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Chapter 55

Seizure Disorders and Treatment Options

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In order to institute appropriate therapeutic strategies for seizure management in cats, the clinician must be aware of the pathophysiology and associated disease processes. Seizure disorders in cats have been reviewed in previous literature.[1-9] A seizure is a clinically detectable manifestation of paroxysmal, excessive, and synchronous discharges of a population of hyperexcitable cerebral neurons. Classification schemes are reviewed for determining seizure type and differential diagnoses. Acquired causes for seizures are emphasized to assist with diagnosis and treatment of seizure disorders in cats.

CLASSIFICATION OF SEIZURES

Further classification of seizure type relies on appropriate use of the term *epilepsy* (recurrent seizures). Recurrent seizures are defined more broadly as epilepsies. Podell, Fenner, and Powers adopted a nomenclature scheme from human epilepsies based on identifiable causes.[10] Primary epileptic seizure (idiopathic) is the term used if an underlying cause cannot be identified. If seizures result from a structural lesion, they are defined as secondary epileptic seizures. The term *reactive epileptic seizure* is used when the normal brain reacts to transient systemic insult or physiological stresses; these seizures are not considered recurrent. Epilepsies also are described as *asymptomatic* (primary, idiopathic) and *symptomatic* (secondary).[11] I use the terminology of primary and secondary epilepsies for this discussion. Secondary epilepsy is common in cats, and appropriate diagnostic tests are necessary to determine the underlying cause.[2,3,5,6]

Primary epilepsy implies recurrent episodes of seizure activity associated with a primary functional cerebral disorder (having a physiological or biochemically related genetic basis). Typically, these seizures are tonic clonic and generalized with no identifiable structural brain lesions. Physical and neurological examinations are normal. Advanced imaging and CSF analysis results are normal. Incidence of primary epilepsy in cats is low when compared with that of dogs.

Secondary epilepsy (also named symptomatic, acquired, or structural) implies recurrent seizure activity caused by acquired but inactive brain diseases that occur after traumatic, ischemic, and encephalitic events. According to some authors,[2,3,9] the term epilepsy should be restricted to recurrent seizures resulting from nonprogressive intracranial causes of either a structural or functional nature. Others classify secondary epilepsy (symptomatic) as recurrent episodes of seizure activity associated with an underlying structural disorder such as inflammation, trauma, ongoing hypoxia or ischemia, or neoplasia.[2,3,9] In cases of secondary epilepsy, partial seizures (focal or complex partial with or without secondary generalization) are observed more commonly and may be accompanied by an abnormal neurological examination with or without lateralization. Secondary epilepsy is thought to be more common in cats than primary epilepsy.[2] *Reactive seizures* arise as a consequence of extracranial metabolic or toxic insults.

CLINICAL SIGNS

Seizure type can be characterized as (1) generalized with major motor activity (i.e., generalized tonic-clonic events), (2) partial with subtle motor manifestations (mild generalized or partial seizures [i.e., limb, facial, or whisker twitching]), or (3) nonmotor (psychic or autonomic activity [i.e., tail chasing, floor-licking, vocalizing]).

Seizures in cats, regardless of the cause, manifest themselves in different ways and are more variable in clinical presentation than in dogs.[1-9] The owner may not notice the ictal phase or actual seizure event readily until the signs are more obvious. The aura or preictal phase may comprise subtle behavioral changes that include aggressiveness, pacing, crying, restlessness, hiding, unusual affection, salivation, frantic running, hissing, growling, and anxiety.[2-6] The aura may last seconds to days, but usually lasts for several minutes.

The ictal phase can be classified further according to seizure type. *Generalized* and *partial* seizures occur in cats. *Generalized seizures* (tonic-clonic or grand-mal seizures) manifest as loss of consciousness, recumbency, and tonic-clonic motor activity. The major motor activity can consist of generalized tonic movements with the limbs in rigid extension and pur-

Figure 55-1. Feline seizures can be comprised of violent motor activity, autonomic release, in addition to facial twitching, salivation, kicking, piloerection, and chewing.

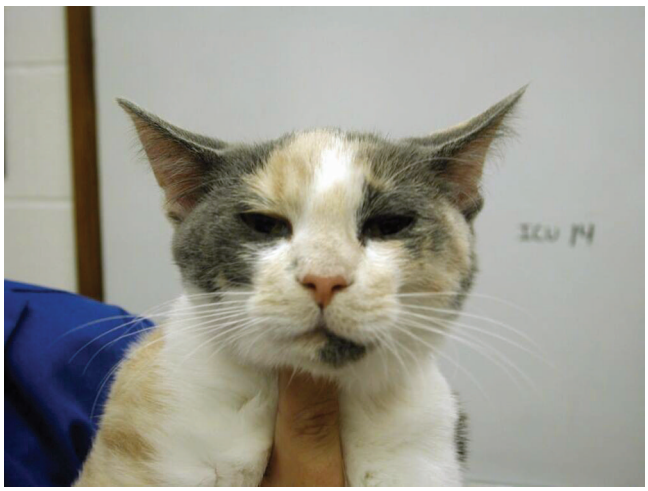

Figure 55-2. Postseizure or postictal cats may appear blind and exhibit inappropriate behavior for a short interval after the seizure event.

poseless limb movements and paddling. Opisthotonus and claw extension in addition to mouth-chomping and pupillary dilation also may be observed. At times, tonic flexion (emprosthotonus) is observed, which may be followed by moderate to severe muscle twitching (clonic phase). The patient may not have loss of consciousness during this type of event. Sometimes generalized seizures can be violent. The cat may jump up into the air as if it were thrown and propel itself forward and from side to side. Autonomic release (urination and defecation) usually accompanies the motor activity in addition to facial twitching, salivation, kicking, piloerection, and chewing (Figure 55-1). Self-inflicted trauma may be observed to include contusions, excoriations, biting of the tongue, or avulsion of the claws. Cats also may exhibit mild or nonconvulsive seizures, which are manifested by impaired consciousness, pupillary dilation, bilateral facial twitching, muscle spasms of the head and neck, and possibly, autonomic release.[2-6,9] The ictus usually lasts from seconds to minutes and sometimes can progress to status epilepticus.

The postictal period is similar to that observed in dogs and can last from seconds to days. This period can manifest as confusion, aimless wandering, pacing, blindness, increased hunger, and changes in sleep/wake patterns (Figure 55-2).

Partial seizures are subdivided into *complex partial seizures* and *simple partial seizures*; complex partial seizures are common in cats. Such events often have lateralizing signs preceding or during the ictus. Cats with complex partial (psychomotor) seizures manifest impaired consciousness with stereotypic motor activity (that may lateralize) and behaviors.[5,6,9] These activities include turning of the head to one side, chewing motions, transient staggering, and ventral flexion of the head. These episodes often are preceded by a short, piteous cry, intermittent episodes of aggression or fright, hissing, growling, raising of a single limb (repetitive movements), tail piloerection, and transient periods of incoordinated, frantic running or bizarre aimless movements. Owners describe their cats as acting like they are "possessed," or in a trance as if they were hallucinating. Compulsive activities such as biting, self-excoriation, and circling can be observed. These episodes of bizarre behavior are distinguished from behavioral issues by the presence of facial twitching, salivation, or a secondary seizure generalization.

Simple partial seizures are characterized by near-normal or normal mentation and the appearance of unilateral motor signs involving a part of or all of the body. Cats with focal seizures often twitch the eyelids, whiskers, and/or ears either in combination or separately. Head-shaking may occur and be accompanied by body jerking. Salivation, urination, and pupillary dilation are transient signs. Continuous vocalization and a brief rise in body temperature can be observed. Hyperthermia ensues as a result of continuous motor activity that can last from minutes to hours. Partial motor seizures are variable in clinical presentation and difficult to recognize for the untrained eye.[2,5,6] Also, partial seizures may progress to tonic-clonic or generalized seizures. Seizures of this type may be more difficult to control because of the prolonged ictal phase. Up to one third of cats have seizures that progress to status epilepticus or cluster seizures. Cats also may have an atypical presentation of nonconvulsive seizures that go undetected for prolonged periods.[2,6,12,13] Requesting the pet owner to videotape these episodes is helpful to document the severity and type of seizure.

DIFFERENTIAL DIAGNOSES

Signalment and initial examination assist with establishment of differential diagnoses. Differential diagnoses for seizure disorders in young cats (less than 4 years of age) include congenital, inflammatory, infectious, toxic, and metabolic causes, whereas in the older cat (over the age of 5), common differential diagnoses include vascular, neoplastic, and infectious inflammatory causes. Exceptions to this guideline do occur; therefore, causes for seizures are assessed on an individual basis.

Secondary or reactive epilepsies are common in cats, whereas in dogs, primary (idiopathic) epilepsy is considered a common differential diagnosis.[2,5,6,9] However, reports have described that at least 50 per cent of cats studied were considered as idiopathic epileptics because the seizure etiology could not be determined after exhaustive diagnostic testing.[1,3] In other words, an underlying cause is suspected but cannot be proven

antemortem. Careful inspection of the brain postmortem may reveal the symptomatic cause.

For the purposes of this discussion, origins of secondary epilepsies in cats are subclassified as *extracranial* or *intracranial*. A disease process of extracranial cause disrupts the normal physiology of the brain. Examples include metabolic disorders, nutritional disturbances, and toxins (Table 55-1). A disease process of intracranial origin disrupts or changes the normal architecture of the brain tissue or vasculature. Examples include neoplasia; inflammatory, infectious, or vascular lesions; congenital anomalies; degenerative disorders; and trauma.

Extracranial Etiologies

Hepatic Encephalopathy

Seizures associated with clinical signs of hepatic encephalopathy (HE) in cats occur relatively infrequently.[2,5,6,14,15] Causes of HE include portosystemic shunting, severe hepatic lipidosis, cholangitis/cholangiohepatitis (either primary or secondary to infectious diseases such as feline infectious peritonitis), neoplasia, and end-stage liver disease. A myriad of metabolic imbalances and toxic substances act synergistically to produce neurological signs. The major contributor to the clinical signs observed is hyperammonemia[5,14] (see Chapter 11). Mercaptans, indoles, and aromatic amino acids also play a role in abnormal neurotransmission and generation of false neurotransmitters available for use in the brain. Increases in excitatory neurotransmitters such as glutamate and alterations in endogenous benzodiazepines have been documented in animals with seizures. High cerebral concentrations of these benzodiazepine-like substances may explain the relative rarity of seizures in cats with HE. The exact role of these metabolic by-products in the generation of seizures has not been determined (Figure 55-3).

Depending on the underlying cause of the HE, most cats will be systemically ill. Neurological signs are consistent with a diffuse forebrain localization and commonly are episodic in onset. If seizures occur, they are accompanied by long periods of abnormal behavior and mentation. Aberrant or bizarre behavior, dementia, aggression, ataxia, head pressing, propulsive circling, blindness, mydriasis, ptyalism, and partial or generalized seizures, may be observed. In cases of portosystemic shunts, the aforementioned signs may occur within hours after eating and often are accompanied by severe ptyalism. Excess salivation is not a manifestation of seizure activity but is theorized to be due to cerebrocortical-mediated abnormal

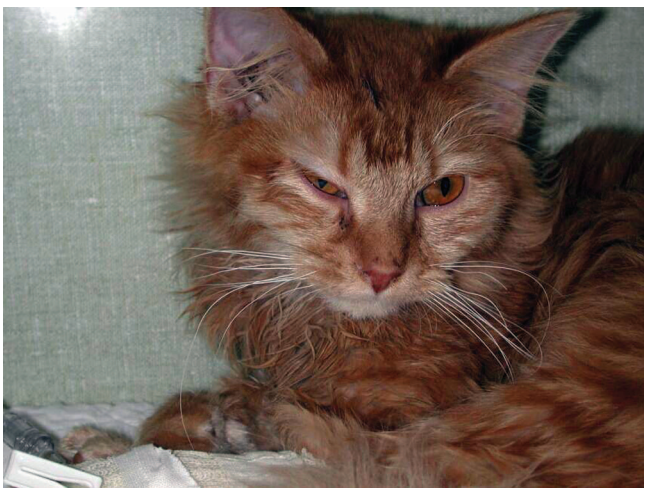

Figure 55-3. A metabolic cause of seizures in young cats is hepatic encephalopathy secondary to an extravascular portosystemic shunt.

Table 55-1 | **Etiology of Feline Seizures**

INTRACRANIAL
Neoplasia
Meningioma
Lymphoma
Glial tumors
Pituitary adenoma/adenocarcinoma
Choroid plexus adenoma/adenocarcinoma
Metastatic
Inflammatory/Infectious
Toxoplasmosis
Cryptococcosis
Blastomycosis
Cladosporium
FIP
FeLV/FIV
Rabies
Aberrant parasite migration (*Cuterebra* larvae or adult *Dirofilaria immitis*)
Other unknown viral causes (nonsuppurative meningoencephalitis)
Vascular
Ischemic encephalopathy
Hypertension
Embolism secondary to underlying cardiac disease
Thromboembolism of unknown cause
Polycythemia (relative versus absolute – primary versus secondary)
Degenerative/congenital/anomalous/malformation
Storage diseases
Hydrocephalus
Traumatic
Immediate
Delayed (posttraumatic epilepsy)
EXTRACRANIAL
Metabolic
Hepatic encephalopathy
Lipidosis
Portosystemic shunt
Cirrhosis/fibrosis
Neoplasia
Cholangitis/cholangiohepatitis
Hyperthyroidism
Hypocalcemia
Primary hypoparathyroidism
Post-thyroidectomy
Hypoglycemia
Insulin-secreting tumor (insulinoma)
Insulin overdose
Sepsis
Severe uremia (end-stage renal disease)
Toxins
Lead
Organophosphates
Ethylene glycol
Nutritional
Thiamine deficiency (terminal stage)
EPILEPSY
Functional
Idiopathic
Genetic
Structural
Postencephalitic
Posttraumatic
Postischemic (FIE, hypoxic event)

behavior.[5,14] Routine complete blood cell counts and serum chemistries in addition to preprandial and postprandial bile acids, resting ammonia levels, abdominal ultrasound, rectal portal scintigraphy and intraoperative portography, and liver biopsy are useful diagnostic aids. Low-protein diets, oral and parenteral antibiotics, antifibrotic agents, and lactulose are indicated for medical treatment of HE depending on the underlying cause.

Surgical correction is the treatment of choice for an extrahepatic shunt in the feline patient.[14] Placement of an ameroid ring constrictor on single extrahepatic portosystemic shunts in cats resulted in a low rate of surgical complication and postoperative mortality.[15] Many cats did have postoperative complications. Neurological complications included central blindness, hyperthermia, frantic behavior, and generalized motor seizures. The pathophysiological mechanism of postligational seizures is poorly understood.[14] Alterations in benzodiazepine concentration have been associated with post-ligational seizures. Animals may decompensate as a consequence of down-regulation of receptors and rapid decrease in concentration of circulating neurotransmitters.

Hypoglycemia

Hypoglycemia in adult cats is caused by insulin overdose, liver failure, sepsis, and rarely, insulin-secreting tumors.[5] The initial signs of hypoglycemia reflect the body's response to decrease of blood glucose rather than the hypoglycemia itself. Increase in sympathetic tone (release of norepinephrine and epinephrine) leads to adrenergic signs of tachycardia, dilated pupils, tremors, irritability, and vocalization (see Chapter 20). Because the brain relies on passive diffusion of glucose, and it is deprived of its energy substrates, signs progress rostral to caudal.[14] The cerebrocortical neurons are more susceptible to the effects of hypoglycemia. Initial forebrain signs of neuroglycopenia include confusion, dullness, and seizures. Caudal fossa signs and death ensue if the condition persists and goes untreated. Routine diagnostic testing and history usually differentiate between insulin overdose, sepsis, and liver disease.

Treatment with intravenous dextrose supplementation and elucidation of underlying cause of the hypoglycemia are key to management of the hypoglycemic patient. Prolonged hypoglycemia causing neuronal death may lead to a permanent seizure focus, and antiepileptic drugs are indicated if seizures persist after correction of the hypoglycemia.[5,14]

Hyperthyroidism

Hyperthyroidism is diagnosed in cats usually older than 6 years of age and can affect the central nervous system (CNS) and peripheral nervous system (PNS). Normally, the brain maintains thyroxine (T_4) and triiodothyronine (T_3) concentrations within a narrow range. The role of hyperthyroidism as a cause for seizures may be linked to the ability of thyroid hormones to decrease the electrical threshold of cerebral tissue directly. Other proposed mechanisms include changes in cerebral oxygen and glucose utilization, altered cerebral blood flow, and altered concentrations of neurotransmitters.[5,14,17] Systemic effects of hyperthyroidism have been discussed elsewhere. CNS signs include restlessness, irritability, aggression, hyperexcitability, aimless wandering, pacing, circling, abnormal sleep/wake patterns, generalized or partial motor seizures, and acute focal neurological deficits (similar to cerebrovascular accidents).[5,17] Diagnosis of hyperthyroidism is based upon elevated T_4 concentrations and nuclear scintigraphy (see Chapter 21). Treatment includes medications that decrease the production of thyroid hormone, radioactive iodine therapy, and surgical excision of the adenomatous thyroid tissue (see Chapter 22). Persistent seizure foci may be a sequela to hyperthyroidism, and the affected cat may require antiepileptic drug therapy after primary treatment for hyperthyroidism.

Hypertension

Normal systolic blood pressure in cats should measure less than 160 mm Hg. Common causes of hypertension in cats are hyperthyroidism, hypertrophic cardiomyopathy, and renal disease. Hypertensive animals usually present with retinopathy and blindness, but similar changes in the brain can lead to focal hemorrhage and atherosclerotic changes.[5,14] Almost half of the cats in one study had other neurological signs in addition to blindness.[18] Seizures, ataxia, nystagmus, sudden collapse, and paraparesis have been reported.[5,14] Diagnosis is based upon documentation of repeatable hypertension and elucidation of the underlying cause of the elevation. Therapy is aimed at reversing the hypertension using oral antihypertensive drugs and treating the underlying cause. Certain antihypertensive drugs (nitroglycerin) can cause cerebral vasodilation, which can worsen the encephalopathy. Permanent seizure foci may be a sequela to the effects of hypertension, and long-term use of antiepileptic drugs may be necessary.

Electrolyte Imbalances

HYPERNATREMIA/HYPONATREMIA. Sodium is the major extracellular osmol. Imbalances can lead to formation of osmotic gradients, which can have profound CNS and PNS effects. Clinical signs of hyponatremia are associated with the degree of the hyponatremia and the rapidity of onset. Clinical signs occur with sodium concentrations below 120 mEq/L. Cerebral edema occurs as a result of osmotic differences between the brain and the extracellular fluid. With chronicity (Na^+ <110 mEq/L), energy metabolism and transport mechanisms may be affected. Neurological signs initially include lethargy and vomiting that can progress to seizures, coma, and death. Rapid correction of chronic hyponatremia may lead to myelinolysis (not described in cats) in the thalamus and pons, a sequela of osmotic shifts and blood-brain barrier disruption.

Hypernatremia can occur as a result of free water loss from the body (adipsia). Clinical signs associated with hypernatremia manifest when the sodium concentration is above 170 mEq/L, which causes an increase in serum osmolality. Ataxia, tremors, myoclonus, tonic spasms, coma, and death can occur. Therapy for hypernatremia and hyponatremia is aimed at correcting the underlying cause in addition to correcting the sodium imbalance as described in the literature.[5,14]

Thiamine Deficiency

Thiamine is an essential, water-soluble B vitamin (B_1) that is a co-factor in the decarboxylation of pyruvate and α-ketoglutarate, and is a necessary co-factor for several steps of the Krebs cycle. Thiamine deficiency interferes with normal energy metabolism in the brain, and a buildup of lactic acid

ensues as the brain is forced into anaerobic metabolism.[5,14] Some fish (tuna and salmon) contain the enzyme thiaminase; if raw fish is prepared at home, cats may develop this deficiency. Central vestibular dysfunction is a classic neurological sign of thiamine deficiency. Generalized seizures usually occur in the terminal stages.[2,5] Diagnosis is based upon history, clinical signs, and response to treatment. Treatment entails thiamine supplementation (either injectable or oral) and supportive care.

Toxic Encephalopathies

LEAD TOXICITY. Common sources of lead include lead-based paint, cages, batteries, grease, and fishing sinkers. Cats are exposed to lead paint chips during home remodeling and ingest the lead through their grooming habits. Chronic exposure to small amounts of lead results in a toxicosis. The effect of lead on the nervous system occurs secondary to decreased blood supply because of capillary and small arteriolar damage. Laminar cortical necrosis is a common histological finding. CNS signs can include altered levels of consciousness, hyperexcitability, excessive vocalization, seizures (either partial or generalized), opisthotonus, paraparesis/plegia, muscle spasms, hyperesthesia, mydriasis, or blindness. Diagnosis is based upon history, clinical signs, and the finding of blood lead levels above 0.35 ppm. Treatment includes removal of lead from the gastrointestinal tract and use of lead chelators such as calcium EDTA.[5]

ORGANOPHOSPHATES AND CARBAMATES. Organophosphates (OP) and the carbamates are acetylcholinesterase inhibitors and common ingredients in flea shampoos and parasite dips. Accumulation of acetylcholine occurs at nerve endings, which results in overstimulation of cholinergic receptors of the somatic, autonomic, and central nervous systems.[5] Clinical signs reflect actions of acetylcholine on muscarinic and nicotinic cholinergic receptors. These signs include vomiting, ptyalism, lacrimation, diarrhea, and, on occasion, hyperactivity and seizure activity. Diagnosis is based upon the history of ingestion and clinical signs. Treatment consists of parasympatholytic agents, supportive care, and antiepileptic drug therapy. Atropine counteracts the muscarinic effects of OP or carbamate toxicity. Pralidoxime chloride (2-PAM, Protopam Chloride, Wyeth-Ayerst) is administered as soon as possible after exposure. 2-PAM disrupts the bond between the OP and acetylcholinesterase to form a complex that is eliminated in the urine. 2-PAM is most effective if administered within the first several hours after exposure before the OP "age" with time. Diphenhydramine is recommended to counteract the nicotinic effects of OP toxicity. More in-depth discussion for treatment is covered in the fourth volume of *Consultations in Feline Internal Medicine,* Chapter 48.

Hypoxia

Transient cerebral hypoxia is much more likely to cause seizures and syncope with seizure-like manifestations in cats than dogs.[9] These events can be precipitated by stress and exercise. Hypoxia often is a sequela of cardiovascular disease, hematological disorders, endocrinopathies, and ischemic events. Diagnosis and treatment are aimed at correcting the primary cause and controlling seizure events with antiepileptic drug therapy if activity persists.

Intracranial Etiologies

Intracranial causes of seizures are divided into structural and functional (idiopathic epilepsy). The literature suggests that structural brain disease is more common in cats than idiopathic epilepsy.[1-9] Structural brain disease in cats used to imply a more guarded prognosis. More recent studies indicate that some of these structural lesions may be nonprogressive, thus having a better prognosis.[3,9] The list of intracranial diseases causing seizures in cats is extensive (see Table 55-1). Selected diseases are highlighted in this chapter.

Neoplasia

Meningioma is the most common CNS neoplasm in cats. Meningiomas are characterized as slow-growing, space-occupying masses that are histopathologically benign in most cases. Masses can occur singly or in a multifocal pattern. Signalment includes cats older than 8 years of age. Male cats are more predisposed than female cats.* Clinical signs vary with lesion location, the forebrain affected most commonly. Clinical signs usually are progressive and lateralizing with a high incidence of focal or partial seizures. Other neurological signs observed are circling (usually toward the side of the lesion), behavior changes, contralateral visual loss, partial cranial nerve deficits, conscious proprioceptive loss, and hemiparesis. Diagnosis and treatment options are discussed in more detail in the fourth volume of *Consultations in Feline Internal Medicine,* Chapter 50.

Primary and secondary CNS lymphoma also can cause seizure activity.[3,5,19-21] The signalment of cats with LSA tends to be young to middle-age (between 7 and 10 years). No sex predilection exists. The forebrain is a common site and presenting clinical signs are similar to those of meningiomas. Other intracranial neoplasms include glial tumors (astrocytomas, oligodendrogliomas), pituitary tumors (adenomas/adenocarcinomas), choroid plexus tumor, medulloblastoma, and gangliocytoma. Metastatic tumors include renal lymphoma and mammary adenocarcinoma.[16,19] (See Chapter 54 for a complete discussion of intracranial tumors.)

Inflammatory Infectious Diseases

Infectious diseases such as feline infectious peritonitis (FIP), feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), and toxoplasmosis are reported as structural causes of seizures in cats.† The multifocal lesion distribution of these diseases may cause focal, partial, or generalized seizures. The incidence of seizures is reported variably in the literature, and seizure activity often is accompanied by concurrent systemic illness (FIP and toxoplasmosis).[22]

According to some reports, the most common structural cause of seizures in cats (47 per cent) is a nonsuppurative meningoencephalitis of an unknown etiology, but suspected to be viral or immune-mediated.[2,8,9] Recurrent seizures were the only clinical sign in the majority of cats in this study and appeared to be self-limiting, but seizures persisted in some cats. It is believed currently that these cases are likely to be the result

*References 3,5-7,16,19,20.
†References 2,3,5,6,8,9,16,22-24.

of a non-FIP virus yet to be identified.[8] Cats of all ages were affected and demonstrated the full spectrum of seizure activity from focal events up to status epilepticus.[9] Results of neurodiagnostic testing were within normal limits. Most cats had an excellent outcome on anticonvulsants, including those with severe and initially refractory seizures. In another study describing nonsuppurative meningoencephalitis, it was the third most frequent diagnosis after neoplasia and FIP as a cause of seizures in cats. In these cases, concurrent systemic illness and mild to moderate changes in cerebrospinal fluid were observed.[12] Symptomatic treatment includes antiepileptic drug therapy and antiinflammatory drugs if other infectious/inflammatory diseases have been excluded.

OTHER INFECTIOUS INFLAMMATORY CNS DISEASES. Besides CNS viral infections, other infectious agents are considered relatively rare in cats and are associated less commonly with seizures as the only clinical abnormality. Often these diseases are rapidly progressive and accompanied by disseminated systemic illness and abnormal neurodiagnostic results.[25] Disease examples include bacterial meningitis/meningoencephalitis, brain abscessation, and subdural empyema.[5,8,9,16] Cryptococcosis is the most common systemic mycosis in cats and has been associated with CNS involvement and seizure development. Cryptococcosis has a predilection for the nasal cavity, and involvement of the cribriform plate and prefrontal lobe is not uncommon.

Vascular Disease

CNS vascular diseases in cats are primary or secondary.[5,13,14,18] Cats with seizures secondary to vascular disease often present with signs of a peracute to acute onset of lateralizing or diffuse forebrain deficits, variable degrees of tetraparesis or paraparesis, and ataxia that improves over a period of days to months. In some instances, clinical signs often improve but then plateau with residual neurological deficits.

Feline Ischemic Encephalopathy

Feline ischemic encephalopathy (FIE) has been described as a cerebral infarction syndrome characterized by a peracute onset of nonprogressive, asymmetrical signs of forebrain dysfunction. Behavior changes and contralateral deficits often are described. Acute onset of cluster seizures or aggression can be the first and predominant clinical signs. Clinical signs improve over weeks to months; behavioral abnormalities may persist. A definitive cause still remains an enigma. Thrombosis or vasospasm of the middle cerebral artery subsequently leads to cerebral ischemia.* Cardiomyopathy-associated thrombosis, FIP-induced vasculitis, aberrant nematode migration, and cerebral *Cuterebra* infection have been proposed as mechanisms. FIE was considered the second most common cause of seizures in cats.[2,9] CSF analysis is characterized by mild elevation in protein concentration with minimal evidence of inflammation. MRI reveals mild to marked asymmetry of the cerebral hemispheres and hydrocephalus ex-vacuo caused by replacement of CSF in areas with parenchymal atrophy.[2]

*References 2,3,5,6,9,12.

Polycythemia

The pathophysiology of polycythemia is related to an increase in erythrocytes causing an increase in blood viscosity. Secondary consequences are impaired blood flow, blood stasis, and tissue hypoxia. Neurological sequelae include seizures (focal, partial, or generalized), behavior changes, and ptyalism. Other systemic signs are polyuria/polydipsia, lethargy, and muscle twitching. Diagnosis is based on determining the underlying cause. Treatment addresses the underlying cause, and palliative antiepileptic drug (AED) therapy is recommended.[2,5]

Trauma

Vehicular accidents, height-related falls, and blunt trauma can cause severe brain injury in cats if they survive the primary impact (Figure 55-4). Clinical signs are dependent upon neuroanatomical location and lesion severity. Neurological dysfunction includes seizures, diffuse or lateralizing forebrain deficits, hemiparesis or tetraparesis, and ataxia. Brain imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) can assess lesion extent and establish options for surgical management. Rapid and aggressive supportive care is essential to outcome for the head trauma patient. Assessment of the whole patient is important, because injuries to multiple systems are not uncommon. Medical management for head trauma consists of providing a functional airway and promoting vascular support with appropriate fluid therapy. Adjunctive therapies consist of osmotherapies with mannitol and/or hypertonic saline, hyperoxygenation, and meticulous patient monitoring. Surgical intervention is recommended for the patient with deteriorating neurological status that is refractory to medical therapies. Clinical signs may improve, but residual neurological deficits are common.[3,5,26]

Malformations and Degenerative Disorders

Hydrocephalus and other primary brain anomalies often have clinical manifestations of seizures. Degenerative disorders such as the lysosomal storage diseases affect cats less than 1 year of

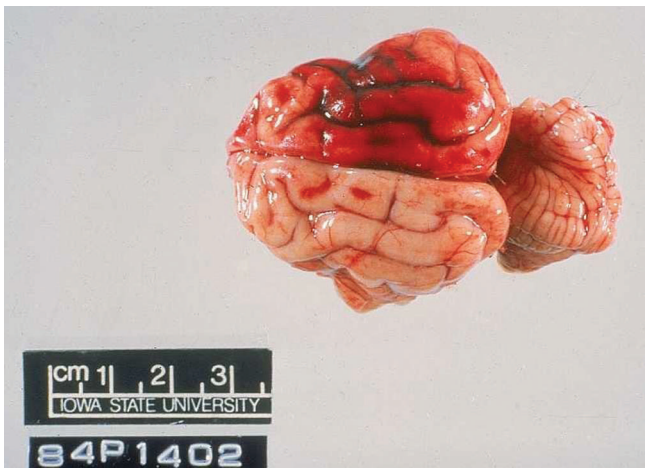

Figure 55-4. Postmortem example of intraparenchymal hemorrhage and cerebral contusions in a cat that sustained severe head trauma as a cause of seizures.

age and are slowly progressive. Seizures usually develop late in the disease course after onset of other neurological deficits and systemic effects.[6,9]

Primary or Idiopathic Epilepsy

A significant percentage of cats have seizures of an undetermined etiology. An underlying cause is suspected but never proven antemortem with routine neurodiagnostic testing. Differential diagnoses include posttrauma, postencephalitis, and postischemic events. The neurological examination is normal in the interictal period, and clinical signs are considered quiescent and nonprogressive. This form of epilepsy probably is more common than pure idiopathic epilepsy in cats. Diagnostic imaging using MRI may reveal evidence of previous trauma. Histopathological studes have shown gliotic scars in cats with previous encephalitis. The incidence of idiopathic epilepsy in cats ranges between 0 per cent and 60 per cent.[2,9] Idiopathic epilepsy is suspected when other pathological causes have been excluded.[2,5,6,9]

DIAGNOSTIC APPROACH

Thorough patient evaluation is essential for determining whether other abnormalities could contribute to the underlying seizure episode. A complete history is a vital component of the patient assessment. The clinician should be aware of the onset of clinical signs, progression, vaccination status, travel history, environment (indoor versus outdoor), drug history, and nutritional status. The seizure episodes are defined thoroughly to determine actual occurrence of a seizure or mimicking clinical signs. Cardiovascular-related syncope, vestibular dysfunction, behavior disturbances, or pain are examples that can mimic a seizure event. Physical examination is important for detecting systemic disorders that may manifest neurological signs secondarily. The neurological examination will determine the presence of neurological dysfunction. The neuroanatomical localization for seizures is the forebrain. The neurological examination also may define the localization as focal, multifocal, or diffuse (Table 55-2). A minimum database for a cat with seizures should include a complete blood count, serum biochemistry profile, urinalysis, preprandial and postprandial bile acids, retinal fundic examination, and tests for FeLV and FIV. Cats older than 5 years of age also should have blood pressure monitoring, thyroid hormone (T_4) screening, thoracic and abdominal radiographs, and cardiac evaluation (ECG and echocardiography). Cats with suspected intracranial disease need further neurodiagnostic testing to evaluate for a possible structural lesion.[1-9,14,20]

Table 55-2 | **Diagnostic Evaluation of Feline Seizures**

History
Previous illness/trauma
Environment (indoor/outdoor/cattery)
Previous therapies
Age at onset of seizures/progression
Type and frequency of seizures
Interictal signs
Nutrition
Physical examination
Neurological examination
Fundic examination
Hematological assessment
CBC/serum chemistry/urinalysis/serum T_4
Bile acids/blood ammonia
FeLV/FIV blood tests
Toxoplasmosis/cryptococcosis serum titers
FIP PCR on blood/CSF
Special chemistries (lead, cholinesterase)
Other diagnostics
Radiography (thoracic/abdominal radiographs/echocardiogram/abdominal ultrasound/thyroid scan/portogram)
ECG/blood pressure
Neurodiagnostics
CT scan
MRI
CSF analysis (cell count/cytology/total protein)

Neurodiagnostic Testing

Ancillary neurodiagnostic testing frequently includes brain imaging (CT or MRI) and CSF analysis. MRI is more sensitive than CT in detection of parenchymal lesions and determining lesion extent.[19] Imaging should be performed before CSF collection. Cisternal puncture would be detrimental in cases of increase in intracranial pressure. Potential risks for herniation have been associated with intracranial neoplasia and inflammatory disease.[2] Abnormalities on CSF analysis indicate presence of a structural brain lesion. These abnormalities can be nonspecific and a definitive diagnosis is made rarely based upon results of CSF analysis alone.[2,5,9,25] Serology performed on CSF for infectious agents such as FIP-inducing coronavirus, *Cryptococcus neoformans*, and *Toxoplasma gondii* may prove more sensitive than similar tests on serum. The main objective for diagnostic testing is to determine viable options for disease-specific medical or surgical treatments, in addition to possible antiepileptic drug therapy.

MEDICAL MANAGEMENT OF SEIZURES

General Principles

AED therapy is initiated if seizures occur more frequently than once a month, if the patient begins to have an acute onset of cluster seizures or status epilepticus, or when the owner has a strong desire to treat the seizures regardless of frequency. AED therapy usually is warranted when seizures are caused by structural lesions of the brain. Long-term maintenance therapy often is indicated with persistent seizure activity.[1-9,27] Realistic goals of AED therapy are to decrease the frequency of the seizures, reduce their severity, and enhance the quality of life for the patient and pet owner. The prognosis should not be based upon the severity of the seizure. Some cats who present with status epilepticus may respond extremely well to anticonvulsant therapy. In my experience, early aggressive therapy is the key to seizure control in acute and chronic situations. Patients refractory to medication need reevaluation for progression of the intracranial disease not addressed previously, assessment of owner compliance, and additional monitoring for drug tolerance. Many owners may have difficulty administering oral medications to their cats and need to be educated about consistency of drug administration and routine drug monitoring. Journal documentation of seizure activity is a useful tool for assessment of medication compliance.

Maintenance Therapy

Phenobarbital

Phenobarbital is the AED therapy of choice for control of seizures in cats. Pharmacokinetics have been well established and most veterinary laboratories perform routine drug monitoring. Phenobarbital is relatively safe and inexpensive and has proven efficacy for seizure control in cats. The recommended dose is 1.25 to 2.5 mg/kg PO q12h. The elimination half-life in cats can range between 43 and 76 hours. Steady-state serum concentration is achieved within 9 to 16 days of starting therapy. Serum drug concentrations ideally should be measured within 2 to 3 weeks of initiating therapy or after a change in dosage. Therapeutic blood levels are similar to those reported in dogs (25 to 40 µg/ml). Optimal recommended therapeutic target range for serum phenobarbital concentrations for cats is between 23 and 30 µg/ml. This target range maximizes seizure control with fewer side effects.[1-9,24,27-29] The pharmacokinetics of phenobarbital in cats are less predictable than in dogs. Phenobarbital is metabolized primarily by the liver. Establishing a baseline of liver function using pre- and post-bile acid testing is recommended before initiating maintenance phenobarbital doses.[6] Serum concentrations should be evaluated every 6 months.[2,7,8] Periodic monitoring of the complete blood count, serum biochemistry profile, and bile acids is recommended. Side effects of phenobarbital include sedation, ataxia, polyphagia, and weight gain. Sedation and ataxia usually are transient and subside within 1 to 2 weeks after initial administration or a change in dose, although exceptions do occur.[6] Cats are considered sensitive to the sedative effects of AEDs, related to a slower elimination rate. The dose should start low and increase incrementally. In my experience, drug-associated polyuria, polydipsia, and polyphagia occur less commonly in cats than in dogs. Rare idiosyncratic reactions include blood dyscrasias (thrombocytopenia, leukopenia), hepatotoxicity, dermatitis, and persistent, unusual behavioral disturbances.[6,24]

Benzodiazepines

Oral diazepam administration has been advocated as a maintenance or adjunctive therapy for seizure control in cats.* In contrast to dogs, diazepam is metabolized in cats more slowly with a half-life that ranges between 15 and 20 hours. Diazepam can be administered every 8 to 12 hours. A recommended dose is 0.5 to 1.0 mg/kg/day PO divided q8-12h. In some cases, the dose can be increased to 2.0 mg/kg and is tolerated safely. Development of drug tolerance is rare in cats, and only a 20 per cent rate of drug resistance has been reported.[3,6] Common side effects include sedation and an increase in appetite. Fulminant hepatic failure associated with oral administration of diazepam has been reported as an idiosyncratic drug reaction and has limited its use as a primary AED.[30] Acute hepatic necrosis can occur as early as 5 days after initiation of the recommended oral dose.[5,6,29] Although fairly uncommon, this side effect frequently is fatal. Liver enzymes and bile acids should be monitored 5 to 7 days after initiation of therapy and every 6 months thereafter.[6]

*References 1-3,5-7,9,24.

Potassium Bromide

Potassium bromide has gained popularity as an adjunctive AED therapy in cats with seizures when phenobarbital alone is ineffective for adequate seizure control.[6-8,27,31,32] Bromide is absorbed in the proximal small intestine and is eliminated through the kidneys. The half-life has been reported to be 13 days in cats, roughly one third the time of that reported in dogs. The steady-state usually is attained within 2 months. Minimum therapeutic concentrations are reached within 3 weeks of initiating therapy. The recommended dose of bromide in cats is 20 to 30 mg/kg PO q24h.[31,32] The target range for serum bromide concentration is between 1.0 and 1.6 mg/ml.[32] Adverse side effects occur in approximately 50 per cent of cats administered bromide. Side effects include polydipsia, vomiting, weight gain, sedation, and coughing. Coughing has a reported incidence in 35 to 42 per cent of cats.[6,8,31-33] A study at Ohio State University reported 11 of 26 cats treated with bromide developed a persistent, nonproductive cough.[33] Coughing is acute in onset and may be associated with dyspnea. Thoracic radiographs reveal mild to marked peribronchial infiltrates, similar to those observed with asthma. Bronchoalveolar lavage has revealed inflammatory changes with eosinophils dominating.[8,33] Withdrawal of the drug often results in resolution of clinical signs; however, three of 17 cats reportedly died from complications associated with drug administration. A thorough history of prior airway disease must be obtained before initiation of bromide therapy. The drug should be discontinued immediately if coughing is reported by the owner.[6]

Adequate and Inadequate Seizure Control

Adequate control of seizures in cats can be monitored by pet owners recording seizure events. Successful management is defined as decrease in seizure severity and frequency and a good quality of life. In my experience, three to four seizures a year is considered acceptable. If seizure severity and frequency are not improved after 3 to 4 weeks of therapy, recommendations include reevaluating the underlying cause and monitoring drug concentrations. If the serum drug concentrations are below or at the low end of the therapeutic range, the dosage is increased incrementally. If drug concentrations are well within the therapeutic range, or if the serum level does not rise with an increase in drug administration (tolerance), adjunctive therapy may be pursued. Options to discontinue AED therapy may be considered when seizure activity ceases for 6 to 12 months.[7] The standard recommendation is to decrease the dose by one third every 2 weeks. In my opinion, if the cat is tolerating the drug and showing minimal side effects, I would not discontinue the medication.

Cluster Seizures and Status Epilepticus

The treatment of status epilepticus in cats is similar to that in dogs.[1-9,27] Intravenous or per rectal diazepam administration at a dose of 0.5 to 1.0 mg/kg often provides cessation of seizure activity. Diazepam alone usually is effective because of its longer half-life. If multiple bolus administration is ineffective, a continuous rate infusion (CRI) of diazepam at 0.5 mg/kg/hr is considered, taking care to protect it from light. I recommend administration of the CRI for up to 2 hours and reassessment of seizure control. Some authors recommend administration of

Table 55-3 | **Summary of Antiepileptic Drug Therapy in Cats**

DRUG	INDICATIONS	ADMINISTRATION	MONITORING	POTENTIAL ADVERSE EFFECTS
Phenobarbital	Identification of a structural lesion Status epilepticus Two or more isolated seizures within a 6-week period The first observed seizure is within a week of head trauma Prolonged, severe, or unusual postictal periods	Initial oral doses 2.5-5 mg/kg PO daily (once or divided q12h) IV loading dose: Total mg IV = (Body weight [kg] × (0.9 L/kg) × (15 µg/ml)	Measure trough serum phenobarbital Therapeutic range is 10-30 µg/mL Evaluate serum chemistry panel at 45 days and every 6 months	Transient: lethargy, behavior change Persistent: polyuria, polydipsia, polyphagia, weight gain, excessive sedation Severe: hepatotoxicity
Potassium bromide	Persistent seizure activity with steady state trough serum phenobarbital concentration > 20 µg/mL for at least 1 month Hepatotoxicity from phenobarbital or primary hepatic disease Severe cluster seizures Poor toleration of adverse effects of phenobarbital	Potassium bromide in capsule formulation at 100 mg per capsule Dose: 20-30 mg/kg/day PO with food as initial dose	Measure trough serum concentrations at 21 days, 90 days and every 6 months after initiation Therapeutic range: 100-200 mg/dL (1.0-2.0 mg/mL) with concurrent phenobarbital: >200 mg/dL (2.0 mg/mL) as sole therapy	Lethargy Polydipsia Polyuria Pancreatitis Ataxia Stupor Cough
Diazepam	IV: Generalized cluster epileptic seizures Status epilepticus PO: Maintenance treatment as for phenobarbital therapy	0.5 mg/kg IV 0.5 to 2.0 mg/kg PO q12h or q8h	Plasma nordiazepam concentration can be measured, but rapid elimination half-life makes interpretation difficult Liver enzyme changes should be monitored at 7, 15, 45 days after start and every 6 months to evaluate for hepatotoxicity	Lethargy and sedation Polydipsia Polyuria Polyphagia Weight gain Idiosyncratic hepatotoxicity
Clorazepate	Maintenance treatment as for phenobarbital therapy	3.75 to 7.5 mg PO q6-8h	As for diazepam	As for diazepam

From Podell M: Antiepileptic drug therapy. Clin Tech Small Anim Pract 13:185, 1998.

the CRI for a minimum of 6 hours.[2,9] A bolus administration or CRI (0.5 to 1.0 mg/kg/hr) of phenobarbitol also can be administered. Propofol also has AED properties. A propofol CRI (0.1 to 0.4 mg/kg/min) can be used short-term in cats. Heinz body production occurs in cats with repeated use of propofol. Heinz bodies are produced as a result of oxidative injury to RBCs. Bolus and CRI administration has potential for severe respiratory depression. Intratracheal intubation and additional ventilatory support may be necessary. Cats may be profoundly sedated after parenteral treatment with AEDs.[9] Monitoring vital indices serially until the cat is acclimated to the AED is important. Additional supportive care includes fluid therapy, temperature regulation, oxygen supplementation, continuous electrocardiogram, and frequent turning. Blood glucose, electrolytes, and urine output are assessed frequently. Choice of a maintenance AED is considered while providing initial seizure control. See Table 55-3 for a summary of AED therapy in cats.

PROGNOSIS

An underlying structural lesion often is the cause for seizures in cats. Prognosis for seizure control is dependent upon the type of structural lesion. The treatment of the acquired cause should be addressed first. No correlation exists between the severity of the seizures and outcome.[2,9,6,24] Side effects and adverse reactions may limit use of some AEDs. In cats with no detectable structural lesion but in which an acquired cause is still suspected, early and appropriate AED management can result in adequate long-term seizure control.

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