

SEIZURES AND EPILEPSY

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A seizure is a paroxysmal, transitory uncontrolled dysrhythmia of brain's gray matter that occurs suddenly and stops spontaneously. It may be characterized by change in consciousness, involuntary motor movements, behavioral change, sensory abnormalities, or autonomic signs. The clinical appearance varies with location and severity of neuronal discharge. There are several areas of the brain that can be damaged to result in seizures: Cerebrum, limbic system, thalamus, hypothalamus. There are 4 stages to a seizure:

1. Prodrome: Behavioral change that precedes ictus by several hours or days. Usually goes unnoticed or can't be detected in the dog.
2. Aura: Actual beginning of ictus. May consist of a behavioral change (restlessness, insecurity, pacing) seconds to minutes before the ictus.
3. Ictus: The seizure.
4. Postictus: Recovery stage (minutes to 1-2 days). Animal may be disoriented, blind, etc.

There are also several types of seizures:

1. Generalized (often called grand mal)

Diffuse, symmetrical, electrical discharge involving the entire cerebral cortex. Most often associated with toxicities, metabolic disturbances, nutritional deficiencies and primary epilepsy.
2. Partial

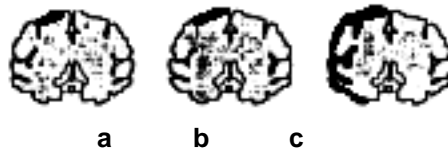
Focal cerebral discharge involving one part of the cerebral cortex only. Most often associated with inflammatory, neoplastic, traumatic or metabolic insults (acquired seizures).
Examples: hysterical running = temporal lobe, limbic system.
unilateral muscle twitch = contralateral frontal lobe
fly biting, star gazing = temporal or occipital lobe.
self mutilation, tail chasing = parietal lobe
episodic chronic vomiting and diarrhea = limbic lobe
3. Partial with secondary generalization
Focal cerebral discharge that becomes a diffuse cerebral discharge. Most often associated with an acquired organic lesion.

GENERALIZED SEIZURE



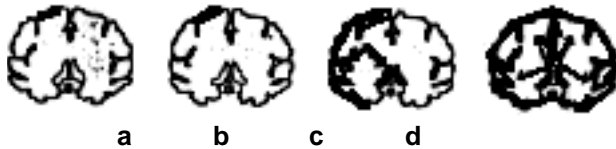
- a. Seizure focus, left cerebrum
- b. Small number of surrounding neurons begin to discharge
- c. Diencephalon is activated
- d. Entire cerebrum shows seizure activity, resulting in generalized symmetrical motor activity

PARTIAL SEIZURE



- a. Seizure focus, left cerebrum
- b. Small number of surrounding neurons begin to discharge
- c. Large numbers of neurons become involved in the seizure discharge. If the abnormal seizure activity involved the left motor cortex, the right side of the body would manifest involuntary movements.

PARTIAL SEIZURE WITH SECONDARY GENERALIZATION



- a. Seizure focus, left cerebrum
- b. Small number of surrounding neurons begin to discharge
- c. Diencephalon is activated
- d. Entire cerebrum shows seizure activity, resulting in generalized symmetrical motor activity

Definitions:

1. Status epilepticus

Continual seizure activity greater than 10-30 minutes in duration or multiple seizures occurring minutes apart with poor or no recovery between the seizures. Can be generalized or partial activity.

Often associated with toxins, acute withdrawal of anticonvulsant drugs, or seizures that are difficult to control.

2. Epilepsy

Epilepsy is characterized by recurrent, spontaneous, transient, paroxysms of hyperactive brain function resulting in seizures. Epileptic disorders can be considered either primary (conditions of intrinsic and presumable hereditary cerebral hyperexcitability with seizures as the only manifestation of abnormal brain function) or secondary (the seizure is the result of a pathologic process that is affecting or has affected normal function of the brain). Many of the cases that we deal with are primary and have been called idiopathic, true, or inherited epilepsy. It is most important to try to establish a secondary cause, such as encephalitis, hypoxia, head trauma, neoplasia, etc. for the dog presenting with seizures. If a secondary cause can not be found and if the neurologic examination is normal, then we can presume that primary epilepsy exists. Most investigators believe that fundamental abnormality in all epileptic conditions occurs in the cerebral cortex including the limbic cortex (hippocampus). Seizures are transient expression of /permanently disordered cortex. Even though epileptic seizures are intermittent, epileptogenic cortical abnormality persists throughout the interictal period. What triggers the clinical expression of the abnormality is not known in the vast majority of the cases. Rarely are we able to establish a "trigger" in our canine cases of epilepsy. In some people, a seizure may be triggered by certain odors, light stimulation, or stress.

3. Refractory epilepsy

I use the term "refractory epilepsy" for those cases that are extremely difficult to control with more conventional anticonvulsant drugs and drug dosages. Primary or secondary epilepsy can develop into refractory epilepsy.

4. Localizing sign

An asymmetrical motor activity (such as jerking of a particular limb at the beginning of a seizure, contracture of one side of the face, or compulsive circling to one side after a seizure) that can give us a clue as to which side of the brain or what parts of the brain may be involved in the seizure focus.

5. Petit mal

A very brief (few seconds) cerebral discharge not readily recognized in animals. EEG pattern is characteristic in people i.e. a generalized 3 per second spike and wave dysrhythmia. This term is often misused to describe a seizure that wasn't severe.

6. Interictal stage: Period between seizures (after complete recovery from a seizure).

7. Epileptogenesis

- A. Seizure threshold: A tendency toward seizures is based upon the normal excitability of neurons which is regulated by the interplay and balance between excitatory and inhibitory neurotransmitters. Each individual has a seizure threshold which, if exceeded, results in a seizure. Some animals likely have a lower seizure threshold because of genetic influences. Seizures can be triggered by fever, estrus, hyperventilation, fatigue, or photic stimulation.
- B. Kindling: Repeated exposure of normal neurons to abnormal electrical discharges will increase their excitability and make them more likely to spontaneously discharge in an abnormal manner. This may explain the eventual loss of seizure control in some epileptics.
- C. Mirror focus: One side of the brain is a mirror image of the other. When a focal epileptic lesion is created experimentally on one side of the cerebrum, abnormal waveforms can be found on EEG recordings on the opposite uninjured side within days to weeks later.

Signalment/History

1. Age

- < 1 year: distemper
lead, other toxins
hypoglycemia
portal systemic shunt
hydrocephalus, lissencephaly
- 5+ years: tumors

2. Breed

Chihuahua: hydrocephalus. Lhasa apso: lissencephaly - Toy breeds: hypoglycemia. German Shepherd, Saint Bernard, Beagles, Irish Setters, Miniature Poodles: primary epilepsy. Miniature Schnauzers: hyperlipoproteinemia. Boxer, Boston Terriers: neoplasia - West Highland White and Cairn Terriers: globoid cell leukodystrophy.

3. Sex

Female: Mammary gland adenocarcinomas may metastasize to brain. **[Seizure threshold is reduced during estrus.]** Male: Prostatic adenocarcinomas may metastasize to brain.

4. History

Extremely important. Be thorough. Get owner to describe seizure. Distinguish seizure from syncope. Onset? Course? Duration? Frequency? Loss of consciousness? Incontinence? Salivation? Try to determine if seizures are generalized, partial, or partial with secondary generalization. Ask about environment, toxins, travel, littermates, flea control. Past history is important. Previous head trauma, infection, seizures? Vaccinations? Diet? For many cases, the key to the diagnosis lies in the history.

Physical Examination (PE)

- Runny nose/eyes in pup: distemper?
- Dome-shaped head and open fontanelles: hydrocephalus?
- Pot-bellied pup with pale mm: hypoglycemia due to parasites?
- Salivation, miosis, urination, defecation: Organophosphate toxicity?
- Physical signs of trauma?
- Ticks: rickettsial encephalitis?
- Normal: primary epilepsy?

Neurologic Examination (NE)

May be difficult to interpret if dog is in post ictal stage. Look for localizing signs as discussed before. Do another complete neurological exam when dog is in interictal stage. Is the dog normal during the interictal stage?

Differential Diagnoses List for Seizures in Dogs

The diagnosis of epilepsy should be distinguished from cardiogenic syncope which can produce motor twitches and even tonic-clonic convulsions. In my experience cardiogenic syncope is most often due to arrhythmias or conduction disturbances but is not a common cause of seizures or epilepsy.

*Discussed with lectures on neurological causes of behavioral changes or coma/stupor. Please refer to those notes. Common causes are in bold print.

Degenerative: None

Anomalous: **Congenital hydrocephalus***, lissencephaly*, lysosomal storage diseases*, **idiopathic primary epilepsy**

Metabolic: Hepatic encephalopathy*, uremia, hypocalcemia, acid-base imbalance, **hypoglycemia**, hypoxia, polycythemia, hyperlipoproteinemia

Neoplastic: **Primary and metastatic brain tumors***

Nutritional:

Inflammatory: Viral **encephalitis (canine distemper***, rabies*, adenovirus*); fungal*, protozoal* or bacterial encephalitis*, **rickettsial*** (Rocky Mountain Spotted Fever, Ehrlichia) encephalitis, **granulomatous meningoencephalitis (reticulosis)***, encephalitis

Idiopathic: **Idiopathic primary epilepsy**

Traumatic: Epilepsy can develop within months to 2 years of severe **head trauma**.

Toxic: Lead*, organophosphates, others

Vascular: Ischemia*

Parasitic: Aberrant migration (rare) of Cuterebra, Dirofilaria

Differential Diagnoses List for Seizures in Cats

Degenerative: none

Anomalous: congenital hydrocephalus*, lissencephaly*, lysosomal storage disease*

Metabolic: **hepatic encephalopathy**, uremia, hypoglycemia, hypocalcemia

Neoplastic: **primary brain tumors***: (meningioma, astrocytoma); metastatic tumors*: (adenocarcinomas, others)

Nutritional: thiamine deficiency*

Inflammatory: **feline infectious peritonitis virus***, systemic fungal infection*, toxoplasmosis*, bacteria*, pseudorabies virus*, rabies virus*, other viruses?

Idiopathic: **feline hyperesthesia syndrome**, epilepsy

Toxic: many; organophosphates most common

Traumatic: head trauma*

Vascular: **ischemic encephalopathy***

Parasitic: aberrant migration of Cuterebra larvae or adult Dirofilaria immitis*

PRIMARY EPILEPSY (Idiopathic, true, genetic)- Common in dogs; rare in cats

Primary epilepsy may be suspected in purebred dogs with generalized seizures which begin before 4 years of age. History should be negative for previous trauma, illness, etc. Diagnosis is confirmed only by studying breeding histories and performing breeding trials.

Signalment: German Shepherds, St. Bernards, Poodles, Irish Setters, Keeshonds, Labrador and Golden Retrievers, Siberian Huskies, Cocker Spaniels, English Cocker Spaniels, Wirehaired Fox Terriers, Beagles, Standard and Miniature Poodles, many other breeds.

Cause: Biochemical neuronal defect??

Complaint: Severe generalized seizure in the larger breeds. Smaller breeds (Poodles) usually tend to have milder generalized seizures and may not lose consciousness.

NE: Normal in interictal stage.

AA: Most AA are normal. Occasionally EEG recording will show changes. Diagnosis is based upon signalment and **exclusion** of other disease processes.

RX: Phenobarbital; bromide.

PX: Good in small breeds, poorer in large breeds. Very poor in St. Bernards, Irish Setters and German Shepherds because seizures usually become refractory to antiepilepsy drugs.

Pathology: Normal except for signs of hypoxia in some cases.

HYPOGLYCEMIA (< 60 mg/dl) - Common

Hypoglycemia is the most common metabolic cause of seizures in small animals. Causes include:

- a) **Stress related hypoglycemia** usually occurs in young animals that are stressed, malnourished, or have a heavy parasite load. It has been observed especially in young toy breeds of dogs. Usually managed by frequent feedings, and proper de-wormings. Dogs usually "grow out of it."
RX: 1/2 cc/lb of 50% dextrose I.V. diluted. Blood transfusion if severely anemic from hookworms; deworm.
- b) **Hunting dog hypoglycemia** occurs sometimes in dogs that are fasted before a hunt.
RX = Karo syrup or honey rubbed on gums or candy bar or some form of sugar. Karo syrup or honey rubbed on gums.
- c) **Hyperinsulinism** can occur from an insulin overdose in diabetics or from an insulinoma (pancreatic or extra pancreatic mass that produces excessive insulin). Most insulinomas (>80%) are Beta-cell adenocarcinomas. This will be discussed in the Endocrinology course.

BRIEF OVERVIEW OF INSULINOMA (SEE ENDOCRINOLOGY NOTES)

Signalment: Middle aged to older dog. Occasional cat, ferret. Complaint: Seizures do not respond well to antiepilepsy drugs; episodic weakness.

AA: **Chemistry:** Resting glucose sample may be low or a 24-72 hr fast may be necessary to demonstrate hypoglycemia.

Amended insulin glucose ratio:

$$\text{Insulin unit/ml} \times 100 \text{ divided by plasma glucose mg/dl minus } 30 \\ = \text{ ratio in } \mu \text{ units/mg. Normal is less than } 30.$$

RX: a) Surgical removal of mass
b) Medical mgt if mass not removed or if metastasis has occurred. Frequent feedings. Diazoxide.

PX: Adenocarcinomas frequently metastasize and hypoglycemia may occur weeks to months later. Better prognosis with adenoma. Brain damage from prolonged hypoglycemia may result in acquired epilepsy. A polyneuropathy is occasionally present causing lower motor neuron weakness.

OTHER METABOLIC CAUSES OF SEIZURES:

HYPOCALCEMIA - Rare

Hypocalcemia-induced tremors and paralysis are more common than seizures.
Causes: excessive lactation, hypoparathyroidism, acute pancreatitis.

HYPOXIA - Rare

Can produce syncope or seizures. Causes: Anemia, cardiac or pulmonary disease, cardiac arrest, toxins.

ACID-BASE IMBALANCES - Rare

Most commonly causes weakness. Alkalosis can decrease seizure threshold.

OSMOLALITY IMBALANCES - Rare

Most commonly causes coma or altered behavior. Ex: Non ketoacidotic hyperosmolar diabetic.

HYPERLIPOPROTEINEMIA- Rare

Most commonly occurs in 2-7 year old miniature Schnauzers, which have defective lipid metabolism. It must be distinguished from other metabolic causes of hyperlipoproteinemia (diabetes mellitus, hypothyroidism, pancreatitis, hyperadrenocorticism). See "**Nutrition Notes.**"

POLYCYTHEMIA - Rare

PUG DOG ENCEPHALITIS-- Occasional

Reported in pugs 9 months to 4 years of age. Most common clinical sign is progressive seizure activity that responds poorly to anticonvulsants. Circling, visual deficits, and intermittent screaming also reported. The course is 1-6 months. CSF may show increased mononuclear cells and increased protein. Histopathology shows a granulomatous encephalitis of the white and gray matter of the cerebrum. Perivascular cuffs of lymphocytes and histocytes are also present. The cause is unknown and the prognosis is poor. Similar disease in Maltese terriers.

TOXICITIES THAT CAN CAUSE SEIZURES: Please refer to toxicology notes.

LEAD: See Cerebral Signs Notes.

STRYCHNINE - Occasional

For more complete description, refer to "**Toxicology Notes.**"

Strychnine is a highly toxic indole alkaloid. It interferes with postsynaptic inhibition in spinal cord and medulla by antagonizing glycine (inhibitory neurotransmitter). The result is generalized, symmetrical rigidity and tonus which can be spontaneous or initiated by stimuli. Onset is 10 min to 2 hrs post ingestion.

RX: Relaxation (valium, pentobarbital, inhalation anesthesia)

Emesis or gastric lavage.

Diuresis (5% mannitol in 0.9% NaCl) or urine

acidification (150 mg/kg ammonium chloride p.o. enhances excretion).

PX: Death (anoxia, exhaustion) in 1-2 hours if untreated. Guarded if not treated early.

ORGANOPHOSPHATES, CARBAMATES - Common

For more complete description, refer to "**Toxicology Notes.**"

The physiologic effect of these toxins is inhibition of AChE (AChE removes toxic amounts of ACh at neuromuscular junction). A small amount of excess ACh causes an increase in function whereas large amount of excess ACh causes a decrease in function. The nerves most affected are motor nerves to striated muscle, preganglionic fibers to autonomic ganglia, and postganglionic cholinergic fibers to smooth and cardiac muscle and the secretory cells. Onset varies with dose and exposure route.

Complaint: Muscle tremors, profuse salivation, lacrimation, involuntary urination, defecation, miosis, vomiting, diarrhea, seizures, weakness and/or ventroflexion of neck. Some organophosphates may also cause a chronic progressive demyelination of peripheral nerves.

RX: Valium to decrease muscle tremors and seizures except in cases of known exposure to chlorpyrifos. Atropine (0.02 mg/lb, one half IV, rest IM) is antidote; dose may have to be repeated several times.

PX: Usually good if treated early.

CHLORINATED HYDROCARBONS - Occasional

Lindane, chlordane, dieldrin, heptachlor, toxaphene, methoxychlor, DDT can either stimulate or depress CNS. The most consistent signs are fasciculations about neck and face but clonic-tonic "seizures" that may be initiated by stimuli are also reported. Treatment is gastric lavage, sedation/anesthesia. Save samples of vomitus or feces for chemical analysis. Tissue samples can also be analyzed (brain, liver, fat, kidney). **See toxicology notes.**

METALDEHYDE - Occasional

Ingestion of snail and slug bait causes CNS depression, seizures, incoordination, muscles tremors, salivation and hyperesthesia, not influenced by external stimuli. Treatment: emetics if dog is still standing, muscle relaxants (Valium or Robaxin), light anesthesia followed by gastric lavage. Aspiration of vomitus is major cause of death. Hepatic insufficiency may occur few days later. Prognosis variable. **See toxicology notes.**

TOAD POISON - Occasional

When dogs grab Bufo marinus toad in their mouths, the toad's parotid gland releases thick, yellow-white toxin which is rapidly absorbed through dog's buccal and gastric mucosa resulting in salivation, cyanosis, seizures. Treatment: rinse mouth immediately. Various drug therapies (**see Current Vet. Therapy**). Toxin = bufotoxins, catecholamines.

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