposite the side of the lesion

polyps, neoplasia (e.g., ceruminous gland adenocarcinoma, squamous cell carcinoma), and toxicity. A review of disorders affecting the central vestibular system can be found in the preceding section on intracranial diseases.

Idiopathic Vestibular Disease

Idiopathic vestibular disease is the most common cause of peripheral signs in cats, accounting for 43% of cases of peripheral vestibular disease in one report.⁹⁶ Clinical signs are often severe, with rolling and rapid nystagmus quite evident. There is no sex or breed predilection, and the average age of affected cats is 4 years, although it may be seen in any age. Interestingly, there is a higher incidence of this disorder in summer and fall, suggesting an environmental or infectious cause. Prevalence is higher in certain regions of the United States, especially the Northeast.

Although usually acute and nonprogressive in nature, there have been some reports of clinical signs progressing for up to 3 weeks.⁹⁶ Signs resolve rapidly without definitive treatment, usually in the first week, although some patients may have a persistent head tilt.⁹⁶ Diagnosis is through excluding other known causes of peripheral vestibular disease; there is no definitive diagnostic testing, nor is there definitive treatment. Some cats may require fluid and antiemetic therapy if vomiting does not resolve the first day.

Nasopharyngeal Polyps

Nasopharyngeal polyps are non-neoplastic, inflammatory growths originating in the middle ear or auditory tube and may potentially lead to peripheral vestibular signs.⁷⁰ They are primarily seen in cats younger than 2 years of age, but reported cases range in age from 2 months to 15 years. In addition to head tilt, ataxia, and abnormal nystagmus, respiratory signs such as stertorous breathing, sneezing, nasal discharge, and upper airway obstruction may be evident. The cause is unknown, but chronic respiratory tract infection, chronic OMI, ascending infection from the nasopharynx, and congenital causes have all been proposed.⁷⁰ Drainage of middle ear secretions through the auditory tube may be

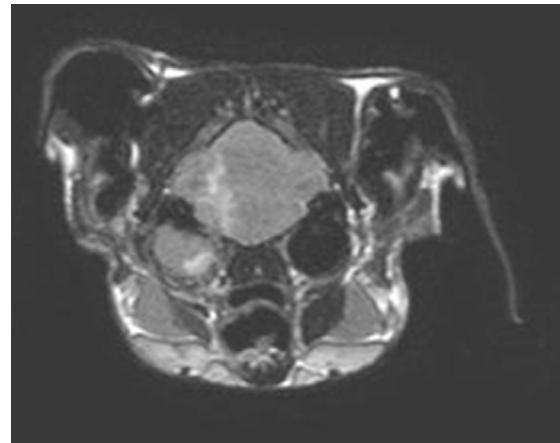


FIGURE 27-15 T1 postcontrast axial magnetic resonance imaging of cat with otogenic encephalopathy. Note the rim of contrast around the abscess in the left brain stem and cerebellum, as well as the mild contrast uptake and soft tissue density within the left bulla.

blocked by the polyp, leading to otorrhea and a misdiagnosis of otitis externa.

Otitis Media-Interna

OMI is one of the primary rule outs for cats with suspected nasopharyngeal polyps as the clinical signs may be identical. OMI may be associated with Horner's syndrome as well as facial nerve paralysis ipsilateral to the affected ear and can be accompanied by pain and signs of otitis externa. Remember that while a thorough otoscopic exam is indicated in all patients presenting with suspected peripheral vestibular dysfunction, the presence of an intact tympanic membrane does not exclude middle ear infection. While the most common etiologic agents in cats are bacterial (e.g., *Pseudomonas* spp., *Staphylococcus pseudointermedius*), *Cryptococcus* infection has also been implicated in a number of cats with OMI and an index of suspicion should be raised in cats living in endemic areas.⁸ Intracranial complications of OMI are well recognized and result from extension of organisms from the inner ear to the brainstem along the nerves and vessels of the internal acoustic meatus (Figure 27-15). This can result in severe, life-threatening disease requiring rapid surgical intervention and aggressive, long

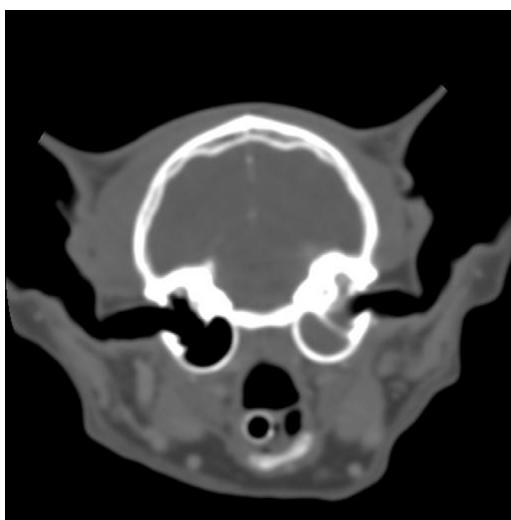


FIGURE 27-16 Computed tomography scan of a cat with unilateral otitis media-interna. There is mild sclerosis of the bony structures around the right bulla.

term medical management based on cultures obtained at the time of surgery.¹³¹

Malignant Tumors

Malignant tumors of the middle and inner ear occur uncommonly but also must be considered on the differential list of patients with peripheral vestibular signs, particularly in geriatric cats. Ceruminous gland adenocarcinoma and squamous cell carcinoma occur with equal frequency in cats and may be accompanied by obvious mass effect, aural discharge, pain, and pruritus.¹⁴⁷

Diagnosis and Treatment of Peripheral Vestibular Disease

Definitive diagnosis of disease of the middle and inner ear may require advanced imaging in the form of CT or MRI (Figures 27-16, 27-17, and 27-18), insofar as plain radiography often results in false-negative results or underestimation of the extent of disease.¹⁰ Imaging of the ear provides vital information about the extent of involvement, the possibility of bilateral disease, and integrity of adjacent structures and assists in ruling out concurrent lesions in the CNS. MRI can provide excellent detail of the structures of the cochlea and semicircular canals as well as the adjacent brain stem and is the imaging modality of choice at the author's institution. CT scanning may be preferable in cases in which the abnormality primarily involves bony structures.

Treatment depends on diagnosis, and in cases of nasopharyngeal polyps, ventral bulla osteotomy (VBO) combined with traction removal of the polyp is recommended.⁷⁰ Prognosis is excellent, although recurrence is possible.



FIGURE 27-17 T1 postcontrast axial magnetic resonance imaging of cat with bilateral otitis media-interna. The bullae are expanded, and there is mild contrast uptake within the homogenous material in both bullae.

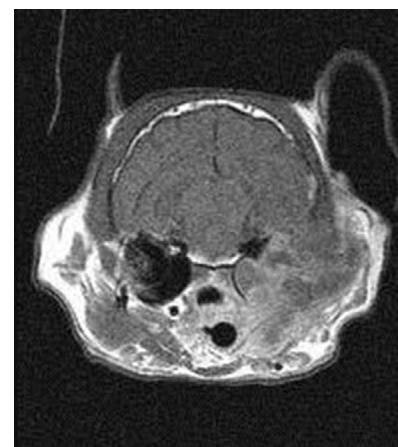


FIGURE 27-18 T1 postcontrast axial magnetic resonance imaging of cat with severe vestibular ataxia, head tilt, and facial paralysis. A mass obliterating the affected bulla and surrounding soft tissue structures is evident. Histopathology was consistent with ceruminous gland adenocarcinoma.

Newly diagnosed cases of OMI require antimicrobial therapy for a minimum of 4 to 6 weeks. Failure to respond to medical therapy or recurrence of OMI warrants surgical intervention (i.e., VBO and antimicrobials based on cultures obtained intraoperatively). Prognosis for malignancies of the ear is fair for ceruminous gland adenocarcinoma and guarded for squamous cell carcinoma after aggressive ear ablation and bulla osteotomy, provided there is no intracranial involvement or lymphatic or vascular invasion.¹⁴⁷

MYELOPATHIES

Feline myelopathies encompass a wide range of diseases and often present a challenge to the clinician, both with respect to attaining a neuroanatomic diagnosis as well

as creating a reasonable list of differential diagnoses. Common cardiovascular and orthopedic conditions can mimic disorders of the spine, making decisions regarding appropriate diagnostic testing particularly taxing. A thorough neurologic assessment is necessary to determine lesion location, with careful attention paid to gait, postural responses, and segmental reflexes. Although many feline patients are reluctant to walk in the clinical setting, the provision of adequate space, a quiet setting, and nonslippery flooring may facilitate the examination. The unique temperament of many cats, difficulty with gait evaluation in this species, and the fact that many live outdoors and thus are less closely observed than other species further impede the assessment of feline patients. Additionally, most of the literature regarding feline myelopathies is based on single cases or small group case reports. Although a description of all spinal disorders is beyond the scope of this chapter, a brief overview of some of the most clinically relevant disorders is presented.

Typically, if the cervical spine is affected, tetraparesis and ataxia are evident, with delayed postural responses in all four limbs. Cats with lesions located between C1 and C5 will show an upper motor neuron/general proprioceptive (UMN/GP) ataxia in all four limbs, whereas those with a C6-T2 myelopathy may have a short-strided gait with decreased tone and segmental reflexes in the thoracic limbs. Those with a lesion between T3 and L3 will have normal thoracic limbs with paraparesis or paraplegia and, if ambulatory, UMN/GP ataxia in the pelvic limbs. Reflexes in the pelvic limbs will be normal to increased, and postural responses may be delayed. Lesions located between L4 and S3 will result in paraparesis/paraplegia, a short-strided gait, postural deficits, decreased tone and reflexes, decreased perineal reflexes, fecal or urinary incontinence (or both), and poor tail tone.

Degenerative Myelopathies

Intervertebral Disk Disease

Although extremely well documented in the veterinary literature in dogs, intervertebral disk disease (IVDD) in cats has been reported only sporadically, with the incidence ranging from 0.02% to 0.12%, compared with dogs, in which the incidence is as high as 2.3%.^{56,92} Although IVDD is clearly less common in the clinical setting in cats than in dogs, necropsy evaluations have revealed that disk extrusion, protrusion, and rupture are commonly found, generally in middle-aged to older cats in all segments of the spine. When clinically significant IVDD is found in cats, it typically affects the thoracolumbar spine, with one study showing a peak incidence at L4-5 (Figure 27-19).⁹² Any age, breed, or sex may be affected, although purebreds appear to be overrepresented and account for approximately 38% of reported cases.



FIGURE 27-19 Sagittal magnetic resonance imaging of the lumbar spine of an acutely paraparetic cat. A degenerate disk with moderate compression of the overlying spinal cord is seen at L4-5.

BOX 27-2

Grading Clinical Signs Caused by Spinal Cord Lesions

- Grade 5: Normal strength and coordination
- Grade 4: Readily stands and walks with minimal paraparesis and ataxia
- Grade 3: Able to stand to walk unassisted but with difficulty; often stumbles and falls but can walk; mild to moderate paraparesis and ataxia
- Grade 2: Unable to stand unassisted; when assisted, able to move the pelvic limbs but constantly stumbles and often falls; moderate to severe paraparesis and ataxia
- Grade 1: Unable to stand unassisted; when assisted, only slight pelvic limb movements; severe paraparesis and ataxia
- Grade 0: Unable to stand unassisted; when assisted, complete absence of any pelvic limb movements, paraplegia

From DeLahunta A, Glass R: *Veterinary neuroanatomy and clinical neurology*, St Louis, 2009, Saunders.

Clinical signs are variable and can include spinal hyperesthesia alone, mild paraparesis, ataxia, paraplegia, urinary or fecal incontinence (or both), and loss of tail or anal tone (Box 27-2). The thoracolumbar spine is typically affected. Involvement of the cervical spinal cord is extremely rare, and to the author's knowledge there is only one case of a surgically treated cervical disk

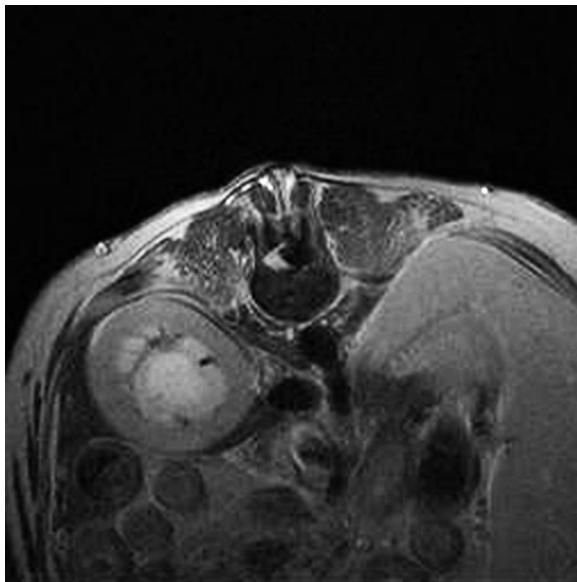


FIGURE 27-20 Axial MRI of a traumatic disc rupture. Note the compression and deviation of the spinal cord by calcified disc material.

in a cat, which succumbed to respiratory arrest several days after a ventral slot at C2-3.⁸⁵

Diagnostic testing can include CT scan or MRI, and most frequently will reveal a single extradural compressive lesion (Figure 27-20). MRI may also reveal loss of the normal signal from the nucleus pulposus of the intervertebral disk, narrowing of the ventral subarachnoid space, and displacement of the spinal cord or epidural fat. With increasing availability of advanced imaging modalities, myelography is becoming less commonly used, but it still remains a viable means of diagnosing this disorder. Plain radiographs are of little value in definitively diagnosing IVDD but may help rule out other causes of myelopathy, such as fracture or osteosarcoma.

As with dogs, treatment options can be tailored to the individual patient depending on clinical signs and owner preference. Conservative management in the form of strict rest, corticosteroids, pain management, and bladder care can be a viable treatment option, especially in patients still able to ambulate. However, recurrence rates with conservative care alone are significantly higher than with surgical management, and gait, bladder, and bowel deficits may persist. Surgical treatment includes hemilaminectomy, dorsal laminectomy, and fenestration, with the majority of reports limited to cases of thoracolumbar IVDD. In a study of thoracolumbar IVDD in 10 cats, all patients undergoing surgical intervention were judged to have an excellent outcome,⁹² whereas in another study five of six cats undergoing hemilaminectomy responded favorably, having good to excellent postoperative recovery.⁶⁶

Other Degenerative Myelopathies

Other degenerative diseases of the spine are extremely rare in cats but include degenerative myelopathy, lysosomal storage diseases, and other inborn errors of metabolism. Degenerative myelopathy, typically seen in large-breed dogs such as the German Shepherd, has been reported in cats and follows a similar clinical course as that seen in canines. Signs are usually slowly progressive and limited to the pelvic limbs, with nonpainful UMN/GP ataxia and paraparesis evident. Bowel and bladder dysfunction may occur late in the course of the disease. The cause is unknown, but feline leukemia virus antigen has been isolated in the spinal cord lesions from some affected cats.¹⁵ Inborn errors of metabolism, such as Niemann-Pick disease, neuroaxonal dystrophy, mucopolysaccharidosis, and other storage diseases, typically have a genetic basis and clinical signs become apparent at a young age.³⁰ Many of these disorders cause skeletal abnormalities, resulting in compressive spinal lesions, whereas others lead to vacuolation within neurons and glial cells with concomitant demyelination. There is no known treatment for these disorders.

Congenital and Developmental Anomalies

Anomalies of the spinal column are infrequently seen in cats and may go undiagnosed or be discovered only incidentally because many cause no clinical abnormalities. Because the embryologic development of the spine is closely related to development of other body systems, a thorough examination of the patient should be performed to assess viability. Although many spinal anomalies occur sporadically, the possibility of a genetic basis in potential breeding animals should be carefully considered. Animals with anomalies of the spinal cord will have clinical signs present from birth, whereas those with vertebral anomalies may not show evidence of a myelopathy until skeletally mature.

The Manx cat has been the subject of numerous reports of spinal anomalies because of its caudal vertebral aplasia specifically selected for in breeding programs. The trait is inherited as an autosomal dominant gene and in the homozygous state is lethal, whereas variable expression is seen in heterozygotes.³⁴ Associated with this anomaly is a high incidence of sacrocaudal spina bifida and meningoceles; meningoceleocele; and myelodysplasia of the caudal lumbar, sacral, and caudal segments.³⁰ Specifically, spina bifida involves failure of the dorsal elements of the vertebrae to form during development and may occur alone in the absence of other clinical signs (spina bifida occulta). Spina bifida may occur in conjunction with meningocele (protrusion of meninges and CSF outside the vertebral canal) or meningoceleocele (protrusion of meninges, CSF, and neural tissue outside the vertebral canal) (Figure 27-21).



FIGURE 27-21 Necropsy of Manx cat, showing cerebrospinal fluid-distended meningocele. (Reprinted with permission from DeLahunta A, Glass R: Veterinary neuroanatomy and clinical neurology, St Louis, 2009, Saunders.)

These are often associated with myelodysplasia, including hydromyelia, syringomyelia, and abnormal gray matter differentiation.³⁴ All these abnormalities could easily be avoided by selecting for Manx cats with normally developed tails. For humane reasons Manx breeders should be strongly encouraged by veterinarians to stop such unethical practices with known deleterious effects.

Clinical findings in Manx and similarly affected cats include abnormal hair growth or dimpling of the skin over the affected spinal segment, an open tract draining CSF, urinary or fecal incontinence (or both), depressed or absent tone and reflexes in the anus and perineum, a “bunny-hopping” gait, and paresis or paralysis. Severely affected animals are usually euthanized, and less severely affected animals may succumb to infections or pyelonephritis. Treatment options are extremely limited and focus on palliative care and bladder management.

Multiple cartilaginous exostosis occurs in younger cats and originates from the perichondrium of flat bones such as ribs, skull, scapulae, and vertebrae.⁵⁹ The nodules are composed of cartilaginous tissue with a bony component and arise from the growth plates. Malignant transformation has been documented. Clinical signs reflect the affected spinal segment, but involvement of the thoracic spine is most common. Radiographically, lesions within the canal may be difficult to visualize, but those on the projecting processes or lamina can be identified with conventional radiography.² Myelography, CT scanning, or MRI is necessary to assess the extent of the lesion (or lesions) and for surgical planning. Prognosis after surgery depends on the severity of clinical signs and whether multiple sites are affected.

Other less common anomalies are sporadically reported, usually as single cases. A retrospective study of 200 cats revealed abnormalities in 46 patients, including block vertebrae, transitional vertebrae, and extra

ribs.⁹⁷ Syringomyelia has also been described and was seen in one kitten in conjunction with hydrocephalus after parvoviral infection. Spinal arachnoid cyst, spinal dermoid sinus, atlantoaxial malformation, hemivertebrae, inborn errors of skeletal growth, and others have also been documented in the veterinary literature.

Metabolic and Nutritional Myelopathies

Metabolic and nutritional myelopathies are rarely reported in cats, with hypervitaminosis A perhaps being the most well described. Cats fed a diet with high levels of vitamin A, such as raw liver, are at risk, and clinical signs result from bony proliferation related to synovial joints.^{34,106} Lesions are often confined to the cervical spine and lead to spinal hyperpathia, tetraparesis, cervical rigidity, Horner’s syndrome, palpable bony masses over the cervical region, lethargy, and weight loss. Lesions can be seen on plain radiographs and consist of multiple exostosis and possible fusion of the spine. Prognosis is extremely guarded, but dietary adjustments may slow disease progression. Other osteodystrophies of suspected nutritional etiology have been reported, as have lesions in the gray matter of the cervical cord in a cat with an extrahepatic shunt.⁸⁴

Inflammatory and Infectious Myelopathies

Infectious meningoelitis has been identified as an important cause of myelopathy in feline patients, representing 32% of cases of spinal cord disease in 208 specimens submitted for histopathologic evaluation.⁸⁴ The majority of cases will occur in cats younger than 2 years of age with clinical signs present for less than 30 days.⁸⁴ Unlike other myelopathies, infectious and inflammatory disease most often affects the cervical spinal cord, perhaps because of extension of inflammatory disease in the brain, insofar as they are often seen in conjunction with intracranial lesions. Although many infectious diseases have the potential to affect the spine, FIP is at the top of the differential list.

Lesions of FIP consist of pyogranulomatous inflammation of the meninges and ependymal cells, spongy degeneration, malacia, and syringomyelia.¹³² Concurrent intracranial signs (e.g., ataxia, seizures) and weight loss, fever, chorioretinitis, and anorexia often accompany the signs of spinal cord dysfunction (e.g., paraparesis, tetraparesis, spinal hyperesthesia). Prognosis is extremely grave. A more comprehensive discussion of FIP is available in the section on encephalopathies.

Other infectious diseases of the spine are seen sporadically and agents include *Cryptococcus*, *Toxoplasma*, bacterial meningoelitis, *Coccidioides*, *Histoplasma*, FIV, rabies, BDV, and others. A FeLV-associated myelopathy was reported in 16 cats with signs consisting of abnormal vocalization, hyperesthesia, and paresis

progressing to paralysis.¹⁵ The clinical course involved gradually progressive neurologic dysfunction resulting in euthanasia. Microscopically, white-matter degeneration with dilation of myelin sheaths and swollen axons was identified in the spinal cord and brain stem of affected animals. Neither neoplastic nor hematologic diseases commonly associated with FeLV infection were present.¹⁵

Noninfectious inflammatory conditions of the spine include idiopathic poliomyelitis and eosinophilic meningomyelitis and can be difficult to distinguish from other forms of myelitis in the absence of additional clinical signs. Because history, clinical signs, and neurologic examination findings can be virtually identical in all of these disorders, the clinician must rely on concurrent systemic signs, potential exposure to an infectious agent, serology, and risk of exposure (e.g., geographical location).

Advanced imaging such as CT scan or MRI should be recommended when attempting to distinguish inflammatory myelopathies from other spinal disorders. However, although these tests are highly sensitive, they are not specific to the etiologic agent responsible for any inflammatory changes that may be evident.

Treatment is aimed at the underlying cause and may include antibiotics, antifungal agents, bladder management, pain control, and corticosteroids. Although the use of corticosteroids in treating infectious diseases may raise concerns for immunosuppression, adjunctive corticosteroid administration in children and adults with bacterial meningitis reduces both morbidity and mortality, and studies suggest that results are best when corticosteroids are administered immediately before the onset of antibiotics. Surgical decompression may be indicated if a discrete compression of the spinal cord is present, such as may be seen with a fungal granuloma.⁴⁴ Prognosis is dictated by specific cause, response to medical management, and neurologic status but in general is extremely guarded.

Spinal Neoplasia

Tumors of the spine represent a wide variety of cancers and are classified as extradural, intradural-extramedullary, or intramedullary. Extradural tumors account for approximately 50% of cases, intradural-extramedullary tumors represent 35%, and intramedullary tumors represent 15%. They may arise from the vertebrae and surrounding soft tissues, meninges, or neuroparenchyma. In a retrospective study of 205 cats affected by spinal disease, 27% were affected by neoplasia, the majority (36%) being diagnosed with lymphosarcoma.⁸⁴ Clinical signs will reflect the segment of spinal cord affected, and care must be taken to do a complete examination to rule out involvement of the brain or other body systems.



FIGURE 27-22 Feline epidural lymphoma. In the top specimen soft, gray-white neoplastic tissue invests the spinal cord. The bottom specimen depicts a similar lesion associated with portion of the spinal cord fixed and removed from the vertebral canal. (Reprinted with permission from DeLahunta A: *Degenerative diseases of the central nervous system*. In Summers BA, Cummings JF, DeLahunta A, editors: *Veterinary neuropathology*, St Louis, 1995, Mosby, p 208.)

Lymphoma, as previously mentioned, is the most common tumor affecting the spine of cats and is typically seen in a younger subset of patients (median age, 24 months) with a short duration of clinical signs (less than 7 days). Reported neurologic signs include spinal hyperesthesia, asymmetric postural deficits, paraparesis and paraplegia, ataxia, tetraparesis, lower motor neuron tail and/or bladder, upper motor neuron bladder, and lack of deep pain.⁸³ Nonspecific abnormalities, such as anorexia, lethargy, weight loss, renomegaly, chorioretinitis, and lymphadenopathy may also be found. There is an association with spinal lymphoma and FeLV infection, and in one report results of FeLV testing were positive in 84.2% (16 of 19) of cases with necropsy confirmation of spinal lymphoma.¹²⁹ Spinal lymphoma has also been found to be associated with FIV.⁷ Extraneuronal lymphoma is commonly found in affected patients, with the most common locations being bone marrow and kidneys followed by liver, skeletal muscle, spleen, lymph nodes, vertebrae, and heart.^{83,142} The majority of clinical cases are located in the thoracolumbar spine and are most frequently reported to be extradural (Figure 27-22). However, histopathologic examination of 33 cats revealed 87.9% to have both intradural and extradural components, with 42.9% of cats examined having concurrent lymphoma in the brain.⁸³

Diagnosis of spinal lymphoma requires a high index of suspicion and careful attention to involvement of other body systems. Hematologic abnormalities are frequently found and include anemia, leukopenia,

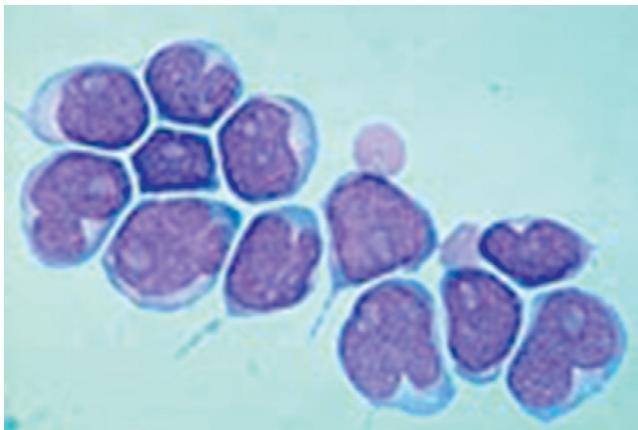


FIGURE 27-23 Large lymphoid cells with dispersed chromatin, prominent nucleoli, and scant cytoplasm in the cerebrospinal fluid of a cat with spinal lymphoma.

thrombocytopenia, and circulating lymphoblasts. Bone marrow involvement is also seen in more than 68% of cases, with the lymphoma being high-grade lymphoblastic or immunoblastic in all cats.¹²⁹ A careful fundic examination, three-view thoracic radiographs, lymph node aspirates if lymphadenopathy is evident, and abdominal ultrasonography are all warranted.

A positive FeLV test raises the index of suspicion for spinal lymphoma, but confirmatory neurodiagnostics are warranted and may include myelography, CT scan, MRI, and CSF analysis. Myelography generally is abnormal, but lesion location (e.g., intramedullary versus extramedullary) may not always be delineated on the basis of this modality alone, and the presence of an extradural lesion does not distinguish lymphoma from other tumor types. CT in combination with myelography is likely to provide greater detail regarding the extent and location of the lesion, whereas MRI increases the ability to visualize the spinal cord and surrounding structures in a less invasive manner. Plain radiographs of the vertebral column are of little value in attaining a diagnosis, with bony lysis being detected very infrequently.⁸³

CSF collected from the lumbar spine may show elevated protein and white blood cells, predominantly lymphocytes, although abnormal CSF is seen more commonly in dogs because of their higher incidence of leptomeningeal involvement. Occasionally, lymphoblasts (Figure 27-23) can be seen, and in one report neoplastic lymphocytes were identified on CSF analysis in 6 of 17 cats evaluated.⁷²

Treatment options depend on tumor location, histologic grade, extent of CNS involvement, and whether multicentric disease is present. Chemotherapy, either alone or in combination with other modalities, has been shown to be beneficial. In one study of cats treated with cyclophosphamide, vincristine, and prednisone, complete remission was attained in 50% of cases, with a

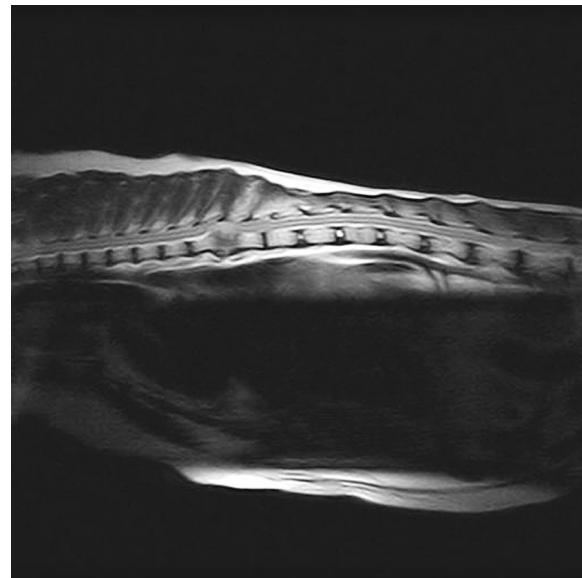


FIGURE 27-24 Magnetic resonance imaging of the spine showing an extraaxial mass lesion in a cat with progressive paraparesis and spinal hyperesthesia.

median duration of remission of 14 weeks.¹²⁹ Surgery in the form of hemilaminectomy or dorsal laminectomy may allow complete removal or cytoreduction of the tumor in some cases, alleviating pain and paresis and providing samples for histologic analysis. When this is combined with chemotherapy, prolonged remission of up to 62 weeks after surgery has been reported.¹²⁹ However, it may not be advisable if intramedullary lesions are present or multiple levels of the spinal cord are involved. Radiation can be used in combination with chemotherapy or surgery (or both) because the spinal cord seems to be relatively resistant to the acute effects of radiation. Long-term prognosis is extremely guarded, despite the greater availability of treatment options and advanced neurosurgical techniques.

Other neoplasms of the spine are rare but include meningioma, osteosarcoma, glioma, malignant nerve sheath neoplasm, meningeal sarcoma, and lipoma (Figure 27-24).^{78,84,111} Median age is typically much higher than in cats with lymphoma (median 12 years), and the clinical course is more protracted because of the slow-growing nature of many of these tumors. Osteosarcoma and meningioma appear to be the most common malignant and benign tumors, respectively,¹¹¹ and accounted for 24% of cases reported in a large retrospective study.⁸³ As with lymphoma, clinical signs reflect the neuroanatomic location, with the most common clinical signs being pain and paraparesis or paraplegia. Unlike lymphoma, conventional radiography can be a useful initial diagnostic tool. Eight of nine cats with confirmed osteosarcoma had bony lysis, and lytic lesions were detected in 14 of 18 cats with other nonlymphoid spinal

neoplasms.⁸³ Vertebral bodies and dorsal lamina are more frequently affected than the dorsal or transverse processes. Additional radiographic signs that may help with antemortem diagnosis include widening of the intervertebral foramen, expansion of the vertebral canal, thinning of the bone, or pathologic fractures. Advanced imaging is indicated even when a lesion is identified on radiography for the purpose of further defining the extent of the lesion and for surgical planning. MRI is considered the superior modality for its excellent anatomic detail and three-dimensional capabilities.

Only a few reports in the veterinary literature address treatment and long-term prognosis in cats with nonlymphoid spinal tumors.^{78,111} Resectability and severity of clinical signs dictate treatment plan, with the primary goal to relieve spinal cord compression, either through surgical management or the use of glucocorticoids. Although surgical intervention may not always achieve complete resection of the mass, cytoreduction will alleviate clinical signs and allow for histopathologic confirmation of tumor type. In a retrospective study of 26 cats undergoing surgery alone for nonlymphoid vertebral and spinal cord neoplasms, the median survival times for malignant (e.g., osteosarcoma) and benign (e.g., meningioma) tumors were 110.5 and 518 days, respectively.¹¹¹ In another report one cat with meningioma was alive 1400 days postoperatively, and another was alive 2190 days after resection of a nerve sheath neoplasm.⁷⁸ Overall, it appears that surgical treatment, even when complete resection is not possible, will palliate clinical signs and may result in sustained quality of life. Data regarding radiation and chemotherapy are lacking in these feline patients, but studies in dogs suggest that one or both of these modalities may prolong MST in some cases.

Spinal Trauma

Many feline patients have access to the outdoors, and thus vehicular accidents and other forms of external trauma to the spine are a common occurrence. Fractures, traumatic disk rupture (discussed previously), luxation, nerve root avulsion, and contusion to the spinal cord are not uncommon. Secondary effects include ischemia, hemorrhage, decreased perfusion, and edema and may have greater potential to damage nervous tissue than the inciting injury.⁷³ The craniocervical, cervicothoracic, thoracolumbar, and lumbosacral junctions appear particularly susceptible to the effects of external trauma,⁷³ but in one report the thoracic and lumbosacral regions were overrepresented.⁸⁴ Careful physical examination is warranted before any neurodiagnostic testing because many of these patients have sustained injuries of the thoracic, abdominal, or pelvic viscera and require immediate stabilization. Concurrent orthopedic injuries are also quite common.



FIGURE 27-25 Myelogram of a cat after being hit by a car. Note the luxation and attenuation of contrast medium at T12-13.

Confirmatory testing begins with conventional radiography and may require sedation, anesthesia, or both. However, the potential for iatrogenic potentiation of spinal trauma exists during handling and positioning of the anesthetized patient, and extreme care must be exercised as such. Complete vertebral radiographs should be taken because a second fracture of the spine is seen in up to 20% of cases.⁷³ Advanced imaging in the form of myelography (Figure 27-25), CT scan, or MRI provides additional information regarding the extent of the injury and may assist in surgical planning and for prognostic purposes.

There is considerable controversy regarding the appropriate treatment of spinal fractures in veterinary medicine, but most practitioners agree that the therapeutic plan must be dictated by the patient's neurologic status. Cats with mild signs such as minor pain, ambulatory paresis, motor deficits, and stable fractures are good candidates for attempting medical management. However, early decompressive surgery may be associated with a more favorable outcome and is considered the best option for animals with unstable fractures, unrelenting pain, severe paresis or paraplegia, or progressive signs. In human studies early surgical intervention reduced complications, length of hospital stay, and cost of care in patients with traumatic spinal injury.⁶⁹ Additionally, early decompression alleviates the compression and thus decreases the cascade of secondary events.⁶⁹

Routine use of corticosteroids has fallen out of favor in recent years for a number of reasons. Dexamethasone, once considered the drug of choice for initial treatment in spinal injuries, has not been shown to inhibit the secondary detrimental effects of trauma on the CNS and is associated with a greater incidence of adverse effects in veterinary patients. Experimental studies in animals suggest that only soluble glucocorticoids (e.g., methylprednisolone sodium succinate) given within 8 hours of injury are of benefit,¹⁰² but adverse effects are common and include gastrointestinal hemorrhage, vomiting, diarrhea, anorexia, and hypotension.



FIGURE 27-26 Radiograph of a kitten with coccygeal separation after having its tail caught in a door.

Supportive care in the form of pain control, bladder expression, physical therapy, appropriate bedding and housing, and management of concurrent injuries may be required in varying degrees. Clinicians and pet owners must be advised of the potentially significant financial and time investment necessary in caring for these patients. Prognosis depends on neurologic status but is considered extremely grave in animals that are paraplegic with loss of deep pain perception.

A unique clinical syndrome in cats results from sacrococcygeal or coccygeal separation (Figure 27-26), a sequela to abrupt pulling of the tail away from the body.⁷¹ Laceration or avulsion of the nerves in the cauda equine leads to varying degrees of compromise to the tail, perineum, pelvic viscera, and pelvic limbs. Clinical signs can range from diminished motor function in the tail alone to signs as severe as complete loss of bowel, bladder, and tail function. Hyperesthesia at the base of the tail is common.⁷¹ Treatment consists of pain control, prevention of urine scald, stool softeners, and bladder management.

The bladder may require manual evacuation if the patient is unable to empty it or if urethral spasm is occurring. Pharmacologic bladder care may include the use of bethanechol, a parasympathomimetic, at 1 to 2 mg/kg, administered orally every 8 hours, to facilitate bladder contraction, or phenoxybenzamine, an alpha-agonist, at 1 mg/kg, administered orally every 8 hours, to relieve urethral spasm. The use of bethanechol alone is strictly contraindicated if increased urethral tone is present because of the risk of bladder rupture.

Tail amputation may be necessary if ischemic necrosis, frequent soiling, or chronic pain is evident.⁷¹ Prognosis may be quite good, especially in those cases with mild signs, but clients must be advised that if no improvement is seen within the first month, the outcome is less favorable.

Vascular Myelopathies

Spinal cord infarction (SCI) is becoming increasingly recognized in veterinary medicine as an important cause of acute myelopathy. Clinical signs are peracute in onset and typically nonprogressive, and the patient may be

monoparetic/monoplegic, tetraparetic/tetraplegic, or paraparetic/paraplegic. Hyperesthesia is not common, although some reports suggest pain at the immediate onset of the infarction. The most well-documented type of SCI in veterinary medicine is fibrocartilaginous embolic myelopathy, in which fibrocartilaginous material derived from the nucleus pulposus gains access to the spinal vasculature.³⁴ The mechanism of action remains controversial, but intervertebral disk degeneration adjacent to the fibrocartilaginous embolic myelopathy is often seen.

Myelographic findings are typically normal, although mild swelling of the spinal cord at the affected site may be appreciated. MRI reveals an intramedullary lesion that is hyperintense on T2 weighting and isointense on T1 weighting with no contrast uptake.⁹⁰ Neutrophilic pleocytosis or cytoalbuminologic dissociation is reported in cases in which spinal fluid was analyzed.¹ Prognosis depends largely on severity of clinical signs, which reflect the degree of ischemic injury and necrosis of the spinal cord. Involvement of the gray matter in the cervical or lumbar intumescence is often associated with a less favorable outcome.³⁴ Many patients recover spontaneously, and those in which improvement is seen within the first week often will go on to make significant improvement.

Other causes of SCI include thromboembolism, hypercoagulable states, vasculopathy, and septic emboli.⁹⁵ An underlying cause should be thoroughly investigated whenever SCI is suspected. Diagnostic workup should include complete blood count, chemistry panel, urinalysis, FeLV and FIV serology, three-view thoracic radiographs, and thyroid panel if indicated. Hypertension has been seen secondary to renal disease in a cat with a cervical infarct,³⁴ so a careful retinal exam for evidence of hemorrhage, as well as blood pressure monitoring, is necessary in some cats. In a series of 13 cats with a diagnosis of SCI, 6 of 13 were found to be hypertensive and seven cats were found to have hypertrophic cardiomyopathy.³⁴ Depending on physical examination and historical abnormalities, coagulation panel, abdominal ultrasound, CSF analysis, or echocardiography may be warranted. MRI is warranted to attain a definitive diagnosis and for prognostic purposes, insofar as the extent of the lesion as seen on MRI, as well as gray matter involvement, may influence outcome (Figure 27-27).

A syndrome of ischemic poliomyelomalacia has been described in cats after abdominal trauma or prolonged vasospasm or embolization of the lumbar arteries.³⁴ Cats typically present with severe neurologic deficits, including paraplegia, absent nociception in the pelvic limbs, absent tail and anal tone, and inability to void. A recent history of abdominal trauma or abdominal surgery is often reported, and clinical signs are acute in nature. Spinal fractures or evidence of external spinal trauma is

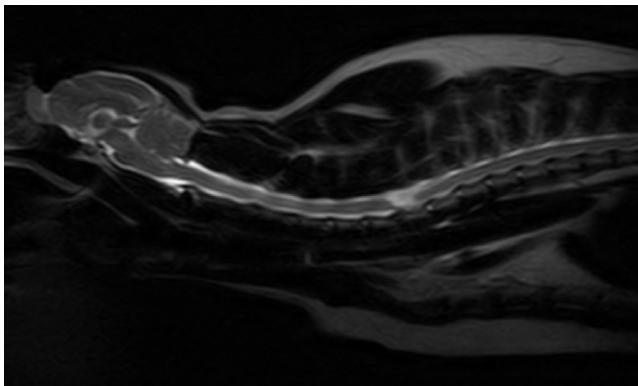


FIGURE 27-27 Sagittal magnetic resonance imaging of a cat with an infarction in the caudal cervical spine. Note the well-defined margins of the lesion, as well as the lack of mass effect. (Courtesy Dr. Kerry Bailey, Oradell Animal Hospital.)



FIGURE 27-28 Severe weakness and cervical ventroflexion in a cat with end-stage renal disease and hypokalemia.

lacking. Evidence of retroperitoneal hemorrhage and, in one cat, an avulsed kidney has been reported. Microscopically, the lesions consist of complete ischemic necrosis of both gray matter and white matter, and such findings have been reproduced experimentally by ligating the aorta at or cranial to the level of the renal arteries.³⁴ There is no known treatment, and prognosis is grave.

NEUROMUSCULAR DISEASES

Disorders of the motor unit are rare in cats and affect skeletal muscle, the neuromuscular junction, or the lower motor neuron. Weakness is the most salient clinical sign common to all these disorders and may vary considerably in severity and distribution, with signs including exercise intolerance, dysphagia, regurgitation, dysphonia, and difficulty jumping.¹²⁰ In addition to weakness, a striking sign often seen in cats is cervical ventroflexion (Figure 27-28), in which the patient is unable to lift the head and the chin rests at the level of the thoracic inlet.⁷⁵

Diagnosis of neuromuscular disorders can be challenging, and a thorough neurologic examination, along with an accurate history, is imperative. A minimum database should include a complete blood count, chemistry panel (including creatine kinase levels), urinalysis, abdominal ultrasound, and possibly thyroid levels. Advanced neurodiagnostics may be indicated as well, including electrophysiologic testing (e.g., electromyogram [EMG], nerve conduction velocities) and nerve and muscle biopsy. This discussion focuses on some of the more common disorders of the motor unit, the diagnostic techniques necessary for making a diagnosis, and therapeutic approaches available for some of these diseases.



FIGURE 27-29 Thoracic radiograph of a myasthenic cat with megaesophagus and regurgitation.

Disorders of the Neuromuscular Junction

Myasthenia Gravis

Myasthenia gravis (MG) is a disorder of neuromuscular transmission resulting from a reduction in the number of acetylcholine receptors at the level of the neuromuscular junction. Acquired MG occurs when antibodies are produced against the acetylcholine receptors, leading to their destruction. Clinical signs may be difficult to distinguish from other neuromuscular disorders and may include generalized weakness and exercise intolerance, collapse, a short-strided gait, and weak palpebral reflexes. Focal signs, including megaesophagus (Figure 27-29) and dysphagia without signs of generalized weakness, may also be seen.¹¹⁷ Abyssinians and the related Somalis are at the highest relative risk for MG, suggesting a genetic basis for this autoimmune disorder.¹¹⁷ A form of acquired MG in cats has been associated with administration of methimazole,¹¹⁹ with clinical signs developing 2 to 4 months after beginning treatment for hyperthyroidism. Congenital MG is extremely

rare and can be diagnosed only through electrophysiologic testing and response to therapy.

The gold standard for confirming a diagnosis of MG is by documentation of antibodies against acetylcholine receptors by precipitation radioimmunoassay (available through the Comparative Neuromuscular Laboratory, University of California; <http://vetneuromuscular.ucsd.edu>). This assay is both highly sensitive and specific. Intravenous administration of edrophonium chloride may temporarily ameliorate clinical signs, but the response of cats to this drug is less reliable than that in dogs.²⁶ In addition to acetylcholine receptor antibody levels, the diagnostic workup should include thoracic radiographs, even in the absence of respiratory signs, on account of the high incidence of thymomas diagnosed in myasthenic cats as well as the potential for megaesophagus. In a retrospective report of 105 cases of acquired MG in cats, 27 of 105 (25.7%) were identified with thymoma. The incidence of megaesophagus is typically lower in cats with MG than it is in dogs because of the different distribution of skeletal muscle in the esophagus of the two species, but megaesophagus was still identified in 14.3% of myasthenic cats in the same study.¹¹⁷

The first line of therapy includes anticholinesterase drugs (pyridostigmine bromide starting at 0.5 mg/kg, administered orally every 12 hours), which help alleviate weakness by prolonging the action of acetylcholine at the neuromuscular junction. Cats may have a greater sensitivity than dogs to the side effects of this drug and may develop ptalism, tremors, respiratory distress, vomiting, and diarrhea, especially at higher doses. If an optimal response to therapy is not seen or unacceptable side effects are observed, corticosteroids may be indicated but should be used with great caution, particularly in cats with megaesophagus. Immunosuppressive doses are not recommended because of the risk of aspiration pneumonia and the potential for corticosteroids to worsen muscle weakness.¹²² Many cats will go into remission spontaneously after months of therapy, and monitoring acetylcholine receptor antibody levels every 3 months is useful in guiding medical management.

Disorders of Muscle

Muscle disorders are uncommonly identified in cats and can be divided into inflammatory and noninflammatory causes.¹²⁰ Noninflammatory myopathies are grouped into those that are primary and those that are secondary to diverse systemic illnesses. Inflammatory myopathies are divided into infectious and noninfectious causes and can appear similar to MG in presentation. The muscle biopsy is the most important diagnostic test for evaluation of muscle diseases¹²² and must be performed before the institution of medical therapy (e.g., corticosteroids).

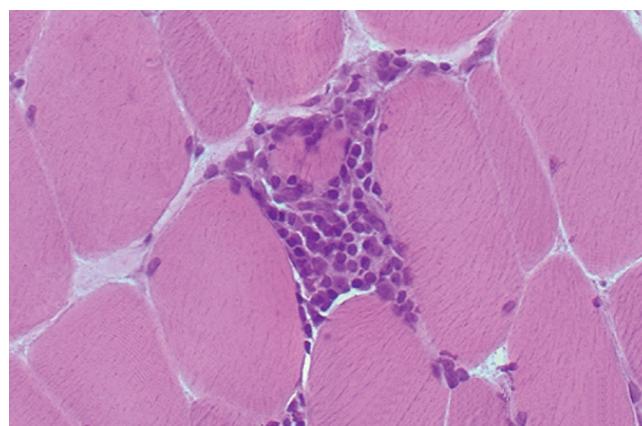


FIGURE 27-30 Muscle biopsy from a cat with polymyositis. Multifocal areas of lymphocytic infiltration are seen. No organisms were present within the biopsies. (Courtesy Dr. Diane Shelton, Comparative Neuromuscular Laboratory, University of California.)

Inflammatory Myopathies

Polymyositis is characterized by myalgia, exercise intolerance, myocarditis, dysphagia, muscle swelling or atrophy, and elevations in serum creatine kinase levels. The degree of elevation of creatine kinase is highly variable, however, and ultimately, a diagnosis of myositis depends on evaluation of muscle biopsy (Figure 27-30).¹²⁰ Additionally, serum CK levels can be significantly elevated in anorectic cats,³⁹ so blood results must be interpreted cautiously in light of the patient's recent nutritional history. Polymyositis can be further divided into either infectious or noninfectious causes (i.e., immune mediated or paraneoplastic). Immune-mediated polymyositis occurs sporadically in cats, but in a review of feline muscle biopsy specimens evaluated at the Comparative Neuromuscular Laboratory, University of California (<http://vetneuromuscular.ucsd.edu>), polymyositis in cats was most often secondary to infectious (FeLV, FIV) or paraneoplastic (prelymphoma, thymoma) disorders.

INFECTIOUS MYOPATHIES

Although not common, *Toxoplasma* infection may manifest as a primary myopathy or can be seen in conjunction with systemic disease, including pneumonia, uveitis, chorioretinitis, intracranial signs, hepatomegaly, vomiting, and diarrhea.¹³⁴ Clinical confirmation requires documentation of cysts on muscle biopsy or through serologic testing. A fourfold rise in IgG over a few weeks or a high IgM titer is suggestive of disease, but many cats can remain positive for IgM over years. Similarly, IgG titers suggest only that the cat has been exposed to *Toxoplasma* and is not a reliable means of diagnosis. PCR can allow for identification of *T. gondii* on tissue, blood, or aqueous humor samples.¹³⁴ Immunosuppression is often a factor in the development of clinically relevant toxoplasmosis in cats, so FeLV and FIV testing should be performed.



FIGURE 27-31 Devon Rex cat with inherited myopathy. Note the typical posture with passive ventroflexion of the head and neck and dorsal protrusion of the scapulae. (Courtesy Dr. Diane Shelton, Comparative Neuromuscular Laboratory, University of California.)

The treatment of choice is clindamycin (25 mg/kg administered orally every 8 to 12 hours) for 2 to 4 weeks, with resolution of clinical signs typically beginning within 1 week after starting therapy.

Other infectious agents reported to cause myositis in cats include *Neospora*, *Clostridium* spp., and *Sarcocystis*. An inflammatory myopathy associated with FIV has been reported and is characterized by elevated creatine kinase levels, abnormalities in EMG testing, mononuclear cellular infiltrates in multiple muscle groups, and myonecrosis.¹⁰⁴ Interestingly, clinical signs associated with these abnormalities have not been reported.

Primary Noninflammatory Myopathies

Primary noninflammatory myopathies are usually associated with abnormalities of the intrinsic metabolic machinery of the muscle or abnormalities in muscle membranes or ion channels.¹²⁰ Many are inherited disorders and have been reported exclusively in certain breeds (e.g., hypokalemic myopathy of Burmese cats, type IV glycogen storage disease in Norwegian Forest cats, and Devon Rex myopathy) (Figure 27-31).

MYOTONIA CONGENITA

Myotonia congenita is characterized by prolonged muscle contraction after cessation of voluntary effort.¹²⁰ This is believed to be due to a chloride channel abnormality inherited as an autosomal recessive trait in some species.¹⁴⁴ Clinical signs include difficulty opening the mouth, muscle hypertrophy, and a stiff gait, with the stiffness decreasing during exercise. Startling of the animal may lead to hyperextension of the limbs and falling to lateral recumbency or spasm of the orbicularis oculi muscle, prolonged prolapse of the nictitating

membranes, and flattening of the ears. Endotracheal intubation may be difficult on account of the inability to open the mouth to a wide angle and narrowing of the glottis caused by muscle spasm.⁵⁴

The diagnosis is supported by characteristic changes on EMG, in which the classic myotonic discharges and “dive-bomber”-like sounds are noted. Further support for the diagnosis is the presence of a sustained contraction of the tongue muscle when tapped, or a “myotonic dimple.” Long-term prognosis is guarded, although affected cats may be able to enjoy some quality of life provided that aspiration pneumonia is avoided.

MUSCULAR DYSTROPHIES

Muscular dystrophies (MDs) are a diverse group of inherited, noninflammatory, degenerative muscle disorders leading to muscle atrophy, hypertrophy of select muscles (e.g., tongue, diaphragm), stiff gait, joint contracture, weakness, exercise intolerance, regurgitation, and dysphagia.¹²¹ The most well-characterized MD in feline medicine is X-linked muscular dystrophy, also called *hypertrophic feline muscular dystrophy* (HFMD), which is associated with an absence of dystrophin and mutations of the dystrophin gene. Other apparently autosomal forms of MD have recently been described, including merosin (laminin alpha-2) deficiency and a unique MD in Sphynx and Devon Rex cats.⁸⁷

Muscle biopsy is characterized by extensive muscle necrosis with large accumulations of macrophages, fibrosis, lipid accumulation, and satellite cells in regenerating muscle.³⁴ Affected cats are typically male, with clinical signs beginning at several months of age. Although cats have been reported to live as long as 5 years, overall prognosis is grave and dysphagia, regurgitation, and dyspnea from hypertrophy of the lingual, pharyngeal, and esophageal musculature as well as the diaphragm will lead to poor nutritional intake and death from aspiration pneumonia.¹²¹

FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

Fibrodysplasia ossificans progressiva is a disorder affecting the epimysium, tendons, and fascia with marked proliferation of fibrovascular connective tissue and associated chondroid and osseous metaplasia.¹⁴³ Clinical signs are characterized by progressive stiffness in the gait, enlargement of the proximal limb musculature, pruritus, and joint pain and are typically seen in young to middle-aged cats of both sexes. Radiographically, multiple mineralized densities (Figure 27-32) can be seen. Muscle biopsy shows collagen proliferation, focal areas of lymphocytic infiltration, and areas of cartilage and ectopic bone formation within the muscle tissue, with the pathologic abnormalities appearing to have originated from the fascial connective tissue. The clinical course progresses rapidly, and there is no known treatment. Prognosis is grave.

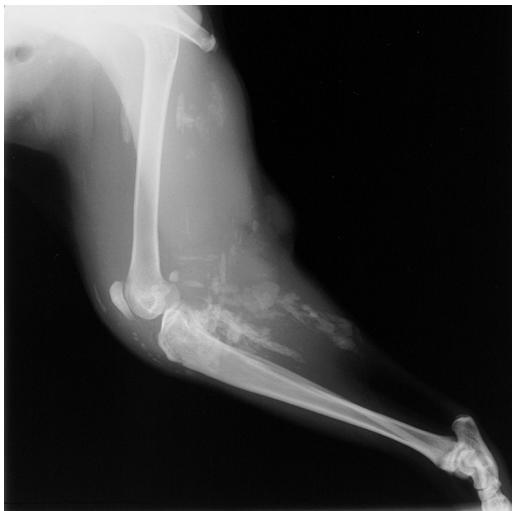


FIGURE 27-32 Lateral radiograph of the pelvic limb showing multifocal mineralized densities in the adjacent musculature in a cat with fibrodysplasia ossificans progressiva. (Courtesy Dr. Diane Shelton, Comparative Neuromuscular Laboratory, University of California.)

Secondary Noninflammatory Myopathies

Secondary noninflammatory myopathies result from nutritional, metabolic, and toxic etiologies. Perhaps the most well recognized of these is hypokalemic polymyopathy, a generalized muscle disorder resulting from low serum potassium levels (1.5 to 3.5 mEq/L), which leads to signs of weakness, cervical ventroflexion (Figure 27-33), myalgia, stiff gait, and a broad-based stance of the pelvic limbs. Reduced potassium intake or increases in the fractional excretion of potassium in the urine secondary to renal disease often precipitate clinical signs. In addition to decreased intake, cats with increased potassium loss through the gastrointestinal tract secondary to vomiting and diarrhea are also at risk.

Other disorders that may give rise to potassium-depletion myopathy include hyperaldosteronism, postobstructive diuresis, diuretic administration, inappropriate fluid therapy, diabetic ketoacidosis, and others. Differential diagnoses include thiamine deficiency, hyperthyroidism, myasthenia gravis, polymyositis, polyneuropathy, hypocalcemic myopathy, and hypernatremic myopathy.⁷⁵ Treatment is aimed at reestablishing normal serum potassium levels and correcting the underlying disorder.

When first examining an adult cat with acute onset of lower motor neuron signs, the clinician should be sure to ascertain whether there has been any recent drug or toxin exposure. Most notably, pyrethrins and organophosphates have been known to result in severe cervical ventroflexion and tremors, as well as seizures. The mechanism of action for these agents is believed to be through the reduction of acetylcholinesterase activity in both the central and peripheral nervous system. Clinical signs can begin within a few hours of exposure, and cats



FIGURE 27-33 Cat with hypokalemia resulting from postobstructive diuresis. Note the typical posture of cervical ventroflexion.

with suspected exposure should be bathed to remove any residual insecticide. Supportive care in the form of muscle relaxants and, if necessary, anticonvulsants, will lead to resolution of signs in 48 hours. Other reported toxins include acrylamide, thallium, chlorpyrifos, vin-cristine, salinomycin, and others.

Disorders of the Lower Motor Neuron

Polyneuropathies of cats can affect sensory, motor, and autonomic neurons with a variety of clinical presentations. Those with involvement of motor fibers will have weakness and muscle atrophy, whereas those with sensory neuropathy may present with ataxia, anesthesia, or paraesthesia.²⁰ Involvement of autonomic neurons may result in ptalism, excessive lacrimation, regurgitation secondary to megaesophagus, urine retention, constipation, and mydriasis. Both inherited and acquired disorders have been reported, and signalment plays a key role in guiding the clinician in differentiating between the two. Definitive diagnosis of polyneuropathy requires electrophysiologic (EMG, NCV, F-waves) testing to confirm the diagnosis and determine the location of the lesion, and nerve biopsy further defines the type of pathology present.²⁰ The ensuing discussion focuses on the more clinically relevant neuropathies seen in feline patients.

Congenital Polyneuropathies

Congenital polyneuropathies are typically seen in cats younger than 1 year of age, with most being progressive and ultimately fatal.²⁰ Clinical signs usually include progressive tremors, paraparesis or tetraparesis, generalized weakness, sensory deficits, and depressed segmental reflexes.²⁰ Concurrent clinical signs, as well as signalment, are critical in helping the clinician arrive at a definitive diagnosis. For example, cats with an inherited primary hyperchylomicronemia develop multifocal neuropathies secondary to lipid deposition and compression of nerves, especially at the level of the intervertebral



FIGURE 27-34 Diabetic cat with polyneuropathy and plantigrade stance. (Courtesy Dr. Diane Shelton, Comparative Neuromuscular Laboratory, University of California.)

foramina. Severe fasting hyperlipidemia and lipemia retinalis are present. Dietary management in the form of a restricted-fat diet results in resolution of clinical signs.⁶⁰

Primary hyperoxaluria is seen in kittens between 5 and 8 months of age, with a rapid course of severe generalized weakness, anorexia, and dehydration.²⁰ This is reportedly an autosomal recessive disorder leading to renal failure from oxalate deposition in renal tubules. The pathogenesis is unclear, but all patients described thus far succumbed to the disease before the age of 12 months.

Other inherited neuropathies include hypertrophic polyneuropathy, glycogen storage disorders in Norwegian Forest cats, and distal axonopathy of Birman cats.²⁰

Acquired Polyneuropathies and Neuronopathies

DIABETIC NEUROPATHY

Neuropathy associated with poorly controlled diabetes mellitus has been well described in the veterinary literature. Symmetric weakness may develop with progressive paraparesis, plantigrade stance (excessive hock flexion), patellar hyporeflexia, and poor postural responses (Figure 27-34).⁶⁸ Clinical signs may progress to involve the thoracic limbs. Functional, structural, and biochemical defects of motor and sensory nerves in both thoracic and pelvic limbs have been identified with Schwann cell injury, leading to demyelination and axonal damage.⁹¹ Strict glycemic control reverses the clinical signs of neuropathy in some cats, although many cats continue to show degrees of clinical weakness even with specific therapy that includes oral hypoglycemic agents or insulin. Acetyl-l-carnitine appears to be of benefit in the treatment of diabetic peripheral neuropathy in humans and has been used in a few cats with persistent clinical signs of neuropathy with subjectively good results.^{27,38,123}

IDIOPATHIC POLYNEUROPATHY

Idiopathic polyneuropathy results in acute onset of generalized weakness; tetraparesis or tetraplegia; decreased segmental reflexes; and, in severe cases, respiratory depression.⁴⁶ Age of onset varies from 3 months to several years, with animals of both sexes affected. The underlying cause is poorly understood, but an immune-mediated basis is suspected. In some cases a toxin (e.g., snake envenomation) or infectious agent may be an inciting factor, and kittens vaccinated against *Microsporum canis* infection have reportedly shown acute flaccid tetraparesis.²⁰ Definitive diagnosis can be attained only by obtaining a representative nerve biopsy; demyelination, axonal loss, and mononuclear inflammation have been reported.⁴⁶ Complete recovery is possible, and treatment with a tapering dose of prednisone over several weeks is recommended. Relapses are not uncommon, however, and cats may ultimately become refractory to treatment with corticosteroids.

FELINE ISCHEMIC NEUROMYOPATHY

Occlusion of the aorta or iliac arteries ("saddle thrombus") is a well-recognized disorder in cats, occurring most often in cats with hypertrophic cardiomyopathy. Clinical signs include acute onset of paraparesis or paraplegia, dysuria, and apparent pain.⁸¹ Occasionally, a thoracic limb lameness of monoplegia may be seen with a thrombus in the brachial artery. Physical examination findings include poor or absent femoral pulses; foot beds and nail beds that are cyanotic and cool; hypothermia; severe weakness distal to the stifle; depressed patellar reflexes; inability to flex or extend the hock; and, in some cases, loss of nociception. Histopathologically, peripheral nerve changes begin at the level of the midthigh and include ischemic degeneration of axons and paranodal and segmental demyelination of the sciatic nerve.³¹ In the cranial tibial muscles, rhabdomyolysis can be noted.³¹ Treatment is aimed at treating the underlying cardiac disorder (see Chapter 20), but prognosis is extremely guarded.

FACIAL PARALYSIS

Facial paralysis affecting one or both facial nerves is commonly seen either alone or in association with myriad disorders. Idiopathic facial paralysis is much less common in cats than in dogs, accounting for only 25% of cases in one report.⁶⁴ Clinical signs include drooling from one side of the mouth, inability to blink on the affected side, and halitosis caused by accumulation of food in the affected oral commissure. A facial droop is not as apparent in cats as it is in dogs. Corneal ulceration may be evident as a result of damage to the parasympathetic fibers responsible for tear production or exposure keratitis resulting from the inability to blink.⁵ On physical examination both the menace response and the palpebral reflex are absent, but sensation to the face remains

intact. When it is a result of disease in the middle ear, facial paralysis may be accompanied by concurrent Horner's syndrome or vestibular signs. A minimum database should include a complete blood count, chemistry panel, otic exam, corneal fluorescein staining, and Schirmer tear test. Advanced imaging (CT or MRI) may be necessary for evaluation of the bullae and brain stem.⁵

ADULT-ONSET MOTOR NEURON DISEASE

Adult-onset motor neuron disease has been seen in cats with slowly progressive signs of generalized weakness, cervical ventroflexion, dysphagia, and muscle atrophy.¹¹⁸ Clinical signs are progressive, and in the end stage spinal reflexes became undetectable. Evidence of denervation can be seen in muscle biopsies, and electrodiagnostics will reveal abnormalities consistent with a neuronopathy. Necropsy examination of the spinal cord in affected cats reveals a decrease in the number of cell bodies in the ventral horn, astrocytosis, and wallerian degeneration in the ventral roots.¹¹⁸ The cause is unknown, but viral, hereditary, immune-mediated, nutritional, and toxic etiologies have all been proposed. Prognosis is grave, but some cats can live many years with mild clinical signs. A similar inherited disorder has been reported in young Maine Coon cats.

DYSAUTONOMIA

Feline dysautonomia (Key–Gaskell syndrome) is a polyneuropathy affecting primarily the autonomic nervous system. Clinical signs include mydriatic pupils that are unresponsive to light, elevation of the third eyelid, dry oral and nasal mucosae, dysphagia, megaesophagus, vomiting, constipation, bradycardia, and incontinence or urine retention (Figure 27-35).^{34,65} Signs are usually acute but may progress over the course of several days or more. The cause is unknown, but a neurotoxin is highly suspected. The disorder was first recognized in cats in the United Kingdom but has been sporadically



FIGURE 27-35 Cat with dysautonomia. Note the elevated third eyelids and dilated pupils. (Courtesy Dr. D. O'Brien, College of Veterinary Medicine, University of Missouri.)

reported elsewhere, including the midwestern United States. Primarily young domestic shorthair cats of either sex are susceptible.

Confirmation of a suspected diagnosis based on clinical signs can be confirmed through administration of 1% pilocarpine drops in both eyes, which will produce constriction of the pupils in affected cats but not normal cats. Alternatively, assays of plasma and urine may reveal reduced amounts of noradrenaline and adrenaline.⁵¹ Histopathologic evaluation of affected animals reveals lesions in both sympathetic and parasympathetic ganglia, with neuronal loss, satellite cell proliferation, and light fibrosis.³¹ Prognosis is extremely poor, and there is no known treatment.⁶⁵

MISCELLANEOUS NEUROLOGIC CONDITIONS

Horner's Syndrome

Horner's syndrome results from loss of sympathetic innervation to the eye and is characterized by miosis, ptosis, enophthalmos, and protrusion of the third eyelid (Figure 27-36).²⁸ Other rare signs of Horner's syndrome include alterations in iris color and change in coat color of Siamese cats secondary to peripheral vasodilation of blood vessels in the skin.⁹⁴ It is helpful to consider that the sympathetic pathway is a three-neuron system, and as such Horner's syndrome can be classified as first, second, or third order.

First-order Horner's syndrome, or upper motor neuron Horner's syndrome, may originate anywhere along the pathway from its origin in the hypothalamus through the lateral tectotegmentospinal system in the cervical spinal cord to its termination in the lateral gray column from T1-3.²⁸ Typically, first-order Horner's syndrome is accompanied by significant neurologic deficits

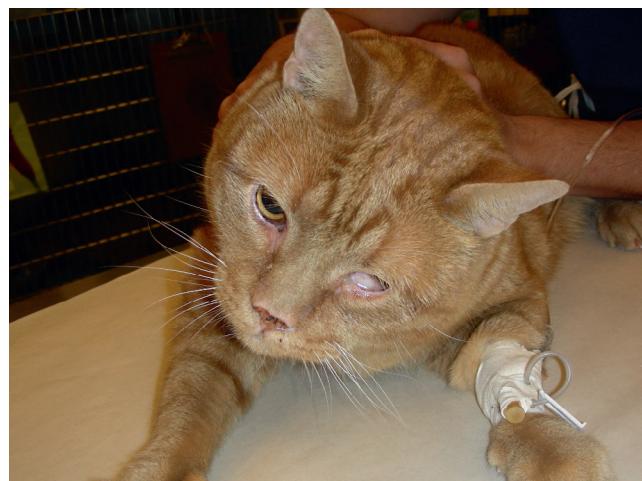


FIGURE 27-36 Cat with classic signs of Horner's syndrome.

and has reportedly been associated with neoplasia, trauma, infarctions, and meningoencephalomyelitis.^{28,63}

Second-order Horner's syndrome (preganglionic) results from a lesion in the pathway beginning from T1-3, through the associated spinal roots and ramus communicans, and up the cranial thoracic and cervical parts of the sympathetic trunk. This trunk travels with the vagus nerve, forming the vagosympathetic trunk, located in the carotid sheath.²⁸ Trauma, aggressive jugular venipuncture, bite wounds, mediastinal lymphoma, and brachial plexus avulsion have all reportedly been the cause of second-order Horner's syndrome.^{28,63}

Third-order Horner's syndrome is most commonly recognized associated with otitis media (Figure 27-37) and results from lesions rostral to the termination of the preganglionic axons in the cranial cervical ganglion, located at the level of the tympanic bulla. In some cases a cause may not be determined, and in a review of 26 cats with Horner's syndrome, a definitive diagnosis could not be attained in 42.3% of cases.⁶³

An initial database should include a thorough otic exam as well as three-view thoracic radiographs to evaluate the mediastinum and other associated structures. A complete neurologic examination can help guide the clinician in determining neuroanatomic diagnosis and whether advanced imaging is necessary. Denervation hypersensitivity of the iris to subpharmacologic concentrations of sympathomimetic drugs is a consequence of Horner's syndrome in dogs and cats and can be used to help predict the site of the lesion in affected patients.⁶³ Instillation of 10% phenylephrine topically will result in mydriasis in less than 20 minutes in cats with third-order Horner's syndrome. In cats with second-order Horner's syndrome, mydriasis will take 20 to 45 minutes to develop, and in those with first-order Horner's syndrome it will take greater than 45 minutes. However, the sensitivity and specificity of this test have not been determined, and the results should be interpreted cautiously, with the history and examination findings being

the most useful means of predicting underlying cause. Treatment of Horner's syndrome is unnecessary, and therapeutic efforts should instead be directed at the primary etiology.

Feline Hyperesthesia Syndrome

Feline hyperesthesia syndrome (FHS) is a poorly understood disorder characterized by myriad clinical signs, including rippling of the skin over the lumbar muscles, excessive grooming, tail chasing, mydriasis, self-mutilation, aggression, frantic biting at the feet and tail base, and vocalization.^{21,101} Palpation of the lumbar musculature may elicit signs of pain. Affected cats commonly stare at their tail, then attack the tail or flanks.²¹ Although all breeds can be affected, Siamese, Burmese, Persian, and Abyssinian cats are more commonly afflicted.⁵⁷ The behavior may be induced by petting or stroking the cat's fur and most commonly occurs in the morning or later in the evening.

Differential diagnoses relate to disorders of the skin, nervous system, musculoskeletal system, and behavioral disorders.²¹ Dermatologic disorders such as flea allergy dermatitis and atopy must be ruled out as possible triggers. Likewise, diseases of the spine, such as IVDD, should be considered and ruled out as a potential source of lumbar pain. Numerous theories point to a compulsive disorder resulting in self-injurious behavior.²¹ Others propose that it is a seizure disorder and best treated with anticonvulsant medication. However, results of EMG and muscle biopsy in five cats with signs of FHS were consistent with an inclusion body myositis/myopathy, suggesting myalgia as a trigger.⁸²

There have been no controlled studies comparing the efficacy of various treatments for FHS, and cat owners must be made aware that a significant trial-and-error period may be necessary before the desired clinical response is attained. The most common treatments used for FHS are flea medications, corticosteroids, anticonvulsants, and anti-anxiety drugs (Table 27-3). The author has not had success with steroids and usually will instead begin treatment with PB (2 mg/kg, administered orally every 12 hours) and increase the dose according to clinical response and drug levels (discussed previously). Alternatively, gabapentin at 10 mg/kg, administered orally every 8 to 12 hours, has both anticonvulsant as well as pain-relieving properties and is considered safe for use in cats. The clinician must be aware that gabapentin pediatric suspension contains xylitol; if a suspension must be used, a xylitol-free product must be obtained from a compounding pharmacy.

Selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (0.5 to 2 mg/kg administered orally every 24 hours) are occasionally recommended when anticonvulsants do not prove effective.²¹ The adverse effects of SSRIs include sedation, anorexia, irritability, vomiting,

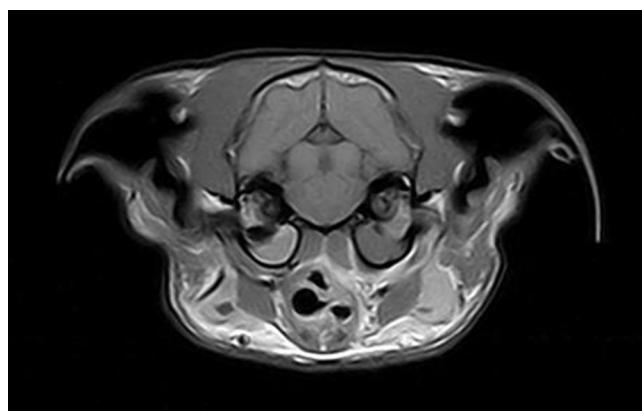


FIGURE 27-37 Magnetic resonance imaging of the cat from Figure 27-36. Note the fluid-filled tympanic bullae bilaterally.

TABLE 27-3 Drugs Used for Treatment of Feline Hyperesthesia Syndrome

Drug	Dose	Comments
Phenobarbital	2 mg/kg, PO, every 12 hours	Increase dose according to response and drug levels; for monitoring, see Table 27-1
Gabapentin	10 mg/kg, PO, every 8 to 12 hours	Ensure suspensions are xylitol free
Fluoxetine	0.5 to 2 mg/kg, PO, every 24 hours	Adverse effects include sedation, anorexia, irritability, vomiting, and diarrhea; inhibition of hepatic cytochrome P450 enzymes
Clomipramine	0.5 to 1 mg/kg, PO, every 24 hours	Adverse effects include sedation, anticholinergic effects, potentiation of arrhythmias, lowering of the seizure threshold

PO, By mouth.

and diarrhea. In addition, SSRIs inhibit the function of the liver cytochrome P450 enzymes, and care should be taken when prescribing concurrent medications that rely on these enzymes for their metabolism (e.g., PB, carbamazepine, benzodiazepines). Tricyclic antidepressants, such as clomipramine (0.5 to 1 mg/kg, administered orally every 24 hours)²¹ can also be used to treat FHS. Adverse effects associated with this drug include sedation, anticholinergic effects, potentiation of arrhythmias in predisposed patients, and lowering of the seizure threshold in patients with seizure disorders.²¹ Long-term medical and behavioral management may be necessary, and cats with FHS often require ongoing adjustments in type or dosage of medication (or both).

Tetanus

Tetanus is a result of sustained muscle contraction without relaxation that is most commonly caused by infection with the anaerobic, ubiquitous organism *Clostridium tetani*.^{24,29} Under certain conditions (e.g., penetrating wound) neurotoxin produced by the bacterium is transported up axons in a retrograde fashion to the level of the spinal cord or brain.²⁴ Ultimately, tetanus toxin (called *tetanospasmin*) acts on inhibitory interneurons, preventing the release of glycine in the spinal cord and gamma-aminobutyric acid in brain stem motor nuclei.²⁹ *Tetanospasmin* may remain bound for up to 3 weeks.²⁹ The main binding site is inhibitory interneurons that act on motor neurons innervating the antigravity extensor muscles.²⁹ Species susceptibility is highly variable, but cats are generally regarded as quite resistant.^{24,29} Nonetheless, there are sporadic reports of this disease in cats,^{77,105,137} and the author has witnessed a handful of cases over the past 10 or more years.

Clinical signs usually are seen 5 to 10 days after wound infection or surgical procedure,^{24,29,77} but can be delayed by up to 21 days.^{77,137} The site where clinical signs first are noted will usually reflect the site of entry of the toxin into the CNS. For example, cats that have developed tetanus after castration will typically develop signs first in the pelvic limbs, after which there will be



FIGURE 27-38 A cat with focal tetanus after suffering a wound to the affected limb. (Courtesy www.felipedia.org/.)

rapid and diffuse spread of the toxin throughout the CNS.²⁹ However, tetanus may remain focal (Figure 27-38), with signs remaining confined to a single extremity where the toxin first entered the CNS.²⁹ In the generalized form the gait is stiff, there is increased muscle tone, and there may be excessive contraction of the facial muscles, known as the classic *risus sardonicus*. Prolapse of the third eyelid, wrinkling of the forehead, and trismus (lockjaw) may also be evident.^{24,29} In the most severe form, the patient is recumbent, with opisthotonus and extensor rigidity in all four limbs, and seizures or respiratory arrest may ensue.^{24,29}

Diagnosis is largely based on history and the classical physical examination findings, and in some cases a recent wound or surgical procedure may not always be evident.²⁴ Treatment is largely supportive, although if a wound is present, débridement and antibiotics to kill any remaining *C. tetani* organisms are indicated. Penicillin G is considered the drug of choice, but amoxicillin-clavulanic acid and metronidazole have also been reportedly effective.¹³⁷ The benefit of tetanus antitoxin in cats remains uncertain insofar as there is too little information in the literature regarding its safety and efficacy. Supportive care depends on severity of signs, and cats severely affected may require muscle relaxants, physical

therapy, bladder management, and nutritional assistance. Recovery can be prolonged, and periods lasting from several weeks to up to 5 months have been reported in affected cats before clinical resolution.^{105,137}

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