

**Practical Neurology
Seizure Disorders
The most common
Neurologic Problem in
Small Animal Medicine**

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Types of Seizures

Generalized Seizure

- Used to be called “grand mal”
- Usually tonic-clonic
- Most common kind of seizure
- Usual loss of consciousness
 - Sometimes partially conscious
- First phase tonic
 - stiff, opisthotonus
 - May be cyanotic
 - Vocalize, salivate, urinate, defecate
 - A minute or so
- Second phase clonic
 - Paddling or jerking of the limbs
 - Chewing movements
 - May be several minutes

Types of Seizures

Generalized Seizure

- Usually tonic-clonic
- Sometimes just tonic
- Sometimes just clonic
- Less common types of generalized seizures:
 - Atonic seizures
 - Sudden loss of muscle tone
 - Myoclonic seizures
 - Generalized brief, shock-like contractions
 - Absence seizures – very rare
 - Formerly called “petit mal”

Types of Seizures

**Focal (Partial) Seizure
(2 kinds)**

- Simple focal seizure
 - Consciousness not impaired
- Complex focal seizure
 - Consciousness is altered
 - Unprovoked aggression
 - Canine rage syndrome
 - Aka Episodic dyscontrol
 - Irrational fear
 - Psychic seizure
 - Aka Psychomotor seizure

Types of Seizures

Focal (Partial) Seizure

- Any body part may be involved
- Depends on the seizure focus location in the cerebrum
 - Facial spasms
 - head movements
 - “yes” or “no”
 - Fly biting
 - Repetitive limb movement
 - Licking or chewing a single area
 - Hypersalivation
 - Vomiting, diarrhea, abdominal pain
 - Limbic epilepsy

Types of Seizures

**Focal/Partial seizures can progress
to Generalized Seizures**

- This can be a clue in the history that distinguishes seizure from other episodes of collapse
 - Starts with a twitching limb or turning head
 - Progresses to generalized seizure

Differential Diagnosis

Episodes resembling seizure

- Syncope
- Narcolepsy
- Stereotypic Behavior
- 4 kinds of tremor
- 3 kinds of ataxia
- Rapidly progressive weakness
- Encephalopathy
- Active sleep
- Pain
- Hyperviscosity Syndrome

Differential Diagnosis

Seizure

- Often spontaneous onset
 - Exercise triggers syncope & progressive weakness
 - Excitement triggers narcolepsy
- Usually self limiting

Differential Diagnosis

Seizure

- Often composed of 3 stages
 - 1 - Pre-ictal – 2 parts
 - Prodrome – hours – normal EEG
 - Long term indication
 - Restless, vocalizing
 - Aura – minutes – abnormal EEG
 - Initial sensation of seizure before observable signs
 - Hiding, agitation, seek owner

Differential Diagnosis

Seizure

- Often composed of 3 stages
 - 2 – Ictal – the seizure (ictus)
 - 3 - Post-ictal – minutes to days
 - Transient abnormalities in brain function
 - Disorientation
 - Restlessness
 - Ataxia
 - Blindness
 - Deafness

Differential Diagnosis

Syncope

- Partial or complete loss of consciousness (confusion)
- Short duration (< 1 minute)
- Lack of clonus, but can have tonic like phase
- Lack of post ictal signs
- Often associated with exercise
- How do you tell the difference?
- Confirmed by cardiac work-up

Differential Diagnosis

Narcolepsy

- Flaccid – no tonic phase
- Loss of consciousness
- Precipitated by excitement
 - Most common incitor?
 - Food/eating

Differential Diagnosis

Stereotypic Behavior

- Repetitive bizarre behavior
 - Tail chasing
- Can usually be distracted
- No pre-ictal or post-ictal phase

Differential Diagnosis

Rapidly Progressive weakness

- Myasthenia gravis
- Exercise induced collapse
- Gradually precipitated by vigorous activity
- May recover fully with time
- No loss of consciousness
- May show postural tremors which might be confused with muscle contractions

Differential Diagnosis

Encephalopathy

- No distinct pre-ictal, ictal and post-ictal phases
- Prolonged neurologic signs
 - Disorientation
 - Ataxia
 - Blindness
 - Abnormal behavior
- Cerebral or hepatic
- Encephalopathy leading to seizures can confuse the distinction

Differential Diagnosis

Active Sleep

- Twitching
- Paddling
- Vocalizing
- No post-ictal signs upon waking

Differential Diagnosis

Pain

- Especially neck pain
- Muscle rigidity
- stiffness
- Crying
- Consciousness not impaired

Differential Diagnosis

Hyperviscosity

- Polycythemia
- High triglycerides

Epilepsy

- Recurrent seizures over time
- A syndrome, not a disease

Different from Provoked seizures

- Aka reactive seizures
- Secondary to metabolic or brain disease, at the time of insult
- Can resolve with underlying cause
 - Hypoglycemia
 - Hypocalcemia
 - Toxicity
 - Trauma

Epilepsy

- Idiopathic epilepsy
 - Aka primary epilepsy
 - No identifiable cause
 - Onset young adult
 - Normal between seizures
 - “well dog with seizures”
 - Normal bloodwork and neurologic exam
 - Neuro exam can be abnormal during post-ictal stage
 - Anticonvulsant therapy can also affect neurologic exam

Epilepsy

- Symptomatic epilepsy
 - Aka secondary epilepsy
 - Identifiable cause of seizures over time
 - Intracranial
 - Congenital storage diseases
 - Hydrocephalus
 - Neoplasia
 - Infectious
 - Inflammatory
 - Trauma
 - Vascular/ischemia
 - Extracranial
 - Hepatic encephalopathy
 - Insulinoma

Epilepsy

- Symptomatic epilepsy
 - Suspect if onset < 1 yrs or >5 years
 - Suspect if focal seizures
 - Sudden onset of cluster seizures
 - Intercital abnormalities on bloodwork or neuro exam
 - “sick dog with seizures”

Breed Predispositions

- Fly snapping seizures
 - Cavalier King Charles Spaniel
- Canine Rage Syndrome
 - Springer Spaniel
- Head Movement partial seizure
 - Boxers and Bulldogs – “no”
 - Doberman Pinschers – “yes”
- Exercise induced collapse
 - Labrador Retriever

Breed Predispositions

- Idiopathic epilepsy
 - Beagle, Belgian tervuren, Keeshond, Dachshund, GSD, Labrador retriever, Golden retriever, Collie
- Status epilepticus
 - Labrador retriever
 - Large dogs
- Narcolepsy
 - Rottweiler
- Tail Chasing
 - Bull terrier

Working Up the Seizure Patient

- **Physical Exam**
- **Neurologic Exam**
 - Avoid post-ictal period
 - Impossible to evaluate if groggy due to anticonvulsants

Working Up the Seizure Patient

- **Laboratory Evaluation**
 - CBC, profile (TG, Ca), electrolytes
 - Thyroid panel
 - TSH, T4, freeT4
 - hypoT4 associated with seizures
 - Phenobarbital can suppress thyroid function
 - Bile Acids if indicated
 - Young animals
 - High liver enzymes, low albumin, low BUN, abnormal cholesterol, low glucose
 - Yorkies, Maltese
 - Blood lead if indicated
 - TG/chol if indicated - lipemic

Working Up the Seizure Patient

- **Advanced Diagnostics**
 - CSF tap
 - Prior to antibiotic, antifungal or anti-inflammatory therapy
 - Easy in any practice with gas anesthesia and a spinal needle
 - Referral for CT or MRI
 - Interictal neurologic deficits
 - Focal/partial seizures
 - < 1 year and normal bile acids
 - > 5 years
 - Any cat
- EEG

Seizure Treatment

When to Treat??

- Single seizure not treated unless status epilepticus
- Provoked seizures not usually treated unless prolonged or severe
- Cluster seizures should be treated aggressively
- Epileptic dogs are better controlled long term when treated early
- Seizures that last longer than a minute or two should be treated
- More than one mild seizure every 2 months should be treated

Seizure Treatment

Client Education

- Medications must be given daily, for life
- Explain side effects & drug interactions (handouts)
- Missed dose should be given as soon as remembered, then back on schedule with next dose
- Owner seizure log – date, time, description, duration
- Dose determined over time by blood tests
- Dose may increase or decrease over time
- Drugs will not reach full effect for weeks to months
- Initial side effects often subside with time

Seizure Treatment

Therapeutic Drug Monitoring

- When steady state achieved after initial treatment
- When steady state achieved after changing dose
- Immediately after loading dose
- When seizure control is suboptimal
- Periodic monitoring, for pre-emptive dose changes (q6-12 months)
 - Induction of liver enzyme can increase PB metabolism rate
 - Prevent poor episodes of control
 - Minimize side effects

Seizure Treatment

Therapeutic Drug Monitoring

- Other drugs added (Phenobarbital)
 - Organophosphate pesticides
 - Ketoconazole
 - Other narcotics
 - Phenothiazines
 - Antihistamines
 - Chloramphenicol
 - Corticosteroids
 - Doxycycline
 - Beta blockers
 - Theophylline
 - Metronidazole

Seizure Treatment

Anticonvulsants

- Dogs
 - Monotherapy
 - Phenobarbital
 - Bromide
 - 2nd line drugs
 - Bromide
 - Phenobarbital
 - Gabapentin
 - Zonisamide
 - Levetiracetam (Keppra)
 - 3rd line drugs
 - Clorazepate
 - Felbamate

Seizure Treatment

Anticonvulsants

- Cats
 - Monotherapy
 - phenobarbital
 - Ancillary drugs
 - Diazepam
 - Bromide
 - Not much information on other ancillary drugs

Seizure Treatment

Phenobarbital

- Half life 40-90 hrs
- 5 half lives to steady state
- Steady state in 10-15 days
- Initial dose
 - 1-2 mg/lb PO BID in dogs
 - Lower if liver disease
 - 1 mg/lb PO BiD in cats
- Check levels in 2-3 weeks
 - Don't use SST
 - Goal is 20-40 ug/ml
 - If control suboptimal, push >30
 - Timing with respect to dose doesn't matter 91% of the time

Seizure Treatment

Phenobarbital

- Side effects
 - Induction of liver enzymes
 - Liver toxicity in dogs only
 - Risk greater if TDL > 35 ug/ml
 - Risk greater with other drugs
 - Bile acids q6-12 months to monitor for toxicity
 - If caught early, toxicity is reversible
 - Altered thyroid tests
 - Decreased T4, fT4
 - Increased TSH
 - No clinical hypothyroidism

Seizure Treatment

Phenobarbital

- Side effects
 - PU-PD
 - Polyphagia and weight gain
 - Increased panting
 - Non-regenerative anemia
 - Dermal necrosis

Seizure Treatment

Bromide

- Na or K bromide
 - KBr preferred for heart disease
 - NaBr preferred for Addison's Dz
- Added to phenobarbital when TDL 20-35 ug/ml does not achieve control
- Half life 24 days in dogs
- Steady State 10-16 weeks in dogs
- Initial Dose
 - KBr 20-35 mg/kg PO SID or divided BID
 - NaBr 17-30 mg/kg PO SID or dBID
 - Higher if on diuretics

Seizure Treatment

Bromide

- Half dose for patients with renal failure
- Loading dose for cluster seizures
 - 400-600 mg/kg
 - Divided into 4-10 doses over 1-5 days (divide BID-QID)
 - Hospitalize the patient
 - If obtunded or anisocoria, skip & resume when alert
 - Start initial dose next day

Seizure Treatment

Bromide

- Check level
 - One week after loading
 - 3 & 6 months after maintenance dose
 - Timing of sample unimportant
 - Ideal range 1-3 mg/ml
 - Can push to 4 when control suboptimal and phenobarbital >35
- If adequate control, phenobarbital can be reduced and eliminated over 4 months when Br > 1.5 mg/ml

Seizure Treatment

Bromide

- Side effects
 - Reversible pneumonitis in cats
 - Way high serum Cl results
 - Dose dependent, resolve with time
 - Rear limb stiffness and ataxia
 - Sedation
 - GI irritation
 - Vomiting, esophagitis, constipation
 - Capsules can help
 - Follow capsules with water
 - Give with food
 - Try NaBr

Seizure Treatment

Bromide

- Side effects
 - Skin rash
 - PU-PD
 - Polyphagia and weight gain
 - Pancreatitis
 - Caution if Hx of pancreatitis
 - Caution in dogs with high TG

Warn owners of side effects that will resolve within a month

Seizure Treatment

Levetiracetam (Keppra)

- Half life 4 hours in the dog
 - Despite the short half life, antiseizure effects persist after serum levels fall off
- Initial dose 20 mg/kg PO TID
- Side effects uncommon
- \$\$\$\$\$

Seizure Treatment

Gabapentin

- Half life 3-4 hours in the dog
- Initial dose 100-300 mg TID
 - Increase every 1-2 weeks until control
 - Up to 1200 mg TID
 - Reduce dose if renal disease
- Or 25-60 mg/kg divided TID-QID
- Do not give within 2 hours of antacids
- Side effects uncommon
 - Little sedation
 - Opiates increase effectiveness and side effects
 - False positive proteinuria on dipstick
- \$\$\$\$\$

Seizure Treatment

Zonisamide

- Half life 15 hours in the dog
- Initial dose 10 mg/kg PO BID
- Therapeutic range for people
 - 10-40 mg/L
- Side effects uncommon in people
 - Drowsiness
 - Ataxia
 - GI upset
 - Known teratogen in dogs
 - Allergy – a sulfonamide
- \$\$\$\$\$

Seizure Treatment

Felbamate

- Half life 5-14 hours in the dog
- Initial dose 15 mg/kg BID-TID
 - Increase every 2 weeks until control
 - Up to 70 mg/kg TID
 - May need to increase with time due to hepatic enzyme induction
- Steady state in 4-6 days
- TDL 15-100 mcg/ml
- Side effects uncommon
 - Little sedation
 - Nervousness at high doses
 - Hepatotoxicity esp. with phenobarbital
- \$\$\$\$\$

Seizure Treatment

Clorazepate

- Can add to phenobarbital and/or bromide in dogs
- Initial dose 0.5-1 mg/kg PO TID
 - SR available but still given TID
- Serum levels often decrease over time
 - Dose increases often necessary
 - Ineffectiveness due to tolerance can occur
- Do not give within 2 hours of antacids

Seizure Treatment

Clorazepate

- Side effects
 - Sedation and ataxia
 - Can increase phenobarbital levels
 - Monitor levels closely
 - Monitor for side effects
 - Enhances effects of narcotics
 - Exacerbates open angle glaucoma
 - liver dz
 - exacerbates fear induced aggression
- \$\$\$\$\$

Seizure Treatment

Monitoring

- CBC, profile, electrolytes q 6-12 months
 - Liver enzymes will be high if on phenoarbital
 - Does not indicate toxicity
- TDL q 6-12 months
- Bile acids q 6-12 months
 - Phenobarbital
 - Felbamate
 - Wean off these drugs if bile acids begin to increase
 - Decrease by 25% each month for 4 months

Seizure Treatment

Drugs not indicated

- **Primidone**
 - Efficacy similar to phenobarbital
 - Greater risk of liver disease
 - No reason to use it in dogs
 - Toxic to cats
- **Short elimination half life**
 - Phenytoin (Dilantin)
 - Carbamazepine (Tegretol)
 - Valproic acid
 - ethosuximide

The Refractory Patient

1. **Repeat TDM for phenobarbital and bromide**
 - Phenobarbital 30-35 ug/ml
 - Bromide 2-4 mg/ml
 - This monitors compliance
2. **Repeat the work-up for underlying cause**
 - Neurologic exam
 - CBC, profile, electrolytes, UA
 - Thyroid panel
 - Bile acids, TG, blood lead if indicated

The Refractory Patient

3. **Consider other causes of episodes of collapse**
 - Syncope, narcolepsy, behavior, tremor, ataxia, weakness, encephalopathy, active sleep, pain, hyperviscosity
4. **Add 2nd or 3rd line drugs**
 - Keppra, gabapentin, zonisamide
 - Clorazepate, felbamate
5. **Advanced Diagnostics – do or repeat**
 - CSF tap
 - Chest x-rays, abdominal US
 - Refer for CT or MRI if possible
6. **Refer for experimental therapies**
 - Vagal stimulator placement

Seizure Treatment

Emergency Treatment

- **Status epilepticus**
 - Continuous seizure lasting > 5 min
 - Multiple discrete seizures without full recovery between
 - Seizure >30 min is deadly
 - Hypoxia, hyperthermia
- **Cluster seizures**
 - Aka serial seizures, acute repetitive seizures
 - More than 3 seizures in 24 hours

Seizure Treatment

Emergency Treatment

Emergency Anticonvulsants

- **Diazepam**
- **Phenobarbital**
- **Propofol**
- **Pentobarbital**
- **Boluses or CRI**

Seizure Treatment

Diazepam (5 mg/ml)

- **Half life**
 - 2-4 hours in dogs
 - Long enough for maintenance in cats
 - But can cause hepatic necrosis in cats
- **Boluses IV or per rectum**
 - 0.5-1 mg/kg IV (1-2cc per 20 lbs)
 - Up to 3 boluses
 - Owners can do per rectum at home
- **CRI if boluses not effective**
 - 0.5-2 mg/kg/hr in D5W or 0.9% NaCl
 - Put 150 ml fluids in the Buretrol
 - Add 7.5-30cc diazepam to the Buretrol
 - Administer at 1 ml/lb/hr

Seizure Treatment

IV Phenobarbital (65 mg/ml)

- 1-3 mg/lb IV bolus
 - Up to 15-20 minutes for full effect
 - Usually causes ataxia
- CRI if bolus not effective
 - 2-4 mg/kg/hr in D5W or 0.9% NaCl
 - Monitor for cardiopulmonary depression

Seizure Treatment

Propofol (10 mg/ml)

- 1-2 mg/kg (1-2cc per 20 lbs) IV bolus
 - Intubate if needed
 - Assist ventilation if apneic
- Anti-seizure CRI if bolus not effective
 - 0.1-0.6 mg/kg/hr in D5W or 0.9% NaCl
- Anesthesia CRI if above not effective
 - Up to 6 mg/kg IV (<3 cc per 10 lb) to effect
 - The CRI 6 mg/kg/hr
 - Monitor for cardiopulmonary depression

Seizure Treatment

Pentobarbital (50 mg/ml)

- 2-15 mg/kg (3.3 cc per 10 lbs) IV bolus
 - Give slowly over several minutes to effect
 - Intubate
- CRI if bolus not effective
 - 0.5-4 mg/kg/hr in D5W or 0.9% NaCl
 - Monitor carefully for cardiopulmonary depression
 - Dysphoria and paddling is common
 - Difficult to distinguish from seizure

Emergency Seizure Protocol

1. Stop the Seizure
2. Provide supportive care
3. Initiate diagnostics
4. Prevent further seizures
5. Treat further seizures
6. If anesthetized, monitor and recover from anesthesia after controlled

Emergency Seizure Protocol

(Handout)

1. Stop the Seizure

- Up to 3 diazepam boluses
 - This will last up to 30 minutes
- If no effect, phenobarbital bolus
- If no effect, propofol low dose bolus
- If no effect, induce anesthesia
 - Isoflurane
 - Propofol CRI
 - Pentobarbital bolus or CRI

Emergency Seizure Protocol

2. Provide Supportive Care

- oxygen
 - By face mask if conscious
 - By tube if intubated
- IV fluids – place catheter
 - 1 ml/lb per hour for maintenance
 - Less if CHF
 - More if dehydrated or shocky
- Monitor temperature
 - Cool if needed
 - Warm with time (anticonvulsant therapy can drop temp)

Emergency Seizure Protocol

3. Initiate Diagnostics

- Draw blood
 - PCV/total solids
 - Check for lipemia – TG/cholesterol
 - Glucose, calcium
 - If already taking bromide or phenobarbital, drug levels
 - prior to emergency phenobarbital administration if possible
- Get pre-fluid therapy urinalysis

Emergency Seizure Protocol

4. Prevent further seizures

- Start PO phenobarbital 1-3 mg/lb
 - if not already given as a bolus
 - If conscious enough to swallow
 - Can give IM if can't swallow
- If on anticonvulsants, consider starting new drug
 - Bromide can be given rectally if can't swallow
 - May cause transient diarrhea

Emergency Seizure Protocol

5. Treat further seizures

- More boluses if sufficient time has passed
- Anticonvulsant CRI if recent boluses ineffective
 - Diazepam CRI first
 - Then add phenobarbital or low-dose propofol
- If still ineffective, consider anesthetic induction
 - Propofol induction
 - Maintain on isoflurane or propofol CRI
 - Or pentobarbital induction
 - Series of boluses or CRI

Emergency Seizure Protocol

6. Monitor and recover

- temperature
- Pulse oximetry
- Respiratory and heart rate
- Turn every 4 hours if under anesthesia
- Express bladder as needed or catheterize with collection system
- If seizures recur on recovery, repeat the process
- Some patients need to be sedated for 24-48 hours
- Tremors on recovery from propofol anesthesia can be confused with seizures