13 Chapter 13 Seizures, Narcolepsy, and Cataplexy

Epilepsy is a disorder of the brain that is characterized by recurring seizures. *Seizures, fits,* and *convulsions* are synonymous terms used to describe the manifestations of abnormal brain function that are characterized by paroxysmal stereotyped alterations in behavior. The term *convulsion* is reserved for seizures with a generalized motor component. *Narcolepsy* is a disorder of the brain that is marked by sudden recurring attacks of sleep. Narcolepsy is discussed at the end of this chapter. *Syncope* is transient loss of consciousness caused by ischemia of the brain. The most common cause in animals is cardiac arrhythmia. The history is usually indicative of syncope rather than seizures, but when in doubt careful auscultation of the heart and an electrocardiogram (ECG) may disclose the problem.

A seizure has several components. The actual seizure is called the *ictus*. Before the seizure (preictally), a period of altered behavior may occur, called the *aura*. People with seizures report varying sensation, apprehension, and so forth during the aura. Animals may hide, appear nervous, or seek out their owners at this time. The ictus usually lasts for 1 to 2 minutes, but variation is considerable. After the seizure (*postictal phase*), the animal may return to normal in seconds to minutes or may be restless, lethargic, confused, disoriented, or blind for minutes to hours. The aura and the postictal phase do not have any relationship to the severity or the cause of the seizures.

The behavioral changes of seizures are composed of one or more of the following involuntary phenomena: (1) loss or derangement of consciousness or memory *(amnesia);* (2) alteration of muscle tone or movement; (3) alteration of sensation, including hallucinations of special senses (e.g., visual, auditory, olfactory); (4) disturbance of the autonomic nervous system (e.g., salivation, urination, defecation); and (5) other psychic manifestations, abnormal thought processes, or moods recognized as behavioral changes (e.g., fear, rage, tail-chasing).[1]

One or more of the aforementioned changes are present in a seizure. For example, loss of consciousness is usually associated with a generalized motor seizure but may not be a part of a seizure with behavioral manifestations. Behavioral or psychic changes are not necessarily seizure disorders; however, if the changes are paroxysmal, seizures are strongly considered. Seizures may occur in any animal, but they have been reported more frequently in the dog.

13.1 PATHOPHYSIOLOGY

Seizures are always a sign of abnormal forebrain function. The dysfunction may be from a primary lesion in the brain or secondary to a metabolic abnormality (e.g., hypoglycemia, toxicity).

Two main categories of seizures include those in which the seizure discharge originates in a circumscribed area of the brain and those in which the discharge appears to involve the two cerebral hemispheres bilaterally and synchronously from the start. Most of the information on the genesis of seizures is taken from models of focal and partial-onset epilepsy.

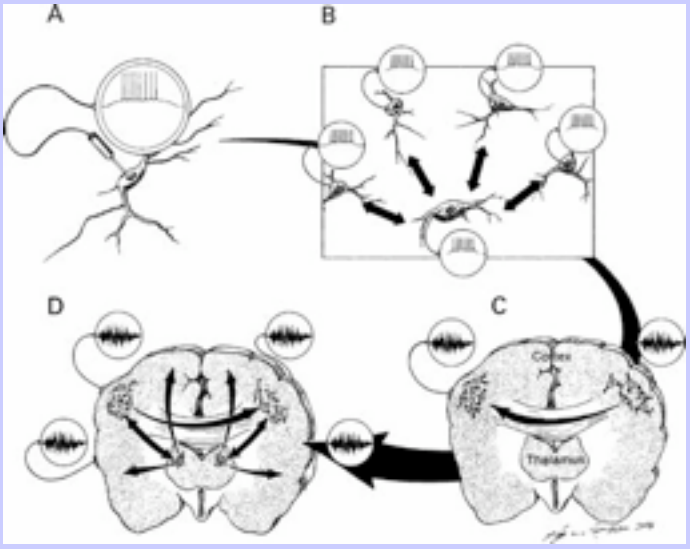
At the cellular level, seizures represent abnormal hypersynchronous discharges of cortical neurons.[2] An imbalance exists between excitatory and inhibitory mechanisms that favor the sudden onset of excitation. Several neurotransmitters play fundamental roles in the pathogenesis of seizures. Gamma-aminobutyric acid (GABA) and glutamate are the primary inhibitory and excitatory neurotransmitter agents. Multiple cellular receptors exist for each agent. Defective inhibition of GABA-$_A$ and GABA-$_B$ receptors may play fundamental roles in the pathogenesis of partial-onset epilepsy. In addition, defective activation of GABA neurons and defective intracellular buffering of calcium may play important roles.[2]

Increased excitability of neurons may follow defects in inhibition or result from conditions or factors that directly promote neuronal excitation. For instance, increased activation of N-methyl-D-aspartate (NMDA) receptors by glutamate, increased synchrony between neurons, and recurrent excitatory collaterals likely play important roles.[2] Glutamate activation of NMDA receptors may aid the development of the paroxysmal depolarizing shift (PDS), a fundamental reaction in seizure foci. Inherited epilepsy may involve changes in receptors for or metabolism of glutamate.[3]

Two components are recognized as the basis for focal seizure disorders: the seizure focus and the spread of the abnormal activity to other areas of the brain. The paroxysmal alterations in behavior are associated with synchronous excessive discharge in large aggregates of neurons: the seizure focus.[4] If the activity of the seizure focus spreads to other parts of the brain, a generalized cerebral dysrhythmia results, which produces the behavioral change that is recognized as a seizure (Figure 13-1).

Seizure foci apparently are present in many persons who do not have seizures. Some populations of neurons in the brain (e.g., the hippocampus) are much more likely to develop seizure activity than others. The seizure focus has been studied extensively in a variety of experimental models and in naturally occurring epilepsy. Neurons in seizure foci are characterized by large-amplitude, prolonged membrane depolarizations with associated high-frequency bursts of spikes: the PDS. These changes cause paroxysmal interictal spikes in the electroencephalogram (EEG).[5,6] The number of epileptic neurons correlates with the frequency of seizures.

Figure 13-1 Spread of seizure activity from a focal area to the entire cerebrum. **A,** Paroxysmal depolarization shift in a neuron. **B,** Spread of activity to surrounding neurons. **C,** Propagation of seizure activity to other cortical areas by axonal conduction. **D,** Generalization of seizure activity through the diencephalon. (From Oliver JE, Hoerlein BF, Mayhew IG, editors: *Veterinary neurology*. Philadelphia, 1987, WB Saunders.)



Generalized seizures may also develop simultaneously in many areas of the brain. The two forms of generalized seizures are tonic-clonic convulsions and absence attacks. The latter types are rarely recognized in animals. Much of the research on generalized seizures has been done in the cat model of generalized penicillin-related seizures. Large doses of parenteral penicillin cause generalized spike-wave discharges on the EEG and behavioral unresponsiveness similar to absence attacks.[4] The cause of the diffuse cortical hyperexcitability is still not clear. Reduction of dendrite inhibition and potentiation of excitation mediated by glutamate and aspartate are suggested mechanisms.[2–4] Alteration of GABA inhibition is likely involved in the transition to generalized convulsions.

Seizures can be generated in any individual by pharmacologic, metabolic, or electrical changes; however, the threshold for stimulation varies widely. Normal individuals may require potent convulsant drugs (e.g., pentylenetetrazol) or electrical shock to exceed the threshold. A lower seizure threshold may allow production of convulsions by conditions such as fever and photic stimulation or minor alterations in body chemistry (e.g., hypoglycemia, hypocalcemia, hyperventilation).

Some individuals have seizures with no apparent stimulus. The range from normal individuals to those who have spontaneous seizures is a continuum without sharply defined boundaries. A lower threshold for seizures may be an inherited trait.

Studies indicate that the expression of individual seizures differs from the development of a lasting seizure-prone state.[7] Antagonists to NMDA prevented the progressive development of seizures but did not block previously induced seizure activity.

324 325

13.2 CLASSIFICATION

The classification of seizures based on clinical signs is helpful from a descriptive standpoint and may also be helpful in localization (Table 13-1).[8]

Gastaut[9] has proposed that generalized seizures be called *primary generalized epilepsy* if no cause can be ascertained and *secondary generalized epilepsy* if any organic cause can be found. Primary generalized epilepsy includes essential epilepsy, true epilepsy, idiopathic epilepsy, genetic epilepsy, and centrencephalic epilepsy. Partial or focal seizures are usually acquired, thus ruling out primary generalized epilepsy.[10]

13.2.1 Generalized Seizures

Tonic-clonic seizures (grand mal, major motor) are common in animals. The seizure frequently is preceded by an aura. The animal falls and becomes unconscious, the limbs are extended rigidly, opisthotonos is usual, and respiration stops *(apnea)*. The tonic phase is usually brief (10 to 30 seconds) and is rapidly followed by clonic limb movements in the form of running or paddling. Chewing movements of the mouth are common. Autonomic activity may start in the tonic or clonic phase of the ictus and may include pupillary dilation, salivation, urination, defecation, and piloerection. The clonic phase may alternate with tonic activity. The ictus usually lasts 1 to 2 minutes. The postictal phase may be a few minutes of rest followed by normal activity or may include confusion, disorientation, restlessness and pacing, and blindness lasting for minutes to hours.

Table 13-1 Classification of Seizures: Clinical Signs

Clinical Manifestation	EEG	Etiology	Anatomic Location
Generalized Seizures, Bilateral Symmetric Seizures, or Seizures Without Local Onset			
Primary generalized, tonic-clonic (grand mal, major motor)	Generalized dysrhythmia from onset, symmetric, often normal interictal unless they are activated or have organic or toxic origin	1. Genetic predisposition 2. Diffuse or multiple organic lesions 3. Toxic or metabolic	1. Unlocalized, multifocal 2. Diencephalic
Absences with or without motor phenomena (petit mal) rare or rarely recognized in animals	Generalized; 3 per second spike and wave dysrhythmia, symmetric (human)	Usually genetic predisposition (human)	1. Unlocalized, multifocal 2. Diencephalic
Partial Seizures or Seizures Beginning Locally			
Partial motor (may generalize to tonic-clonic seizure); signs depend on site of discharge	Focal dysrhythmia (spikes, slow waves), may generalize secondarily	Acquired organic lesion (see Tables 13-2 and 13-3)	Focal cortical or subcortical
Psychomotor (may generalize or appear as complex behavioral change: running, fear, aggression)	Dysrhythmia related to temporal lobe	Acquired organic lesion (see Tables 13-2 and 13-3)	Limbic system (hippocampus, temporal or pyriform lobe)

Modified from Oliver JE Jr: Seizure disorders in companion animals. *Compend Cont Educ Pract Vet* 2:77–86, 1980.

Generalized tonic-clonic seizures in cats can be violent.[11] Cats may be propelled into the air, and self-inflicted trauma may occur (contusions, excoriations, avulsion of nails, and biting the tongue). Mild generalized seizures in cats are characterized by pupillary dilation, facial twitching, and, less frequently, salivation and urination.

Careful questioning of the owner is required to determine whether the episode described is actually a seizure. Owners frequently confuse syncope or acute vestibular syndromes with seizures. If the event is repetitive and has the same appearance each time, it is likely a seizure. Next the clinician needs to know whether the seizure starts as generalized, symmetric activity or if it has a focal component. The aura should not be confused with focal seizure activity. Any indication of focal motor activity preceding the generalized seizure, such as chewing, forced turning of the head, or clonic jerks of muscle groups, indicates a focal component, even if it generalizes secondarily. Primary generalized seizures cannot be localized anatomically. Whether the seizure focus is single or multiple, the generalized signs preclude localization.

325

326

Absences, or petit mal seizures, either are very uncommon in animals or, more likely, are not easily recognized. They are characterized by a brief (seconds) loss of contact with the environment that occurs without motor activity. Variations in humans include minor motor components such as facial twitching, loss of postural tone, and autonomic activity. Redding[12] reported one dog with absence attacks and characteristic EEG changes (4-Hz spike-wave complexes). Unless these attacks are frequent or the owner is very observant, they are usually not recognized.

13.2.2 Partial Seizures

Partial motor seizures (focal motor, Jacksonian) reflect the activity of a local seizure focus in an area producing motor activity. Movements are restricted to one part of the body, such as the face or one limb. Partial seizures frequently spread, resulting in a generalized convulsion. The focal component of the seizure onset is the key differential diagnosis feature. Because partial seizures are invariably acquired, primary generalized epilepsy is not considered in the differential diagnosis. The true Jacksonian seizure, which includes a focal onset followed by a slow progression of motor activity to adjacent structures, ultimately terminating in a generalized motor seizure, is rare in animals. The motor area of the cerebral cortex of domestic animals is small, allowing seizure activity to generalize rapidly. Patients with partial motor seizures are more likely to have focal EEG abnormalities in interictal periods than are those with generalized seizures. Partial sensory and autonomic seizures are not commonly recognized. Partial motor seizures are presumed to arise from a seizure focus near a primary motor area, usually the frontal cortex. In animals, partial motor seizures are indicative of a lesion in the contralateral cerebral hemisphere (e.g., a left thoracic limb seizure indicates a right cerebral cortex lesion).

Psychomotor seizures may have a predominance of autonomic signs.[1,9,10,13] Animals that have repetitive episodes of “fly biting” may be having focal sensory seizures in the visual cortex; however, psychomotor seizures with a sensory component are the generally accepted explanation.[14]

Psychomotor seizures (complex partial seizures, behavioral seizures) are paroxysmal episodes of abnormal behavior.[13–15] Examples include hysteria, rage, autonomic reactions such as salivation, and hallucinations such as fly biting. Visceral activity such as diarrhea, vomiting, and abdominal discomfort may correlate with lesions of the limbic system.[13] The most frequent locations are probably the hippocampus, the amygdala, and the temporal cortex. These areas commonly are involved in inflammatory diseases such as canine distemper and rabies and are damaged in tentorial herniation of any cause (see Chapters 12 and 15).

Complex partial seizures are recognized in several canine breeds and have been extensively studied in the bull terrier.[16] Behavioral changes such as compulsive tail chasing, rage, trances, preoccupations, fears, hyperactivity, sound sensitivities, and phobias have been described. EEG abnormalities include multiple epileptiform spikes characterized by high-amplitude, low-frequency discharges.

Many affected dogs have concurrent hydrocephalus demonstrated on computed tomography (CT) examination. Clinical signs develop at 6 to 13 months of age and occasionally in older dogs. No abnormalities in zinc, copper, and iron metabolism have been detected. The syndrome in bull terriers may reflect an inherited form of temporal lobe epilepsy similar in many respects to previously described cases of psychomotor epilepsy.

Complex partial seizures occur in cats.[11] They are characterized by lack of response to sensory stimuli and a trance-like state. Unilateral facial twitching, turning the head to one side, and repetitive movements of one limb have been reported. Bizarre behavior, such as inappropriate hissing, growling, and running blindly into objects, and compulsive behavior, such as self-chewing, biting, and circling, have been observed in association with facial twitching and salivation.

Differentiating psychomotor seizures from functional behavioral changes is difficult. Psychomotor seizures are usually preceded by an aura and followed by a postictal phase. The ictus is stereotyped and repetitive. Autonomic components of the ictus are common.

13.3 DISEASES

Seizures can be caused by any process that alters normal neuronal function. As with all neurologic diseases, the differential diagnosis is formulated in broad categories. The most likely diseases within each category then are considered. Tables 13-2 and 13-3 outline the major categories of diseases that are likely to produce seizures.

13.3.1 Idiopathic (Genetic)

Primary generalized epilepsy *(idiopathic)* has no demonstrable pathologic cause and may be inherited. Although it may occur in a number of species,[17] the most comprehensive studies have been those of humans and dogs.[17–25] Primary generalized epilepsy is rare in cats.[11]

Table 13-2 Causes of Seizure Disorders of Dogs and Cats*

Classification	Most Frequent Causes	Diagnostic Tests
Degenerative (15)	Storage diseases	Breed, biopsy
Anomalies (12)	Hydrocephalus	PE, CT, EEG, ventriculography
	Lissencephaly	Breed, PE, EEG
Idiopathic (13)	Genetic	Breed, age, history
	Unknown	Absence of other causes
Inflammation/infectious (15)	Viral: canine distemper, rabies, FIP	History, PE, CSF analysis, CSF titers
	Bacterial: any type	
	Mycotic: cryptococcosis	
	Protozoal: toxoplasmosis, neosporosis	
	Rickettsial: RMSF, ehrlichiosis	
	Granulomatous meningoencephalitis	
	Immune meningoencephalitis	
	Nonsuppurative encephalitis (cats)	
	Aberrant parasites	
Metabolic (15)	Electrolyte: hypocalcemia	CBC, biochemical profile, UA, free bile acids, glucose-insulin pairs, hepatic biopsy
	Carbohydrate: hypoglycemia	
	Renal failure	
	Hepatic failure, portacaval shunt, microvascular dysplasia	
Neoplastic (15)	Primary: gliomas, meningiomas	NE, CT, MRI
	Metastatic	
Nutritional (15)	Thiamine deficiency	History, response to treatment
Toxic (15)	Heavy metal: lead	History, blood lead levels
	Organophosphates	History, NE, cholinesterase levels
	Chlorinated hydrocarbons	History, NE, PE
	Strychnine	
	Tetanus	
	Toad poisoning	
	5-hydroxytryptophan	

Traumatic (13)	Acute: immediately after head injury	History, PE, NE, CT, MRI
	Chronic: weeks to years after head injury	History, EEG, CT, MRI
Vascular (12, 13)	Infarctions	History, NE, CT
	Arrhythmias	Auscultation, ECG

Modified from Oliver JE Jr: Seizure disorders in companion animals, *Compend Cont Educ Pract Vet* 2:77–86, 1980.

CBC, Complete blood cell count; *CSF,* cerebrospinal fluid; *CT,* computed tomography; *ECG,* electrocardiogram; *EEG,* electroencephalography; *FIP,* feline infectious peritonitis; *MRI,* magnetic resonance imaging; *NE,* neurologic examination; *PE,* physical examination; *RMSF,* Rocky Mountain spotted fever; *UA,* urinalysis.

* Numbers in parentheses refer to chapters in which disease classes are discussed.

In animals, primary generalized epilepsy usually occurs in the form of generalized tonic-clonic seizures. Absence attacks are common in humans but are apparently rare in dogs.[23] Breeds of dogs known to have a genetic basis for epilepsy are listed in Table 13-4. Also listed are those breeds reported to have a high incidence of seizure disorders but for which genetic studies have not been documented. Whether these breeds have genetic epilepsy has not been proven. A study at the University of Pennsylvania, School of Veterinary Medicine, found no evidence of an increased incidence of epilepsy in any breed. The incidence of seizures in all breeds closely matched the frequency of admission to the hospital for all problems.[26] The diagnosis of primary generalized epilepsy does not prove inheritance. Only careful breeding studies can prove a genetic trait.

Inherited epilepsy also has been reported in Brown Swiss and Swedish Red cattle.[27] A hereditary syndrome characterized by recurrent seizures and the gradual development of cerebellar ataxia occurs in purebred and crossbred Aberdeen Angus cattle. The seizures start in young calves but decline in frequency in those that survive to approximately 15 months of age. Most cattle are clinically normal by 2 years of age. Pathologic changes have been found in the Purkinje cells of the cerebellum.[28]

327

The first seizure in a dog with primary generalized epilepsy usually occurs between the ages of 6 months and 5 years.[1] Early onset of seizures in puppies conceived by breeding two epileptic Labrador retrievers has been described.[29] Three puppies of a litter of 10 had seizures beginning at 8 to 9 weeks of age. Eventually, five of eight surviving pups had seizures. In a large beagle colony, 29 dogs had their first seizure at a mean age of 30 months (range, 11 to 70 months).[19] Many dogs with abnormal EEGs did not have seizures by 6 years of age but may have been at risk of future seizures. An incidence of 1% to 2% is reported from two university teaching hospitals.[30,31]

328

Table 13-3 Causes of Seizure Disorders of Large Animals*

Classification	Most Frequent Causes	Diagnostic Tests
Degenerative (15)	Storage diseases (bovine, ovine)	Breed, biopsy
Anomalies (12)	Hydrocephalus	PE, CT, EEG
	Hydranencephaly	
Idiopathic (13)	Genetic (bovine)	Breed, age, history
	Unknown	Absence of other causes
Inflammation (15)	Viral: infectious bovine rhinotracheitis, pseudorabies (bovine, porcine), rabies (all), hog cholera, viral encephalomyelitis (equine)	History, species, PE, CSF analysis, titers
	Bacterial: thromboembolic meningoencephalitis (bovine), any type	
	Aberrant parasites (all)	
Metabolic (15)	Electrolyte: hypocalcemia, hypomagnesemia, water intoxication (porcine)	PE, CBC, biochemical profile, and UA
	Carbohydrate: hypoglycemia, ketosis, pregnancy toxemia (ovine)	
	Renal failure	
	Hepatic failure	
Neoplastic (15)	Primary: gliomas, meningiomas	NE, CSF, CT
	Metastatic	
Nutritional (15)	Thiamine (ruminants)	History, NE, response to treatment
Toxic (15)	Heavy metal: lead, arsenic	History, blood lead levels, tissue levels
	Organophosphates	History, NE, cholinesterase levels
	Chlorinated hydrocarbons	History, NE, tissue levels
	Strychnine	
	Tetanus	
Traumatic (13)	Acute: immediately after head injury	History, PE, NE
Vascular (12)	Infarction	History, NE
	Arrhythmias	Auscultation, ECG

CBC, Complete blood cell count; *CSF,* cerebrospinal fluid; *CT,* computed tomography; *ECG,* electrocardiogram; *EEG,* electroencephalography; *NE,* neurologic examination; *PE,* physical examination; *UA,* urinalysis.

* Numbers in parentheses refer to chapters in which disease classes are discussed.

Table 13-4 Breeds with Primary Generalized Epilepsy

Genetic Factor Proved or Highly Suspected
Beagle
Dachshund
German shepherd dog (Alsatian)
Horak's laboratory dog
Keeshond
Belgian tervuren
Aberdeen Angus cattle
Brown Swiss cattle
Swedish Red cattle
High Incidence of Seizure Disorders
Arabian foal
Boxer
Cocker spaniel
Collie
Golden retriever
Irish setter
Labrador retriever
Miniature schnauzer
Poodle
Saint Bernard
Siberian husky
Wire fox terrier

The clinician can make a diagnosis of primary generalized seizures only by excluding other causes. No positive diagnostic findings can substantiate the diagnosis. The breed, the age, and the history may be highly suggestive, especially if a familial history of seizures exists (Tables 13-4 to 13-6). EEG abnormalities are not consistent.

13.3.2 Degenerative

328

329

Deficiencies in specific enzymes cause abnormal cellular metabolism with the accumulation of metabolic products within the neurons. These storage diseases may produce seizures as one part of the clinical syndrome (see Chapter 15).

Table 13-5 Common Causes of Seizures at Different Ages

Age/Disease Class	Cause
<1 Yr	
Degenerative	Storage diseases
Developmental	Hydrocephalus
Toxic	Heavy metals: lead, organophosphates, chlorinated hydrocarbons
Infectious	Canine distemper, encephalitis, other infectious diseases
Metabolic	Hypoglycemia: transient, enzyme deficiency, portacaval shunt, hepatic encephalopathy
Nutritional	Thiamine, parasitism
Traumatic	Acute
1–3 Yr	
Genetic	Primary generalized epilepsy (may start at approximately 6 mo)
	Others as above
>4 Yr	
Metabolic	Hypoglycemia: secondary to beta-cell tumor
	Hypocalcemia: hypoparathyroidism
	Hepatic encephalopathy: cirrhosis
Neoplastic	Primary or metastatic brain tumor
Vascular	Cardiovascular: arrhythmia, thromboembolism

Modified from Oliver JE Jr: Seizure disorders in companion animals, *Compend Cont Educ Pract Vet* 2:77–86, 1980.

Table 13-6 Causes of Seizures by Breed Predisposition

Breed	Cause
Alsatian (German shepherd dog)	Genetic
Beagle	Genetic
Belgian tervuren	Genetic
Boston terrier	Hydrocephalus, neoplasia
Boxer	Neoplasia
Cairn terrier	Globoid cell leukodystrophy
Chihuahua	Hydrocephalus
English setter	Lipodystrophy
German shepherd (Alsatian)	Genetic
German shorthaired pointer	Lipodystrophy
Irish setter	Genetic (suspected)
Keeshond	Genetic
Lhaso apso	Lissencephaly
Maltese	Portacaval shunts
Miniature pinscher	Hydrocephalus
Miniature schnauzer	Hyperlipoproteinemia, portacaval shunts
Pekingese	Hydrocephalus
Poodle, miniature and standard	Idiopathic
Poodle, toy	Hydrocephalus
Saint Bernard	Idiopathic
West Highland white terrier	Globoid cell leukodystrophy
Yorkshire terrier	Hydrocephalus, portacaval shunts

Modified from Oliver JE Jr: Seizure disorders in companion animals, *Compend Cont Educ Pract Vet* 2:77–86, 1980.

13.3.3 Developmental

Disorders in this group may or may not be inherited but are distinguished from primary generalized (genetic) epilepsy by involving demonstrable pathologic changes in the brain. Hydrocephalus is the most common developmental disorder that causes seizures (see Chapter 12). Other developmental defects that may produce convulsions are lissencephaly and porencephaly (see Tables 13-5 and 13-6).

Lissencephaly is a congenital absence of the convolutions of the cerebral cortex.[32,33] It has been reported in lhasa apso dogs, wire fox terriers, and Irish setters, and in one cat. Affected animals may have behavioral, visual, and slight proprioceptive deficits in addition to seizures.

Porencephaly is a cystic malformation of the cerebrum that usually communicates with the lateral ventricle or the subarachnoid space. It may be congenital or acquired (degenerative).

13.3.4 Inflammatory/Infectious

Any inflammatory or infectious disease has the potential to cause seizures if it invades the forebrain. The most prevalent diseases are listed in Tables 13-2 and 13-3. Canine distemper virus is probably the most common infectious cause of seizures in dogs. Seizures may appear without any noticeable clinical illness or may occur long after a clinical illness has been resolved.

329

330

Granulomatous meningoencephalomyelitis (GME) is a common inflammatory cause of seizures in dogs. A nonsuppurative meningoencephalomyelitis was reported as a common cause of seizures in cats from Canada.[11] The diagnosis of inflammatory central nervous system (CNS) disease requires cerebrospinal fluid (CSF) examination, CSF serology, advanced imaging, and in some cases EEG. Inflammatory or infectious diseases are discussed in Chapter 15.

13.3.5 Metabolic

Failure of one of the major organs or of the endocrine glands may produce alterations in the electrolytes or glucose or the accumulation of toxic products, which results in seizures (see Tables 13-2, 13-3, and 13-5).[34] Hypoglycemic syndromes and hepatoencephalopathy are the most common diseases in this category. Some animals have a lower seizure threshold. Relatively minor alterations may cause seizures in these instances. The major metabolic disorders are discussed in Chapter 15.

13.3.6 Neoplastic

Intracranial neoplasia, either primary or metastatic, can cause seizures. The seizure activity is caused by an abnormality in neurons adjacent to the neoplasm that are compressed or distorted or that have an insufficient blood supply. Brain tumors are not electrically active.

Seizures may be the first sign of brain tumor. A neurologic deficit may not be apparent until weeks to months after the onset of seizures, especially if the mass is in the cerebral cortex. Neoplasia as a cause of seizures is relatively common in dogs and cats older than 5 years of age, and the incidence increases as animals age. Older animals with a sudden onset of seizures should be considered to have a tumor until proved otherwise. CT and magnetic resonance imaging (MRI) are the diagnostic procedures of choice. Neoplasia is discussed in Chapter 15.

13.3.7 Nutritional

Seizures may be the terminal manifestation of a number of nutritional disorders. The B complex vitamins are most frequently incriminated. Thiamine deficiency causes polioencephalomalacia in ruminants, which is discussed in Chapter 15. Thiamine deficiency in dogs and cats causes hemorrhage and necrosis in the brainstem.

Animals that are fed most commercial rations do not develop thiamine deficiencies. Dogs that are fed only cooked meat develop paraparesis that progresses to convulsions. Early treatment with thiamine reverses the clinical progression of the disease. Thiamine deficiency in cats has been attributed to fish-based cat foods that

contain thiaminase. Supplementation with thiamine eliminates the problem. Cats typically have a seizure syndrome that is characterized by ventroflexion of the head, ataxia, behavioral changes, dilated pupils, and eventually coma. Because thiamine toxicity is unlikely, giving thiamine to cats with seizures is the best treatment. A dose of 50 to 100 mg is given intravenously the first day; thereafter, daily intramuscular injections are given until a response is obtained or another diagnosis is established.[1]

13.3.8 Toxic

Many toxins affect the CNS, and most can cause seizures. The diagnosis usually depends on the history, identification of the toxic substance from analysis of body tissues or intestinal contents, and the response to treatment.

Lead poisoning is a frequent intoxication in animals. Other clinical signs may include depression, tremor, and ataxia, which sometimes are associated with gastrointestinal signs. Seizures are often associated with behavioral signs. Peripheral blood changes may include nucleated erythrocytes (red blood cells [RBCs]) and basophilic stippling of RBCs without anemia. The changes in the RBCs are transient and may not be present in chronic lead poisoning. Blood lead determination is diagnostic. Calcium ethylenediamine tetraacetic acid (CaEDTA) is used in treatment.[35]

Strychnine causes a tonic seizure that is exacerbated by stimulation. The animal remains conscious unless respiration stops. Strychnine blocks inhibitory interneurons in the spinal cord, causing a release of motor neuron activity.

Organophosphate and chlorinated hydrocarbon insecticides are a common cause of seizures.

Seizures induced by the toxin produced by the *Bufo marinus* toad have been reported.[36] Although several species of *Bufo* toads exist worldwide, most reports in the United States are from southern Florida, Colorado, Arizona, Texas, and Hawaii. The incidence was highest during warm months of the year. In addition to seizures, neurologic signs include stupor, ataxia, nystagmus, extensor rigidity, and opisthotonos. Hyperemic oral mucous membranes and ptyalism are common findings. The toxin is released from the toad's parotid glands and is readily absorbed through the oral mucosa. Intoxication may be fatal. The oral cavity should be lavaged with tap water. Diazepam is used to control seizures and extensor rigidity. Intravenous fluids and diuretics are given to promote urinary excretion of the toxin. Overall mortality is low in animals treated within a few hours of intoxication.

330

331

In dogs, 5-hydroxytryptophan toxicosis has been reported as a cause of seizures.[37] It is a precursor to serotonin, a common CNS neurotransmitter. The signs in dogs are similar to the “serotonin syndrome” as described in humans. In addition to seizures, neurologic signs include depression, tremors, hyperesthesia, transient blindness, and ataxia. Gastrointestinal signs include vomiting, diarrhea, ptyalism, and abdominal pain. Hyperthermia is also a common finding. Signs develop within minutes to hours following accidental ingestion of dietary supplements containing the agent. Most dogs develop signs within 1 hour. Treatment includes decontamination (induction of emesis, gastric lavage, and oral administration of activated charcoal), fluid therapy, thermoregulation, and parenteral administration of anticonvulsant agents (diazepam or phenobarbital). The serotonin antagonist cyproheptadine may be useful as adjunct therapy. A dose of 1.1 mg/kg administered orally or rectally every 1 to 4 hours is suggested.[37]

Toxic disorders are discussed in Chapter 15.

13.3.9 Traumatic

Seizures may be seen immediately after acute head trauma as the result of direct neuronal injury. Posttraumatic seizures may occur many weeks to several years after a head injury. Posttraumatic epilepsy may be focal or generalized, depending on the location of the brain lesion. The focus develops secondary to a scar in the brain at the site of the initial injury. The focal abnormality may be recognized on EEG. The diagnosis is based on the correlation of historical information with the development of seizures and the elimination of other causes. Treatment is directed at controlling the seizures.

13.4 PLANS FOR DIAGNOSIS AND MANAGEMENT OF SEIZURE DISORDERS

Most animals with seizures have a similar history of episodic convulsions. Therefore a protocol for diagnosis and a plan for management and treatment that includes a defined database are useful.[8,38]

13.4.1 Database

The recommended database is formulated at two levels to rule out the two major groups of problems causing seizures: (1) extracranial abnormalities such as metabolic, toxic, and nutritional problems; and (2) intracranial diseases such as encephalitis, brain tumors, anomalies, degenerative diseases, and traumatic injuries. Idiopathic or primary generalized epilepsy is assumed from the history, signalment, and exclusion of other causes (Table 13-7). The minimum database can be obtained at any veterinary clinic with an access to pathology services. The specific serum chemistry analyses can be modified to fit those available in an automated service. The only expense other than the initial examination is the cost of laboratory studies. The risk to the patient is minimal.

331

The minimum database screens for primary neurologic disease (neurologic examination) and metabolic or systemic disorders (physical examination, laboratory examination).

332

Table 13-7 Database for Seizure Disorders

Minimum Database
Patient profile
Species, breed, age, sex
History
Immunizations: kind, dates, by whom
Environment
Age at onset
Frequency, course
Description of seizure: general or partial, duration, aura, postictus, time of day, relation to exercise, food, sleep, or stimuli
Previous or present illness or injury
Behavioral changes
Physical examination
Complete examination of systems, including specifically:
Musculoskeletal: Size, shape of skull, evidence of trauma, atrophy of any muscles
Cardiovascular: Color of mucous membranes, evidence of arrhythmias, murmurs
Funduscopic examination
Neurologic examination
Complete examination: Note time of last seizure; if it was within 24-48 hr and neurologic examination is abnormal, repeat in 24 hr
Clinical pathology

CBC Urinalysis BUN, ALT, ALP, calcium, fasting blood glucose levels (GGT, SDH in large animals), free bile acids Others as indicated (e.g., blood lead level, Coggin's test)
Complete Database
Computed tomography or magnetic resonance imaging
CSF analysis: Cell count, total and differential; protein levels; pressure
Skull radiographs: Ventrodorsal, lateral, frontal
EEG
ALP, Alkaline phosphatase; *ALT,* serum alanine transaminase; *BUN,* serum urea nitrogen; *CBC,* complete blood cell count; *CSF,* cerebrospinal fluid; *EEG,* electroencephalogram; *GGT,* γ-glutamyltransferase; *SDH,* sorbitol dehydrogenase.

The more complete database includes CSF analysis, CT, MRI, and EEG (see Table 13-7). CSF analysis can be performed at most clinics. EEG, CT, and MRI usually are not available except at referral centers. CT is available to many veterinarians through local hospitals or mobile units. CT and MRI are the best tests for the detection of organic brain lesions such as neoplasia and infarcts. These tests are performed when the minimum database indicates the presence of neurologic disease, when an older animal experiences a sudden onset of seizures, or if the seizures have not been controlled with medication. These procedures are not recommended as a part of the minimum database in dogs younger than 5 years of age because of the low yield in animals with normal findings, the increased risk of required anesthesia, and the increased cost to the client.

Because cats most commonly have secondary epilepsy, CSF examination and CT or MR imaging are important in determining the cause of seizures in this species. The most common causes of seizures in cats are organic brain diseases such as nonsuppurative meningoencephalitis, feline ischemic encephalopathy, and neoplasia.[11]

In large part, CT and MR imaging have replaced the various contrast-enhanced procedures for evaluating structural alterations in the brain. Arteriography and ventriculography are no longer used because of the risk and poor diagnostic results. Ventriculography may be helpful in the diagnosis of hydrocephalus. CT is helpful. Ultrasonography can be used in animals with persistent fontanelles.[39]

13.4.2 Plan for Management

A minimum database should be completed for every patient that has more than one seizure. Patients that have had only one isolated seizure should be given thorough physical and neurologic examinations. If no abnormalities are found, the owners should be advised to watch for further seizures.

Information from the minimum database yields one of three findings: (1) a definitive diagnosis, (2) a possible cause of the seizures that requires further tests to confirm, or (3) no suggestion of the cause (Figure 13-2).

Seizures occur episodically; therefore, the veterinarian frequently must evaluate an animal without ever seeing the convulsion. The history must be taken carefully and must include a complete description of the seizures and their frequency, duration, and severity. The first goal is to determine that the animal is having convulsions. For example, transient vestibular dysfunction and drug reactions may resemble seizures. The most frequent problem to be confused with seizures is *syncope* (transient loss of consciousness). Syncope is caused by a loss of the blood supply to the brain or hypoglycemia. Cardiac arrhythmia is the most common cause. Acute vestibular episodes may also be mistaken for seizures. Vestibular disease usually causes other deficits, such as a head tilt or ataxia. We encourage all owners to videotape the episodes for our review. This greatly aids in the diagnosis and treatment of seizures, especially those that include complex behavioral signs.

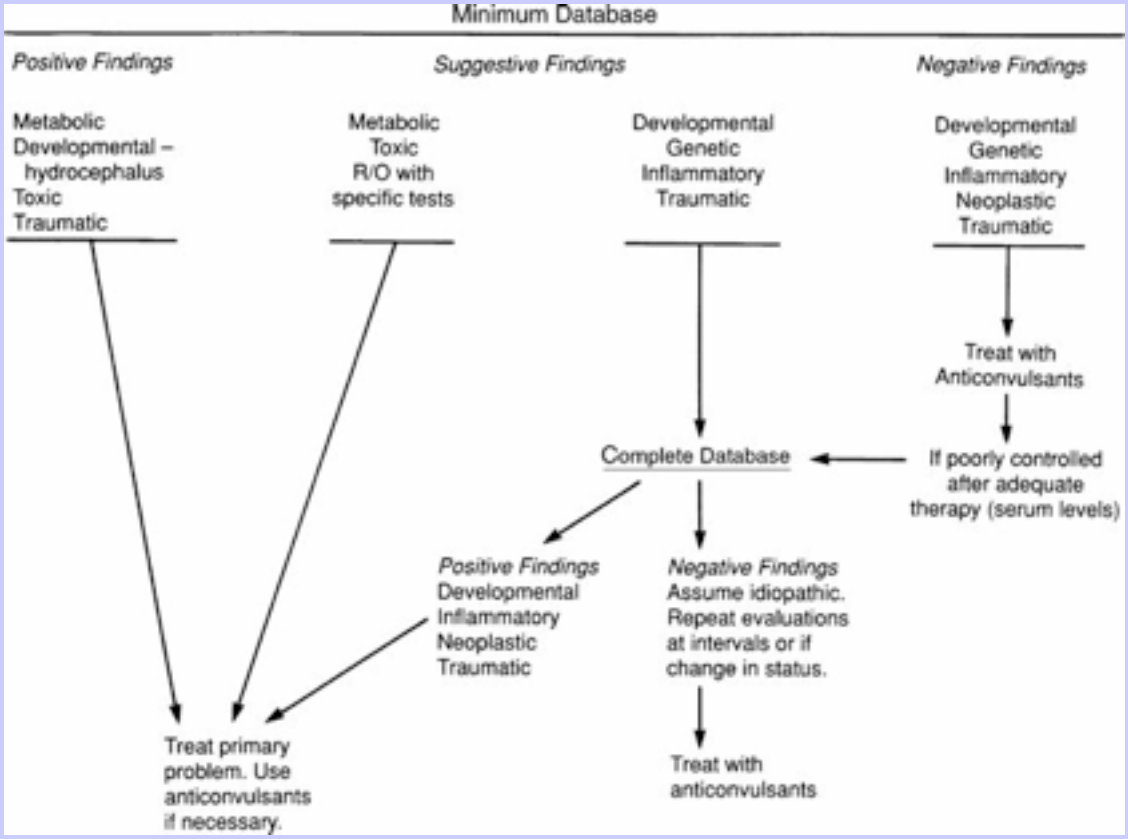
The history also provides information related to the onset and the progression of the disease (see Figure 13-2). Seizures, by definition, are acute in onset; however, the owner may be able to recognize a chronic progression of signs, with seizures being only one component. The diagnostic tests that are most likely to be useful in each disease are listed in Tables 13-2 and 13-3. The minimum database rules out most metabolic diseases. Other diseases may or may not be suggested by the minimum database.

Positive findings include evidence of a metabolic or toxic disease or an abnormal neurologic examination indicating CNS disease. Suggestive findings include some indication of metabolic abnormality that may require further tests. For example, serum albumin and urea nitrogen levels may be low, suggesting liver disease. In the absence of positive or suggestive findings in the minimum database, the animal should be treated with anticonvulsants. Generally, we recommend anticonvulsant therapy in dogs and cats when single seizures occur more than once every 6 weeks and when cluster seizures occur.

Failure to control the seizures after adequate therapy (see Plans for Treatment) warrants a complete database to rule out neurologic disease. Any change in neurologic signs also indicates a complete evaluation. Dogs older than 5 years of age or cats of any age most likely have an acquired disease. Brain tumors must be high on the list of rule-outs in all older animals, even when no neurologic signs are present. The safest and most accurate method of diagnosis is CT or MRI. Therefore, we recommend a scan for all these animals. If the findings are negative, CSF analysis and EEG should be done (see Table 13-7).

Some breeds have primary generalized epilepsy that is difficult to control. The most common examples are German shepherd dogs, Saint Bernards, Labrador retrievers, and Irish setters.[1,10] Negative findings on the complete database for an animal that has been poorly controlled with adequate anticonvulsant medication suggest a poor prognosis. The treatment can be altered by changing the dosage or the drugs, by combining drugs, or by changing the schedule of administration. Periodic reevaluation may reveal a progressive disease that was missed originally.

Figure 13-2 Plan for the diagnosis and management of seizures. Positive findings confirm the diagnosis, negative findings eliminate the diagnosis. *R/O,* Rule out. (Modified from Oliver JE Jr: Protocol for diagnosis of seizure disorders in companion animals, *J Am Vet Med Assoc* 172:824, 1978.)



13.4.3

Plans for Treatment

Successful treatment depends heavily on client education and cooperation. Treatment failures are usually the result of (1) progressive disease, (2) refractory epilepsy, or (3) inadequate client education or poor client compliance leading to subtherapeutic drug concentrations. Clients need to understand the importance of therapeutic drug monitoring to successful seizure management. A progressive disease is identified by repeated examinations. Refractory epilepsy is expected in the breeds that have been listed previously.

The client should understand that successful treatment may be manifested by (1) a reduction in the frequency of seizures, (2) a reduction in the duration of seizures, or (3) a reduction in the severity of seizures. Although complete elimination of seizures is certainly a goal, it is not a realistic expectation for most animals.

The client should be given the following basic rules for treating epileptic animals:

1. Do not judge the efficacy of the medication for at least 2 weeks. Give the medication a chance.
2. Do not change or discontinue the medication suddenly. Status epilepticus (SE) may follow.
3. Phenothiazine tranquilizers are *contraindicated* in epileptics because they lower the threshold for seizure activity.
4. Allow for changes in the animal's environment (e.g., give more medication when increased excitement is expected).
5. Medication may be required for life. Do not decrease dosages rapidly or too soon after seizure control is achieved.
6. No single drug or combination works in all cases. Adjustments in the dosage, the schedule, or the combination of drugs probably will be required. Finding the right combination usually occurs by trial and error, but monitoring therapeutic serum levels helps to eliminate the guesswork. 333 334
7. Good seizure control is more difficult to achieve in certain large-breed dogs.
8. The severity of seizure disorder in cats is not a good predictor of outcome.

We usually do not recommend treatment for animals that have had only one seizure. Knowing the frequency and severity of the seizures is useful in assessing the response to treatment. We usually do not treat animals while we are establishing a diagnosis unless the seizures are frequent or severe or occur in clusters.

We do recommend treating seizures if they are recurrent or intense, especially if they tend to cluster. Our general guidelines are to treat all animals that experience single seizures more frequently than once every 6 weeks. Dogs, especially large-breed dogs, with cluster seizures are at increased risk for developing SE, and we usually initiate anticonvulsant therapy in these cases. Owners should be advised that each time a seizure discharge spreads, it increases the probability that it will spread again. This phenomenon is called *kindling* and can be suppressed with appropriate anticonvulsant therapy.

The final decision about treatment must be made by the client. In essence, if the client feels that the seizures are more of a problem than is giving the medication, treatment is in order.

13.4.4 Antiepileptic Drug Therapy

The strategies of antiepileptic drug therapy have been described by Podell.[40] These strategies include:

1. Modulate membrane action of GABA
2. Reduce excitatory transmission
3. Modulate membrane cation conductance.

Most of the commonly used anticonvulsant agents (phenobarbital, potassium bromide, and diazepam) increase GABA-activated Cl^- conductance, which enhances the inhibitory action of GABA. Several new anticonvulsant agents used in people act to modulate sodium or calcium channels or reduce glutamate-mediated excitation.[40]

The ideal anticonvulsant should suppress seizures completely without side effects or toxicity and be reasonable in cost because life-long therapy is usually required. Unfortunately, such a drug is not known.

13.4.4.1 Phenobarbital

Phenobarbital is the initial drug of choice for treating seizures in dogs and cats.[41–44] In large-breed dogs, some clinicians prefer to initiate treatment with potassium bromide. Phenobarbital is effective, inexpensive, and convenient for administration. The usual starting dosage is 2.5 mg/kg orally twice daily. Some dogs require 5 mg/kg orally twice a day to achieve therapeutic blood levels. Absorption and excretion differ considerably between individuals, and this is especially important in cats. The lower dosage is used if seizures are infrequent and occur as single episodes. Higher dosages are recommended if seizures are frequent or tend to cluster. The dosage is adjusted according to seizure control, side effects, and serum concentrations.

Sedation may occur but usually disappears in the first week. Polyphagia, polydipsia, and polyuria may be seen in some patients. Hepatotoxicity occurs in a small number of cases, but it is less frequent than with most other anticonvulsants.[45]

The peak concentrations of phenobarbital occur 2 to 3 hours after oral administration, and the lowest (trough) concentrations occur just before the next dose. Generally, phenobarbital reaches steady-state concentrations in 2 weeks. Assessing trough concentrations of phenobarbital once every 2 to 3 weeks until serum concentrations are in the therapeutic range of 15 to 45 µg/ml is considered ideal for therapeutic drug monitoring.[41–43] Recent studies indicate, however, that timing may not be clinically important. In a study of 33 epileptic dogs treated with twice-daily phenobarbital, 91% of all samples taken at 0 (trough), 3, and 6 hours post treatment were within the therapeutic range.[46] Many dogs need levels near the high end to achieve control. Generally, we try to maintain serum concentrations in the range of 20 to 40 µg/ml. Dosages as high as 10 to 20 mg/kg per day may be needed in some dogs to maintain these therapeutic blood levels. The response to treatment is more important than the blood level, but monitoring serum levels of phenobarbital may help to determine the cause of inadequate seizure control. Monitoring for evidence of hepatotoxicity or other side effects is strongly encouraged. Routine blood counts and serum chemistries are usually recommended at 6-month intervals; however, a report on monitoring of human epileptics indicates that this grants little benefit, except in high-risk patients.[47] High-risk groups include those with known or presumed biochemical disorders, adverse drug reaction histories, or neurodegenerative diseases.

13.4.4.1.1 Side Effects.

Hepatotoxicity occurs in a small number of dogs treated with phenobarbital.[45] Whether this represents a direct dose-dependent hepatotoxicity or an idiosyncratic drug reaction is still debated among clinicians; however, dogs with serum concentrations above the therapeutic range (>45 µg/ml) are at greatest risk. Several studies in normal and epileptic dogs document that phenobarbital induces hepatic enzyme production in the absence of liver failure.[48,49] When serum levels were maintained in the range of 20 to 40 µg/ml, both alkaline phosphatase (ALP) and alanine aminotransferase (ALT) were increased following 29 weeks of treatment at 5 mg/kg every 12 hours. Concentrations of ALP may be above the normal reference range, whereas ALT levels are usually in the high normal range. Gamma-glutamyl transferase (GGT) may be transiently increased. Aspartate transaminase (AST), free bile acids (fBA), and bilirubin are not affected. Moderate hepatomegaly may be detected on abdominal radiographs, but hepatic ultrasonography is usually normal. Hepatic enzymes return to normal within 6 to 8 weeks following discontinuation of phenobarbital

treatment.[49] Hepatic enzyme induction must be considered when dogs are monitored for hepatotoxicity. The presence of bilirubinuria, bilirubinemia, hypoalbuminemia, and increased concentrations of free bile acids are the best indicators of possible hepatotoxicity. Serum ALT concentrations that are consistently above normal ranges are also indicators of possible hepatotoxicity.

Life-threatening neutropenia and thrombocytopenia have been reported in dogs treated with phenobarbital.[50] Clinical signs resolved when the drug was discontinued. Although the exact mechanism is unknown, it is speculated that phenobarbital most likely induces an immune-mediated reaction directed at cells in circulation rather than suppression of hematopoiesis in the bone marrow.[50]

Several studies have demonstrated the effects of long-term phenobarbital treatment on the thyroid and adrenal axis of normal and epileptic dogs.[48–52] Both serum thyroxine (T_4) and free thyroxine (fT_4) are decreased compared with nontreated dogs. Up to 40% of treated dogs have T_4 concentrations below the normal range. Canine thyroid-stimulating hormone (cTSH) concentrations were either not affected or only mildly increased. Serum triiodothyronine (T_3) concentrations were not affected. Phenobarbital may increase hepatic thyroxine metabolism, decrease thyroxine synthesis and secretion, and alter thyroxine protein binding. The effect is dose related because dogs with phenobarbital levels below 15 µg/ml developed few or no changes in T_4 of fT_4 concentrations. Whereas phenobarbital alters dexamethasone suppression testing in humans, studies in dogs generally show little or no effect on adrenal function tests.[48]

Animals that cannot be controlled with adequate levels of phenobarbital may be given combination therapy. It is most commonly combined with potassium bromide in dogs and benzodiazepines in cats. Phenobarbital is continued while other drugs are added to the regimen. Guidelines for use of the few alternative drugs available are not clearly documented by controlled trials in most cases. Because these drugs are not approved for use in animals, owner consent should be obtained.

13.4.4.2

Potassium Bromide

Potassium bromide (KBr) is a safe and effective anticonvulsant in dogs. It is the first-choice alternate therapy for phenobarbital and is commonly used as the initial anticonvulsant in large-breed dogs.[53–56] Like phenobarbital, it enhances the activity of GABA. KBr was the principal anticonvulsant for humans in the late 1800s until phenobarbital was introduced in the early 1900s. The therapeutic range is not far from the level that produces toxic side effects, such as skin eruptions, sedation, and weakness. These problems rarely have been seen in animals, despite the increased use of KBr. The initial dosage of KBr is 20 to 40 mg/kg per day.[53–56] Chemical-grade KBr can be used in capsules or dissolved in water (100 to 500 mg/ml), which is mixed with food. KBr is slow to reach steady state and has a long half-life (Table 13-8). Higher levels of chloride in the diet, especially one that promotes urolith dissolution, increase the rate of renal excretion of bromide.[55] Bromide toxicity has been reported in an epileptic dog with renal insufficiency.[57] Two to 3 weeks are required to reach therapeutic levels. Steady state is reached in about 4 months.

The KBr levels in the serum should be determined 30 and 120 days after initiating therapy. Therapeutic trough concentrations are 0.8 to 3.0 mg/ml (880 to 3000 µg/ml).[56,58] The time to reach steady-state concentrations can be decreased by giving loading doses of KBr. The loading dose ranges from 450 to 600 mg/kg for a target serum level of 1.0 to 1.5 mg/ml. The loading dose is divided into equal doses given once a day for 5 days. On day 6, serum bromide levels are measured. Smaller loading doses can be continued for 5 days if the KBr

concentration is less than 1 mg/ml. Drug concentrations are again assessed.[58] If in the therapeutic range, maintenance doses are administered, and KBr levels are reassessed in 1 month. KBr combined with phenobarbital has controlled seizures in dogs refractory to phenobarbital alone or to other anticonvulsant therapies.[54,56,58] Serum phenobarbital levels should also be monitored every 6 months and the dosage reduced by 25% if toxic levels are found. When combined with phenobarbital, KBr serum levels of 810 to 2400 µg/ml and serum phenobarbital levels of 9 to 36 µg/ml reduced seizures by 50% or greater in 72% of treated dogs. 335
Forty-five percent of these dogs had no seizures with phenobarbital concentrations below 20 µg/ml.[59] 336

Table 13-8 Anticonvulsant Drugs for Dogs and Cats

Drug	Dosage (mg/kg)	Therapeutic Serum Concentration (µg/ml)	Half-Life (H ± Se)	Time to Steady State (D)
Phenobarbital*	1.5–5 q12h	20–45	70 ± 16	10–18
Potassium bromide*	20–60 q24h or divided	1000–1500	25 (days)	4 (mo)
Diazepam (cats)	0.5–1 q12h	200–500 (ng/ml)	1.5–2	
Clonazepam*	0.02–0.5 q12h	0.02–0.08	1.4 ± 0.3	
Valproic acid*	60 q8h	40–100	1.7 ± 0.4	6–10
Primidone*	10–15 q8h (dog)	5–15 (human)	9–12	6–8
Chlorazepate*[40]	2–4 q12h	20–75 µg/L	5–6	1–2
Felbamate*[40]	20 q8h	30–100 mg/L	5–6	1–2
Gabapentin*[40]	30–60 q8–12h	4–16 mg/L	2–4	1
Topiramate[40] (human)	5–10 q12h	2–25 mg/L	12–30	3–4
Zonisamide*[40]	4–8 q12h	ND	15–20	3–4
Levetiracetam[40] (human)	500–4000 mg/day	ND	7–10	2–3

q, Every.

* Data for dogs.

13.4.4.3 Benzodiazepines

Diazepam is the most commonly used drug in this class. It is used in the treatment of SE, cluster seizures, and toxic seizures and may be used as an add-on drug in the long-term treatment of epilepsy. The benzodiazepines enhance the activity of GABA. Diazepam has a quick onset of action when given parenterally to both dogs and cats. In the dog, the duration of action is very short, and tolerance can rapidly develop, making it less useful for long-term management of epilepsy in this species. Diazepam has a longer half-life in cats, and tolerance is not common in this species, making it a more effective drug for long-term management of feline

epilepsy. In the cat, dosages of 0.5 to 1.0 mg/kg three times daily are effective.[58] Phenobarbital and diazepam are the only anticonvulsants we recommend for cats, although some neurologists report satisfactory results with KBr (Table 13-9). Diazepam can be hepatotoxic, especially in cats.

Clorazepate can be used for monotherapy, but it is most commonly combined with phenobarbital for long-term seizure control in dogs and cats. The dosage is 2.0 to 4.0 mg/kg every 12 hours. Clorazepate may increase phenobarbital concentrations in the serum, usually within 1 month after initiating therapy.[40,58]

Clonazepam, a longer-acting benzodiazepine, is effective for short-term control of refractory seizures. The beneficial effect seems to last for only a few months. Hepatotoxicity can be a problem in dogs receiving clonazepam for longer than a few months. Currently, we use it during the time that KBr is reaching therapeutic effect (1 to 3 months), and then we stop it. The dosage is 0.5 mg/kg twice daily.

13.4.4.4

Primidone

Primidone is largely metabolized to phenobarbital, and a small portion is metabolized to phenylethylmalonamide (PEMA). Phenobarbital is the primary component found in the serum and is assumed to be the primary active agent.[41,44,60] Primidone at a dosage of 50 mg/kg daily produces blood levels of phenobarbital of 10 µg/ml, which is subtherapeutic. Although primidone and PEMA concentrations are much lower, they may have an additive effect.[60]

336

337

Table 13-9 Protocol for Anticonvulsant Medication

Dogs
Phenobarbital, 2.5-5 mg/kg b.i.d.Reduce dosage after 1 wk if sedation is a problem. Measure serum levels after 2 wk to establish a baseline standard. Increase dosage to maintain control as needed and measure serum levels 2 wk after changes in dosage.
If seizures are not controlled, add *potassium bromide* (KBr) in a dosage of 40 mg/kg once a day in addition to the phenobarbital. Serum levels of KBr (1000-1500 mg/dl) may be reached in about 4 mo. If seizures are frequent or severe, clonazepam (0.5 mg/kg b.i.d.) may be used during the time KBr is reaching therapeutic levels.
See text for other alternatives.
Cats
Phenobarbital as above.
Diazepam, 0.5-1 mg/kg b.i.d. or t.i.d. (may be combined with phenobarbital).
Horses and Food Animals
Phenobarbital as above.
Phenytoin, 20 mg/kg b.i.d., for horses only (not approved or tested).
b.i.d., Twice daily; *t.i.d.,* three times daily.

The efficacy of primidone for patients with seizures has been demonstrated clinically for years; however, several studies indicate that it has little or no advantage over phenobarbital, and hepatotoxicity is more frequent.[41,61] Side effects include depression, polydipsia, polyphagia, and hepatic necrosis. The side effects may be dramatic, but they are usually transient. One half to twice the recommended dose may be used, depending on the individual animal's response. Larger animals should be started on a lower dose until tolerance is induced. Primidone is not approved for use in food animals or horses because the dosage and the anticonvulsive effects are unknown.

13.4.4.5

Phenytoin

Phenytoin is frequently used in humans, but its use in animals is limited because of studies showing marked species differences in the metabolism of the drug. The pharmacokinetics vary, depending on the route of administration, pretreatment, and treatment with other drugs. The action of the drug also differs among individuals, even of the same breed.[60] The approximate plasma half-life of phenytoin is 22 to 28 hours in humans, 3 to 4 hours in dogs, and 24 to 108 hours in cats. In addition, blood concentrations of phenytoin in the dog do not reach therapeutic levels (10 μg/ml, based on human clinical and canine research data) at the dosages prescribed for humans.[60,62] Laboratory studies indicate that at least 35 mg/kg three times daily are needed to reach therapeutic levels in the dog.[62] In another study, therapeutic levels were achieved with 3 to 5 mg/lb three times daily, but the reported concentrations were only 1.5 to 3.0 μg/ml.[63] The variability in serum levels and the short half-life make phenytoin of little benefit in most dogs.

13.4.4.6

Miscellaneous Anticonvulsant Drugs

Mephobarbital is longer acting than phenobarbital and is given once daily. Its efficacy is essentially the same as that of phenobarbital because it is metabolized into two molecules of phenobarbital. Mephobarbital offers a once-a-day medication schedule at a greater expense.

Sodium valproate, in combination with phenobarbital, has been useful in a limited number of cases. The half-life is short, and therapeutic levels are difficult to achieve. Some evidence indicates that brain levels may be higher and that other metabolites may have some effect. Sodium valproate may be tried in combination with phenobarbital at a dose of 60 mg/kg.[42,64]

Paramethadione and related drugs of that group are given primarily for absence seizures in humans. Paramethadione is reportedly effective for tonic-clonic seizures at a dosage of 10 to 60 mg/kg daily.[65]

Nimodipine is a calcium channel antagonist that penetrates the blood–brain barrier. It has anticonvulsant activity in models of experimental epilepsy. Nimodipine was ineffective in controlling seizures in 10 dogs with idiopathic epilepsy when administered at a dose of 2.5 mg/kg every 12 hours.[66]

Several new anticonvulsant drugs are available for use in humans and have been used on a limited basis in dogs (see Table 13-8). These drugs are expensive at present, and no reports of clinical trials in dogs or cats have appeared. The following are the recommendations adapted from Podell[40]:

1. Felbamate enhances sodium channel inactivation, enhances GABA activity, and reduces glutamate-mediated excitation. It is used to treat partial seizures at a dosage of 20 mg/kg every 8 hours. Blood dyscrasias and liver disease are potential side effects.

2. Gabapentin also enhances sodium channel inactivation, enhances GABA activity, and reduces glutamate-mediated excitation. A dosage of 30 to 60 mg/kg every 8 to 12 hours is suggested for generalized and partial seizures. Sedation is the primary side effect.

3. Topiramate has activity similar to felbamate. It is used as an add-on drug for generalized and partial seizures. Gastrointestinal upsets and irritability are the primary side effects. A dosage of 5 to 10 mg/kg every 12 hours has been suggested.

4. Zonisamide primarily reduces current through calcium[2] channels. It is used as an add-on drug for the treatment of generalized and partial seizures. A dosage of 4 to 8 mg/kg every 12 hours has been suggested. Sedation, ataxia, and anorexia are potential side effects.

5. Levetiracetam enhances GABA inhibition and is used as an add-on drug for generalized and partial seizures. The side effects are few, and a dosage of 500 to 4000 mg daily has been suggested.

A protocol for the treatment of seizures is outlined in Table 13-9.

13.5 STATUS EPILEPTICUS AND SEVERE CLUSTER SEIZURES

Status epilepticus is the condition of rapidly recurring seizures with incomplete recovery between episodes. This is a serious emergency that can result in death of the patient. Causes of SE include (1) toxicities or metabolic abnormalities, (2) sudden withdrawal of anticonvulsant medications, (3) ineffective anticonvulsant medications, and (4) progressive brain diseases. The risk factors for development of SE have been studied in dogs with primary epilepsy.[67] Dogs weighing 28.9 kg (63.6 lbs) or more were at increased risk compared with dogs weighing 17.4 kg (28.3 lbs) or less. One or more episodes of SE were predictive of future attacks. The mean life span of dogs with SE was 8.3 years compared with 11.3 years in epileptic dogs with no history of SE.[67]

337
338

Animals with SE may develop permanent brain damage and become refractory to anticonvulsant drugs. During severe seizures like those that occur in SE, transient brain hypoxia can occur. Hypoxia can produce central laminar necrosis and may result in permanent neurologic signs such as cortical blindness and mental retardation. Hyperthermia, commonly present in dogs with SE, enhances neuronal swelling and cerebral edema. Treatment for cerebral edema with mannitol and glucocorticoid steroids may be useful in some cases.

Cluster seizures represent individual convulsions that occur close together with short periods of normalcy between episodes. Animals experiencing cluster seizures are at increased risk of developing SE. In a study of 156 epileptic dogs, 66% and 16.5% had generalized cluster seizures and SE, respectively.[68] Of the 156 dogs studied, 52 and 68 had primary or secondary epilepsy, respectively. Fifty dogs had toxic epilepsy, low anticonvulsant drug concentrations, or undetermined causes. A poor prognosis was associated with the diagnosis of GME, loss of seizure control within 6 hours of initiating treatment, or development of SE.

Table 13-10 Protocol for Treatment of Status Epilepticus

1. Stop the seizure. Administer diazepam, 10-50 mg in 10-mg boluses IV. Diazepam usually gives at least temporary remission, allowing time for succeeding steps. Clonazepam may also be used in a dosage of 0.05-0.2 mg/kg for a longer duration of action. If seizures are not controlled, administer phenobarbital sodium (2-4 mg/kg IV at 30-min intervals). If neither is effective, administer sodium pentobarbital to effect (estimated dosage, 10-15 mg/kg). Pentobarbital must be given cautiously because diazepam and phenobarbital may potentiate its effect. Ultrashort-acting barbiturates should not be used because they may potentiate seizure activity.
2. When the seizures have stopped, ensure ventilation of the patient. An endotracheal tube should be placed if the patient is unconscious.
3. Place an IV catheter, draw blood for hematology and chemistry analysis, and start IV fluids. Measure blood glucose levels as soon as possible.
4. Give 50% dextrose IV (2-3 ml for toy breeds, 50 ml for giant breeds). If the seizures are not violent or if interictal quiet periods occur, you may perform steps 3 and 4 first. Hypoglycemia is the one cause of status that can be treated directly.
5. Ruminants and cats should be given thiamine IV in 0.5- to 1-g doses, repeated several times in 24-48 hr.
6. If you suspect hypoglycemia, give an IV calcium preparation. Carefully monitor the heart rate.
7. Once the seizures are under control, evaluate the animal for etiology of seizures. If a cause is found, treat the specific disease.
8. Monitor the body temperature. If it reaches 105° F, cool the animal with ice to a temperature of 103° F. Maintain the temperature in a normal range.
9. Continue to control the seizures. Intravenous or intramuscular phenobarbital should be given until oral medication can be used. The normal movements of anesthetic recovery should not be mistaken for seizures.
IV, Intravenous

A protocol for the treatment of SE is presented in Table 13-10. The same protocol can be used for treatment of cluster seizures, except pentobarbital is seldom required to control the seizures. Diazepam, administered per rectum, has been used to treat cluster seizures and to prevent the development of SE.[69] Owners are given injectable diazepam (5 mg/ml) to give at a dose of 0.5 mg/kg per rectum. The drug is given after an initial generalized seizure and when a second or third seizure occurs within 24 hours of the first seizure. Diazepam is well absorbed from the rectum within 10 minutes of administration, and the availability is about 65%.[69] This protocol may greatly decrease visits to emergency clinics for treatment of recurrent seizures in dogs receiving adequate doses of anticonvulsants.

13.6 NARCOLEPSY AND CATAPLEXY

Narcolepsy is a brain disorder characterized by recurring sudden attacks of sleep.[70] *Cataplexy* (loss of muscle tone) commonly accompanies the attacks and may be the most common feature of attacks. Two other components occurring in humans—sleep paralysis and hallucinations—are difficult to verify in animals because of their subjective nature.[70]

Dogs with narcolepsy typically have episodes in which they suddenly collapse, often while excited or during emotional stimulation. Eating is the most common precipitating factor in reported cases. The dog starts to eat and suddenly falls to the ground asleep. Noise, shaking, or other stimuli may arouse the animal, and often it resumes eating only to fall asleep again. Continual stimulation, such as petting or shaking, may prevent the attack. The episodes often are repeated many times a day.[70–73] Narcolepsy also has been reported in ponies, horses, and a Brahman bull.[74,75]

Normal sleep is characterized on the EEG by a change from low-voltage, fast-wave activity in the animal that is awake to high-voltage, slow-wave activity in the animal that is asleep. Rapid eye movement (REM) sleep develops after approximately 90 minutes of slow-wave sleep and may recur intermittently thereafter. REM sleep is associated with dreaming and is characterized by eye movements, occasional facial movements, and desynchronized low-voltage, fast-wave activity of the EEG.[76]

The sleep attacks of narcolepsy are the same as REM sleep with no intervening slow-wave sleep. Partial attacks and cataplectic episodes may occur without EEG changes.[71]

Narcolepsy has occurred in humans after CNS infection or trauma, and an immune mechanism is suspected in some cases.[73] Narcolepsy/cataplexy has been reported in a young dog with distemper encephalitis.[77] We have documented narcoleptic/cataplectic attacks in dogs with ehrlichial encephalitis that resolved with doxycycline therapy. A biochemical alteration of the neuronal membrane is presumed. Studies in dogs with narcolepsy have demonstrated some biochemical abnormalities.[78–81] Numbers of dopamine and muscarinic receptors are increased, but the numbers of benzodiazepine receptors do not change. The reticular activating system of the rostral brainstem presumably is associated with sleep, and the more caudal portions of the reticular formation in the pons are associated with cataplexy.

A genetic basis for narcolepsy in some breeds is suspected. An autosomal recessive inheritance has been demonstrated in Doberman pinschers and Labrador retrievers.[81] Numerous other breeds of dogs have been diagnosed as narcoleptics, but breeding studies have not been done or have been inconclusive.

A diagnosis usually can be made by observation of the characteristic signs if cataplexy is a prominent part of the syndrome. In the absence of cataplexy, the problem probably will not be recognized by the owner. The EEG is the only available diagnostic test. Sleep beginning with REM sleep is characteristic. Polygraphic recording of the EMG, eye movements, and EEG simultaneously for extended periods is the most definitive test.[82]

Anticholinergic compounds increase the frequency and duration of cataplectic attacks in narcoleptic animals but have no effect on normal animals.[82] A dose of physostigmine salicylate (0.025 to 0.1 mg/kg administered intravenously) produces cataplectic attacks in susceptible animals.

Treatment with stimulants is partially effective. Dextroamphetamine (5 to 10 mg three times daily) and methylphenidate (Ritalin, 5 to 10 mg two or three times daily) have stopped the sleep attacks but have produced undesirable behavioral changes in some cases.[70,82] Excessive somnolence is not a significant problem for most dogs; therefore, managing the cataleptic episodes is of more importance. Imipramine at a dosage of 0.5 to 1.0 mg/kg three times daily is more effective in preventing cataplexy.[82] A combination of methylphenidate and imipramine is recommended to control sleep attacks and cataplexy. The medication should be given at a dosage that reduces attacks without completely eliminating them because complete elimination may require dangerously high dosages.

Giving the medication intermittently also reduces the development of tolerance. Protriptyline at a dosage of 10 mg once a day was effective in controlling hypersomnia in a dog.[83] This dog did not have cataplexy.

Combining amphetamines and imipramine is potentially dangerous because amphetamines cause a release of catecholamines and imipramine blocks their reuptake. Hypertensive episodes can result. A balanced regimen of therapy must therefore be developed for each individual to attain a relatively normal sleep/wakefulness cycle.

13.7 Case Histories

Seizures are a common neurologic problem in dogs. Most patients with seizures do not have other neurologic deficits. The following case histories demonstrate the approach to management. Localizing signs of brain disease are not present in these cases because they are discussed in other chapters. After reading the history and the preliminary laboratory data, the student should develop a plan for further diagnosis or treatment of each case and then read our assessment.

13.7.1 CASE HISTORY 13A

13.7.1.1 Signalment

Canine, miniature poodle, male, 18 months old.

13.7.1.2 History

The dog has received all vaccinations on schedule and has had no major medical problems. The first seizure occurred 2 months ago. The second seizure was observed last night at approximately 6:00 PM. *339*

340

The owner describes the seizure as follows: The dog seemed somewhat apprehensive for approximately 30 minutes, seeking attention from the owner. Suddenly he fell down, extended all four limbs, and arched the head and the neck. After about 30 seconds he started making running movements of the limbs with some chewing movements of the mouth. Some salivation occurred, and the dog urinated. The owner tried to hold and rub the dog, and the movements stopped after about 1 minute. In about 2 or 3 minutes, the dog was able to get up. He seemed a little disoriented for a few minutes, and then he seemed normal.

Other than during the two seizures, the dog appeared to be healthy. He is fed a variety of commercial dog foods twice daily. Water consumption and urination are thought normal.

13.7.1.3 Physical and Neurologic Examinations

No abnormalities are found.

13.7.1.4 Laboratory Examination

The complete blood cell count (CBC) and the chemistry profile (see Table 13-7) are normal.

13.7.2 CASE HISTORY 13B

13.7.2.1 Signalment

Canine, cairn terrier, male, 6 years old.

13.7.2.2 History

The dog has had no serious illnesses and has had booster vaccinations annually. Ten weeks ago the dog had a generalized motor seizure that lasted about 5 minutes. The dog seemed blind and confused for about 4 hours afterward. Two weeks ago, the dog had a second seizure. Since that time he has not acted “right.” His appetite is diminished, and he does not play the way that he did, and he has urinated and defecated in the house several times, which he has not done for years. Last night he had another seizure that lasted over 5 minutes. Today he is very depressed.

13.7.2.3 Physical Examination

No abnormalities are found other than depression.

13.7.2.4 Neurologic Examination

The dog can be coaxed to walk, but he prefers to lie down. The gait is good, with a suggestion of slight symmetric dysmetria. The limbs seem to be lifted a bit high and to be put down with increased force. No ataxia is present, however. The postural reactions also seem slightly dysmetric. The spinal reflexes are normal, as are the cranial nerves, although the menace reaction seems a little sluggish. This response is considered within normal limits when the depression is taken into account.

13.7.3 CASE HISTORY 13C

13.7.3.1 Signalment

Canine, German shepherd dog, female, 4 years old.

13.7.3.2 History

All vaccinations, including annual boosters, have been given. No major illnesses have occurred. Generalized motor seizures started 18 months ago. The first few were 2 to 3 months apart, but recently they have been 2 to 3 weeks apart. Several recent seizures were prolonged (approaching SE) and were controlled with general anesthesia. Several anticonvulsants, including phenobarbital, phenytoin, and primidone in dosages that appear to be adequate, have been used in the last year, with no apparent control of the seizures. The seizures have occurred at various times of day, including at night when the dog is asleep. Laboratory evaluations performed on several occasions by the referring veterinarian have not revealed any abnormalities. The owner feels that neither he nor the dog can continue to tolerate these seizures.

13.7.3.3 Physical and Neurologic Examinations

No abnormalities are found.

13.7.3.4 Laboratory Examination

No abnormalities are found.

13.7.4 CASE HISTORY 13D

13.7.4.1 Signalment

Feline, domestic short hair, female, approximately 14 months old.

13.7.4.2 History

The cat took up residence at the owner's home 6 months ago. She was vaccinated for the usual feline diseases, including rabies, at that time. She has not been ill except for seizures, which started 6 weeks ago. The first seizure, which occurred in the evening, was described as a brief period during which the cat suddenly looked “glassy eyed,” stiffened all four limbs, and arched the neck. The seizure lasted less than a minute. The second and third seizures were similar and occurred about 1 week apart. In the last 3 weeks, the cat has had at least two seizures per week. The last two were generalized motor seizures. The most recent seizure was described as starting like the first one. The cat then twisted to the right, urinated, and began paddling, first with the right limb and then with all four limbs. The seizure lasted approximately 2 minutes, and the cat acted dazed and depressed for approximately 2 hours.

13.7.4.3 Physical Examination

No abnormalities are found.

13.7.4.4 Neurologic Examination

The only abnormality is a slight anisocoria, with the left pupil slightly smaller than the right. Both pupils are reactive to light, although the right seems slightly slower to react than the left. The iris and the fundus appear normal.

13.7.5 CASE HISTORY 13E

13.7.5.1 Signalment

Canine, dachshund, male, 6 months old.

13.7.5.2 History

The dog suddenly became lethargic and exhibited a staggering gait. The owners believe that the onset of signs occurred shortly after he was seen eating some unknown substance in the front yard. Observation of the dog for several days revealed the following pattern of behavior: The dog suddenly collapses to the ground while walking. He appears to be asleep for a few seconds and then awakens, gets up, and behaves normally. While eating, the dog collapses with food in his mouth, wakes up in less than a minute, and continues eating. This pattern might be repeated every 2 to 3 minutes during a meal. The dog can be aroused from sleep easily by noise or touch. No other abnormalities are observed. The dog has not been ill previously and has had all vaccinations.

13.7.5.3 Physical and Neurologic Examinations

Other than the behavior just described, no abnormalities are found.

13.7.5.4 Laboratory Examination

All tests, including an ECG, are normal.

13.7.6 ASSESSMENT 13A

The seizures are generalized tonic-clonic (grand mal, major motor; see Table 13-1). To the owner's knowledge, they have occurred twice. The seizures are single and are of short duration. No history of illnesses or injuries is present, and the physical, neurologic, and laboratory examinations are normal. Although a genetic basis for epilepsy has not been demonstrated in miniature poodles, hereditary epilepsy is suspected because of the relatively frequent occurrence of seizures in this breed without specific cause.

Nothing in the database justifies further diagnostic tests at this time. We would recommend prophylactic medication to determine if the seizures can be prevented. If the owner feels that giving medication is a serious problem, we would suggest observing the animal closely for further seizures and then starting medication if another seizure occurs. The owner should be warned that the dog probably will have more seizures and that medication is the preferred alternative. The medication of choice is phenobarbital.

13.7.7 ASSESSMENT 13B

A 6-year-old dog with a sudden onset of seizures probably has an acquired brain problem. The disorder appears to be progressive. The depression suggests brain abnormalities, which may be primary or secondary to metabolic or toxic abnormalities. Dysmetria, especially when it is subtle and occurs in a terrier, may or may not be significant. It could indicate a diffuse abnormality with cerebellar involvement. A laboratory profile is indicated.

13.7.7.1

Laboratory Examination

Packed cell volume	37%
Hemoglobin	14.5 g/dl
White blood cells (WBCs)	10,950/µL
Neutrophils	7400/µL
Lymphocytes	2400/µL
Monocytes	450/µL
Eosinophils	700/µL
Nucleated RBCs	3 per high-power field
Some polychromasia	
Serum plasma protein	6.5 g/dl
Albumin	3.3 g/dl
Serum urea nitrogen	14 mg/dl
Alkaline phosphatase	80 IU/L
Alanine aminotransferase (ALT)	30 IU/L
Calcium	9.9 mg/dl
Glucose	95 mg/dl
Urinalysis	Normal

No evidence indicates systemic infectious disease (normal WBCs and differential). Severe liver disease is unlikely (normal ALT and alkaline phosphatase, serum albumin, and serum urea nitrogen levels). Calcium and glucose levels are normal. The only unusual findings are nucleated RBCs and polychromasia with a normal packed cell volume and hematocrit (no anemia). This finding is suggestive of lead poisoning. A sample of whole blood was submitted, and 65 mg of lead per 100 ml was reported. These results are diagnostic of lead poisoning. Chelation therapy with calcium ethylenediamine tetraacetic acid (EDTA) was successful. The source of the lead was not found for several weeks, until the owners discovered a thoroughly chewed and very old bowling trophy under a bed.

13.7.8

ASSESSMENT 13C

The history is typical of a form of epilepsy, presumably genetic, that is seen in German shepherd dogs and a few other large breeds. The seizures begin in early adult life and are severe. They often are multiple and are refractory to anticonvulsant therapy. CT or MR imaging and CSF analysis should be recommended to rule out causes of secondary epilepsy. If phenobarbital is ineffective, as in this case, KBr in combination with phenobarbital is the best alternative. The prognosis for significant control is poor, but some dogs can be managed effectively. Phenobarbital and bromide plasma concentrations should be monitored.

The owner declined diagnostic evaluation. The dog's seizures were satisfactorily controlled with KBr therapy for a period of 2 years. Then the dog became increasingly refractory to anticonvulsant therapy and the owner elected euthanasia.

13.7.9 ASSESSMENT 13D

Seizures in cats usually are acquired *(secondary epilepsy)*. Unfortunately, most of the causes are diseases with a poor prognosis. The progression from a partial motor seizure to generalized seizures also suggests primary brain disease. Anisocoria frequently occurs in cats that have had positive tests for feline leukemia virus (FeLV). The signs also may be associated with feline infectious peritonitis (FIP, usually the “dry” form). Meningiomas also may cause seizures without other signs in the early stages. The age of the cat is more suggestive of viral diseases than of neoplasia.

13.7.9.1 Localization

Cerebral or diencephalic. Rule-outs are (1) FIP, (2) FeLV, and (3) meningioma.

13.7.9.2 Plan

Laboratory examination, titers for FeLV and FIP, CSF analysis, EEG. The significant findings are:

WBCs	16,000/µL
Segmented neutrophils	6700/µL
Bands	2500/µL
Lymphocytes	6000/µL
Eosinophils	800/µL
Serum protein	9.0 g/dl
Albumin	3.0 g/dl
Globulin	6.0 g/dl

341

342

CSF	
Protein	110 mg/dl
Cells (total)	240/mm^3
Neutrophils	130/mm^3
Lymphocytes	110/mm^3
EEG: Generalized high-voltage slow waves with spikes randomly superimposed	
FeLV: Positive	
FIP titer: Positive at 1:1600	

All these findings are characteristic of FIP. If costs are a factor, the laboratory examination (serum protein) and FeLV and FIP tests are adequate for diagnosis. Treatment of the CNS form of FIP has been uniformly unsuccessful. Many of these cats have either uveitis or retinal lesions, or both, and a strong presumptive diagnosis can be made from the clinical examination alone.

13.7.10 ASSESSMENT 13E

The behavior of this dog is typical of narcolepsy/cataplexy. The EEG is useful for documenting the changes. Clinical management requires long-term therapy because the disease is not reversible. A brief trial with therapy at home was unsatisfactory for this client, and euthanasia was performed.

13.8 References

1. JE Oliver, Jr.: Seizure disorders and narcolepsy. In Oliver, JE, Hoerlein, BF, Mayhew, IG (Eds.): *Veterinary neurology*. 1987, WB Saunders, Philadelphia.

2. JE Cavazos: In *Pathogenesis of epilepsy. Proceedings of the 19th ACVIM Forum*. 2001, American College of Veterinary Internal Medicine, 423–426.

3. SR Platt: In *The role of glutamate in neurologic diseases. Proceedings of the 19th ACVIM Forum*. 2001, American College of Veterinary Internal Medicine, 427–429.

4. P Gloor, RG Fariello: Generalized epilepsy: some of its cellular mechanisms differ from those of focal epilepsy. *Trends Neurosci*. **11**, 1988, 63–68.

5. ME Russo: The pathophysiology of epilepsy. *Cornell Vet*. **71**, 1981, 221–247.

6. TP Bleck, HL Klawans: Convulsive disorders: mechanisms of epilepsy and anticonvulsant action. *Clin Neuropharmacol*. **13**, 1990, 121–128.

7. SF Stasheff, WW Anderson, S Clark, et al.: NMDA antagonists differentiate epileptogenesis from seizure expression in an in vitro model. *Science*. **245**, 1989, 648–651.

8. JE Oliver, Jr.: Seizure disorders in companion animals. *Compend Cont Educ Pract Vet*. **2**, 1980, 77–85.

9. H Gastaut: Clinical and electroencephalographic classification of epileptic seizures. *Epilepsia*. **10**(suppl), 1969, 512–513.

10. TA Holliday: Seizure disorders. *Vet Clin North Am*. **10**, 1980, 3–29.

11. AD Quesnel, JM Parent, W McDonnell, et al.: Diagnostic evaluation of cats with seizure disorders: 30 cases (1991-1993). *J Am Vet Med Assoc*. **210**, 1997, 65–71.

12. RW Redding: Electroencephalography. In Oliver, JE, Hoerlein, BF, Mayhew, IG (Eds.): *Veterinary neurology*. 1987, WB Saunders, Philadelphia.

13. EB Breitschwerdt, JE Breazile, JJ Broadhurst: Clinical and electroencephalographic findings associated with ten cases of suspected limbic epilepsy in the dog. *J Am Anim Hosp Assoc*. **15**, 1979, 27–50.

14. SL Crowell Davis, M Lappin, JE Oliver: Stimulus responsive psychomotor epilepsy in a Doberman pinscher. *J Am Anim Hosp Assoc*. **25**, 1989, 57–60.

15. H Gastaut, M Toga, R Naquet: Clinical, electrographical and anatomical study of epilepsy induced in dogs by the ingestion of agenized proteins. In Baldwin, M, Bailey, P (Eds.): *Temporal lobe epilepsy*. 1958, Charles C Thomas, Springfield, Ill.

16. NH Dobman, KE Knowles, L Shuster, et al.: Behavioral changes associated with suspected complex partial seizures in Bull Terriers. *J Am Vet Med Assoc*. **208**, 1996, 688–691.

17. MJ Falco, J Barker, ME Wallace: The genetics of epilepsy in the British Alsatian. *J Small Anim Pract*. **15**, 1974, 685–692.

18. A Van der Velden: Fits in Tervuren shepherd dogs: a presumed hereditary trait. *J Small Anim Pract*. **9**, 1968, 63–70.

19. SW Biefelt, HC Redman, JJ Broadhurst: Sire and sex-related differences in rates of epileptiform seizures in a purebred beagle dog colony. *Am J Vet Res*. **32**, 1971, 2039–2048.

20. GA Hegreberg, GA Padget: Inherited progressive epilepsy of the dog with comparisons to Lafora's disease of man. *FASEB J*. **35**, 1976, 1202–1205.

21. T Tomchick: Familial Lafora's disease in the beagle dog. *FASEB J*. **32**, 1973, 8–21.

22. ME Wallace: Keeshonds: a genetic study of epilepsy and EEG readings. *J Small Anim Pract*. **16**, 1975, 1–10.

23. TA Holliday: Epilepsy in animals. In Frey, HH, Janz, D (Eds.): *Handbook of experimental pharmacology*. **vol 74**, 1985, Springer Verlag, Berlin.

24. JG Cunningham, GC Farnbach: Inheritance and idiopathic canine epilepsy. *J Am Anim Hosp Assoc*. **24**, 1988, 421–424.

25. J Borden, L Manuelidis: Movement of the X chromosome in epilepsy. *Science*. **242**, 1988, 1687–1691.

26. GC Farnbach: Seizures in the dog, Part I: basis, classification, and predilection. *Compend Cont Educ Pract Vet*. **6**, 1984, 569–576.

27. CL Chrisman: Epilepsy and seizures. In Howard, JL (Ed.): *Current veterinary therapy: food animal practice*. 1981, WB Saunders, Philadelphia.

28. R Barlow: Morphogenesis of cerebellar lesions in bovine familial convulsions and ataxia. *Vet Pathol*. **18**, 1981, 151–162.

29. VA Gerard, CN Conarck: Identifying the cause of an early onset of seizures in puppies with epileptic parents. *Vet Med*. **86**, 1991, 1060–1061.

30. TA Holliday, JG Cunningham, MJ Gutnick: Comparative clinical and electroencephalographic studies of canine epilepsy. *Epilepsia*. **11**, 1971, 281–292.

31. SE Bunch: Anticonvulsant drug therapy in companion animals. In Kirk, RW (Ed.): *Current veterinary therapy VIII*. 1983, WB Saunders, Philadelphia.

32. KG Braund: Degenerative and developmental diseases. In Oliver, JE, Hoerlein, BF, Mayhew, IG (Eds.): *Veterinary neurology*. 1987, WB Saunders, Philadelphia.

33. CE Greene, M Vandevelde, K Braund: Lissencephaly in two lhasa apso dogs. *J Am Vet Med Assoc*. **169**, 1976, 405–410.

34. JE Oliver, BF Hoerlein, IG Mayhew: In *Veterinary neurology*. 1987, WB Saunders, Philadelphia.

35. JN Kornegay, IG Mayhew: Metabolic, toxic, and nutritional diseases of the nervous system. In Oliver, JE, Hoerlein, BF, Mayhew, IG (Eds.): *Veterinary neurology*. 1987, WB Saunders, Philadelphia.

36. BK Roberts, MG Aronsohn, BL Moses, et al.: *Bufo marinus* intoxication in dogs: 94 cases (1997-1998). *J Am Vet Med Assoc*. **216**, 2000, 1941–1944. 342

37. SM Gwaltney-Brant, JC Albretsen, SA Khan: 5-hydroxytryptophan toxicity in dogs: 21 cases (1989-1999). *J Am Vet Med Assoc*. **216**, 2000, 1937–1940. 343

38. JE Oliver, Jr.: Protocol for the diagnosis of seizure disorders in companion animals. *J Am Vet Med Assoc*. **172**, 1978, 822–824.

39. JA Hudson, ST Simpson, DF Buxton, et al.: Ultrasonographic diagnosis of canine hydrocephalus. *J Vet Radiol*. **31**, 1990, 50–58.

40. M Podell: In *Strategies of antiepileptic drug therapy. Proceedings of the 19th ACVIM Forum*. 2001, American College of Veterinary Internal Medicine, 430–432.

41. D Schwartz Porsche, W Loscher, HH Frey: Therapeutic efficacy of phenobarbital and primidone in canine epilepsy: a comparison. *J Vet Pharmacol Ther*. **8**, 1985, 113–119.

42. SB Lane, SE Bunch: Medical management of recurrent seizures in dogs and cats. *J Vet Intern Med*. **4**, 1990, 26–39.

43. GC Farnbach: Serum concentrations and efficacy of phenytoin, phenobarbital, and primidone in canine epilepsy. *J Am Vet Med Assoc*. **184**, 1984, 1117–1120.

44. HH Frey: Use of anticonvulsants in small animals. *Vet Rec*. **118**, 1986, 484–486.

45. B Dayrell Hart, SA Steinberg, TJ VanWinkle, et al.: Hepatotoxicity of phenobarbital in dogs: 18 cases (1985-1989). *J Am Vet Med Assoc*. **199**, 1991, 1060–1066.

46. RE Levitski, LA Trepanier: Effect of timing of blood collection on serum phenobarbital concentrations in dogs with epilepsy. *J Am Vet Med Assoc*. **217**, 2000, 200–204.

47. JM Pellock, LJ Willmore: A rational guide to routine blood monitoring in patients receiving antiepileptic drugs. *Neurology*. **41**, 1991, 961–964.

48. PB Muller, J Taboada, G Hosgood, et al.: Effects of long-term phenobarbital on the liver in dogs. *J Vet Intern Med*. **14**, 2000, 165–171.

49. TL Gieger, G Hosgood, J Taboada, et al.: Thyroid function and serum hepatic enzyme activity in dogs after phenobarbital administration. *J Vet Intern Med*. **14**, 2000, 277–281.

50. G Jacobs, C Calvert, A Kaufman: Neutropenia and thrombocytopenia in three dogs treated with anticonvulsants. *J Am Vet Med Assoc*. **212**, 1998, 681–684.

51. LB Kantrowitz, ME Peterson, LA Trepanier, et al.: Serum total thyroxine, total triiodothyronine, free thyroxine, and thyrotropin concentrations in epileptic dogs treated with anticonvulsants. *J Am Vet Med Assoc*. **214**, 1999, 1804–1808.

52. CL Gaskill, SA Burton, CJ Hans, et al.: Effects of phenobarbital treatment on serum thyroxine and thyroid-stimulating hormone concentrations in epileptic dogs. *J Am Vet Med Assoc*. **215**, 1999, 489–496.

53. Schwartz Porsche D, Boenigk HE, Lorenz JH: Bromid Therapie bei den Epilepsien des Hundes: Erste Erfahrungen. Kurzreferate, regionale Arbeitstagung Nord DVG Fachgruppe. Kleintierkrankheiten. Timmendorfer Strand, 1987.

54. D Schwartz Porsche: Epidemiological, clinical, and pharmacokinetic studies in spontaneously epileptic dogs and cats. In *Proceedings of the 11th American College of Veterinary Internal Medicine Forum*. 1986, American College of Veterinary Internal Medicine, Washington, DC, 61–63.

55. A Sisson, RA LeCouteur: Potassium bromide as an adjunct to phenobarbital for the management of uncontrolled seizures in the dog. *Prog Vet Neurol*. **1**, 1990, 114–115.

56. M Podell, WR Fenner: Bromide therapy in refractory canine idiopathic epilepsy. *J Vet Intern Med*. **7**, 1993, 318–327.

57. ES Nichols, LA Trepanier, K Linn: Bromide toxicosis secondary to renal insufficiency in an epileptic dog. *J Am Vet Med Assoc*. **208**, 1996, 231–236.

58. DM Boothe: Anticonvulsant therapy in small animals. *Waltham Focus*. **4**, 1995, 25–31.

59. LA Trepanier, A Van Schoick, WS Schwark, et al.: Therapeutic serum drug concentrations in epileptic dogs treated with potassium bromide alone or in combination with other anticonvulsants: 122 cases (1992-1996). *J Am Vet Med Assoc*. **213**, 1998, 1449–1453.

60. HH Frey, W Loscher: Pharmacokinetics of antiepileptic drugs in the dog: a review. *J Vet Pharmacol Ther*. **8**, 1985, 219–233.

61. GC Farnbach: Efficacy of primidone in dogs with seizures unresponsive to phenobarbital. *J Am Vet Med Assoc*. **185**, 1984, 867–868.

62. JE Sanders, RA Yeary: Serum concentrations of orally administered diphenylhydantoin in dogs. *J Am Vet Med Assoc*. **172**, 1978, 153–156.

63. LJ Pasten: Diphenylhydantoin in the canine: clinical aspects and determination of therapeutic blood levels. *J Am Anim Hosp Assoc*. **13**, 1977, 247–254.

64. LA Nafe, A Parker, WJ Kay: Sodium valproate: a preliminary clinical trial in epileptic dogs. *J Am Anim Hosp Assoc*. **17**, 1981, 131–133.

65. AJ Parker: A preliminary report on a new antiepileptic medication for dogs. *J Am Anim Hosp Assoc*. **11**, 1975, 437–438.

66. DP O'Brien, ST Simpson, RC Longshore, et al.: Nimodipine for treatment of idiopathic epilepsy in dogs. *J Am Vet Med Assoc*. **210**, 1997, 1298–1301.

67. M Saito, KR Munana, NJH Sharp, et al.: Risk factors for development of status epilepticus in dogs with idiopathic epilepsy and effects of status epilepticus on outcome and survival time: 32 cases (1990-1996). *J Am Vet Med Assoc*. **219**, 2001, 618–623.

68. SW Bateman, JM Parent: Clinical findings, treatment, and outcome of dogs with status epilepticus or cluster seizures: 156 cases (1990-1995). *J Am Vet Med Assoc*. **215**, 1999, 1463–1468.

69. M Podell: The use of diazepam per rectum at home for the acute management of cluster seizures in dogs. *J Vet Intern Med*. **8**, 1995, 68–74.

70. CD Knecht, JE Oliver, R Redding, et al.: Narcolepsy in a dog and a cat. *J Am Vet Med Assoc*. **162**, 1973, 1052–1053.

71. JW Richardson, P Fredrickson, S Lin: Narcolepsy update. *Mayo Clin Proc*. **65**, 1990, 991–998.

72. MM Mitler, O Soave, WC Dement: Narcolepsy in seven dogs. *J Am Vet Med Assoc*. **168**, 1976, 1036–1038.

73. AE Katherman: A comparative review of canine and human narcolepsy. *Compend Cont Educ Pract Vet*. **2**, 1980, 818–822.

74. CR Sweeney, JC Hendricks, J Beech, et al.: Narcolepsy in a horse. *J Am Vet Med Assoc*. **183**, 1983, 126–128.

75. GM Strain, BM Olcott, RM Archer, et al.: Narcolepsy in a Brahman bull. *J Am Vet Med Assoc*. **185**, 1984, 538–541.

76. A Wauquier, JL Verheyen, WAE Van Den Broeck, et al.: Visual and computer-based analysis of 24 h sleepwaking patterns in the dog. *Electroencephalographr Clin Neurophysiol*. **46**, 1979, 33–48.

77. C Cantile, M Baroni, M Arispici: A case of narcolepsy-cataplexy associated with distemper encephalitis. *J Vet Med Assoc*. **46**, 1999, 301–308.

78. MM Mitler, WC Dement, C Guilleminault, et al.: Canine narcolepsy. In Rose, FC, Behan, PO (Eds.): *Animal models of neurological disease*. 1980, Putman Medical, Kent, Great Britain. 343

79. Delashaw, JB Jr., AS Foutz, C Guilleminault, et al.: Cholinergic mechanisms and cataplexy in dogs. *Exp Neurol*. **66**, 1979, 745–757. 344

80. S Bowersox, K Kilduff, L Zeller DeAmicis, et al.: Brain dopamine receptor levels elevated in canine narcolepsy. *Brain Res*. **402**, 1987, 44–48.

81. B Fruhstorfer, E Mignot, S Bowersox, et al.: Canine narcolepsy is associated with an elevated number of α-receptors in the locus coeruleus. *Brain Res*. **500**, 1989, 209–214.

82. TL Baker, MM Mitler, AS Foutz, et al.: Diagnosis and treatment of narcolepsy in animals. In Kirk, RW (Ed.): *Current veterinary therapy VIII*. 1983, WB Saunders, Philadelphia.

83. A Shores, R Redding: Narcoleptic hypersomnia syndrome responsive to protriptyline in a labrador retriever. *J Am Anim Hosp Assoc*. **23**, 1987, 455–458.