Seizure Disorders in dogs and Cats

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I. Seizure Definition: Brain disorder characterized by a paroxysmal cerebral dysrhythmia (EEG diagnosis), sudden in onset, which ceases spontaneously, and has tendency to recur. Synonym = convulsion, epilepsy, fit. Seizures arise from abnormal neuronal activity originating in the cerebral cortex. They are nonspecific, sudden event characterized by involuntary muscle tone (tonus) or muscle movement (clonus) or abnormal sensations or behavior lasting seconds to minutes (ictal period)

II. Incidence: approximately 1% (0.1 to 2%, mean 0.82%) of all canine diseases, rare in cats.

III. Any activity that is involuntary, episodic and recurrent should be considered as a possible seizure disorder - i.e.

A. Loss or deranged consciousness

B. Increased or decreased voluntary muscle tone (tonic seizure) or movement (clonic seizure)

C. Visceral muscle activity

D. Episodic altered behavior

IV. Seizure classification - Partial vs. Generalized

A. Partial or Focal Epilepsy

1. Epileptogenic focus originating from a focal area of the cerebral cortex, that does not tend to spread over the cortex.

2. Signs are associated with the location of an irritative focus within the brain. Focal seizures are more common in cats than dogs and may subdivided into simple or complex partial seizures

a. Simple partial seizures are associated with localized motor or sensory abnormalities without a change in consciousness. Focal facial twitching, head turning, or excessive pawing or biting at a body part. Cyclic vomiting, diarrhea, salivation (visceral epilepsy)

b. Complex partial seizures have a significant change in behavior accompanying the focal motor or sensory signs (also termed psychomotor seizures). ”Fly biters, incessant howling, excessively restless.

3. Jacksonian epilepsy (marching fit) begins in one group of muscles and spreads sequentially to others. Stays ipsilateral until one entire side is involved.

B. Generalized Seizures (Grand Mal) Convulsion, non-convulsive (petit mal-very rare, loss of consciousness only).

1. Most common form in dogs and cats

2. No localizing signs

3. Components - aura, ictus, post-ictal phase.

a. Aura - short period when animal senses fit is coming.
Psychic stage - Restless, seek attention, hide, licking, salivating.

b. Ictus - Actual seizure period usually 1-2 min - visceral + somatic motor activity.

1) Animals are unconscious, have dilated pupils, salivate, chewing activity, tonic and/or clonic, or rarely atonic in terms of muscular activity. Visceral signs (defecation and urination) are common.

2) Whether a seizure remains partial, or generalizes, depends on its spread from a focal area to the diencephalon. Once activity

reaches the diencephalon, it spreads to contralateral cortex and generalizes.

3) Cortical UMN activity discharges to entire LMN in brainstem and cord.

c. Post-ictal phase

1) Post seizure period when animal appears abnormal but not seizing. Duration and characteristics highly variable between animals but similar in a given animal.

2) Pacing, hungry, agitated, sleepy, blind.

3) May last few minutes to several days. No correlation with severity of fit.

4. Seizures may be "isolated" single seizure in 24 hrs, "cluster" seizure-2 or more in 24 hrs, or "continuous" in which convulsion lasts 30 minutes or more with no recovery (status epilepticus)

V. Pathogenesis

A. Initiated in small irritative focus, usually cortical areas.

B. Intermittant, spontaneous depolarization --> seizure.

C. Interference with normal sodium/chloride pump mechanisms, imbalance between excitatory (glutamate) and inhibitory (GABA) cerebral control mechanisms.

D. Metabolic diseases interfere with O_2 and glucose availability.

E. Idiopathic epilepsy

1. Genetically predisposed, reduction in seizure threshold.

2. Normal animals require potent stimuli to induce seizures (Electric shock, drugs).

3. Mildly epileptic individuals need less strong stimuli to seize (fatigue, exercise, fever, excitement, photic stimuli, estrus).

4. Very low seizure threshold group - require no obvious stimuli at all, spontaneously seize (idiopathic epileptics).

VI. Etiology

A. Extracranial (Reactive epileptic seizures RES) vs. Intracranial (Primary and Secondary Epileptic Seizures)

B. Extracranial (reactive)-cause for seizure originates outside the cranium
Patients usually normal during interictal phase

1. Hypoglycemia - insulinomas, young puppies, hunting dogs, Addisons, sepsis, hypothyroidism, hepatic failure

2. Hepatic encephalopathy - acquired, congenital

3. Hypocalcemia

4. Hypoxia - cardiovascular disease, pulmonary disease, anemia. Repeated hypoxia can lead to organic lesions.

5. Renal failure

6. Hyperkalemia

7. Hyperlipoproteinemia (Schnauzers)

8. Intestinal parasitim - Possibly associated with hypoglycemia and hypocalcemia.

9. Toxicities - lead, chlorinated hydrocarbons, mercury, hexachlorophene, organophosphates, strychnine

10. Dogs with their first seizure at less than 1 or greater than 5 years of age, have an interictal interval less than 4 weeks, or have a partial seizure as the first observed seizure, carry a high suspicion for non-idiopathic cause for epilepsy being identified.

C. Secondary Intracranial Causes (an identifiable, organic lesion is present)
Patients usually have abnormalities detectable during the interictal period and this suggests organic brain disease exists.

1. Inflammatory: Viral, fungal, protozoal, bacterial, parasitic rikettsial, GME, Distemper is the most common cause of inflammatory seizures in dogs.
2. Neoplastic
    a. Focal signs during interictus common. Some tumors are "silent", except for seizure activity
    b. Signs are usually slowly progressive.
    c. CSF is abnormal. Increased pressure, increased protein, occasionally cellular.
    d. EEG abnormalities seen with cortical lesions.
3. Malformations - Hydrocephalus, occipital dysplasia
4. Trauma - fits may occur acutely or as long as 2 years post trauma. Cerebral scarring.is presumed to be the cause for seizures.
5. Neuronal degeneration - thiamine deficiency in cats
    a. All fish diets high in thiaminase.
    b. Prolonged anorexia
    c. Generalized fits, especially after handling
    d. Rx. 50 mg thiamine per day, 3-4 days, reverses signs.
6. Neurogenic, non-epileptic disorders that may resemble epilepsy
    a. Narcolepsy
    b. Myasthenia
    c. Vestibular disease

D. Primary Epileptic Seizures “Idiopathic epilepsy”

a. Syndrome
b. No known or demonstrable cause identified, likely genetic or genetically influenced in nearly all breeds
c. Exclusion diagnosis
d. Breeds in which a genetic predisposition has been identified: Beagles, Belgian Tervurens, Keeshounds, Dachshunds, British Alsations, German Shepherds, Border Collies, Golden Retrievers.
e. First seizure occurs between 6 mo and 5 years of age.
f. Intermittant seizures at fairly regular intervals (days to weeks to months). No external triggers for seizures have been able to be documented, although owners and veterinarians often associate excitement, fear, and other possible events with seizure activity.
g. Normal during interictus
h. Well controlled by Rx - 2/3 in small breeds,1/3 in large breeds
i. Seizure characteristics
    1) Short aura
    2) Ictus lasts 30 sec to 2 min
    3) Post-ictus - depressed, blind, ataxic, hyperactive, etc.

j. Cause unknown
    1) Genetic predisposition
    2) Genetics determines seizure threshold

k. Seizures often increase in frequency or severity with time ("kindling" effect).

VII. Examination of Seizure Patients

A. Signalment - Age, sex, breed

1. Age = < 6 mo.
    a. Extracranial causes (Reactive epilepsy)
        1) Lead and other intoxications
        2) Hypoglycemia
        3) Hypocalcemia
        4) Hepatic encephalopathy (congenital shunt)
        5) Parasitism
    b. Intracranial causes (Secondary Epilepsy)
        1) Distemper
        2) Toxoplasmosis
        3) Hydrocephalus
        4) Occipital Dysplasia?
        5) Trauma
2. Age = 6 months - 5 years
    a. Intracranial (Secondary Epilepsy)
        1) Neoplasia
        2) Inflammatory - fungal, bacterial, viral
        3) Trauma
        4) Vascular
    b. Intracranial Primary Epilepsy: **Idiopathic (70%)**
    c. Extracranial (Reactive epilepsy)
        1) Toxicity
        2) Metabolic diseases (Hypoglycemia, hypocalcemia, hepatic coma)
        3) Cardiovascular diseases (syncope)
3. Age = >5 yrs
    a. Intracranial (Secondary Epilepsy)
        1) Neoplasia is most important
        2) Inflammatory-rare, GME (granulomatous meningoencephalitis)
        3) Traumatic
        4) Vascular
    b. Extracranial (Reactive Epilepsy)
        1) Toxicity
        2) Metabolic diseases (hypoglycemia, hypocalcemia, liver failure
        3) Cardiovascular (rare)

B. History - Careful history important

1. One of the most important diagnostic aids in seizure disorders.
2. Accurate description of seizure is critical
    a. Localizing signs - focal = organic disease
    b. Prognosis and therapy

c. Seizure characteristics
1) Frequency - static, increasing, decreasing
2) Duration - when started, how long do they last, any change since onset, how many at a time?
3) Behavioral changes
4) Severity - what does animal do?
5) Aura present? Post-ictal characteristics
6) Normal during interictus

3. Past medical history
a. Trauma; birth, later on
b. Infectious diseases (distemper)
c. Non-CNS neoplasms (mammary, hemangiosarcoma)
d. Prior neurological signs unassociated with seizures that have progressed to fits = organic, progressive CNS disease.
e. Known metabolic diseases

VIII. Physical Exam

A. Primary purpose is to determine if seizure is due to intracranial or extracranial disease (cardiac, infectious, hepatic, renal). Most common extracranial causes.
1. Hypoglycemia
2. Hepatoencephalopathy
3. Hypoxia
4. Lead

B. Neurological abnormalities present during interictal period suggest intracranial disease. Focal signs suggest neoplasia, infarct, trauma. Absence of interictal neuro signs occurs in both intra and extracranial causes of seizures. However, most extracranial causes of seizures have few if any interictal neurological signs.

IX. Diagnostic Evaluations

A. Clinical Path: Hematology, Biochemistry,Urinalysis:
1. CBC, UA, BUN, glucose, electrolytes, ALT, SAP, Lead, bile acids?

B. Fundic exam

C. EEG

D. CSF

E. Skull radiographs, CT/MRI

F. Negative findings on the Hx, Px, lab tests = idiopathic epilepsy

X. Therapy

A. Client education
1. What a seizure is
2. What epilepsy is - idiopathic?
3. Control vs. cure
4. Breeding epileptics (NOT)
5. Medical management

B. Principles of therapy
1. Control vs. cure - 2/3 well, 1/3 in giant breeds
2. < number < frequency and/or severity of seizures
3. Treat primary disease if known (tumor, hypoglycemia, infection, etc.)
4. Idiopathic seizure disorders and many organic brain diseases causing seizures are treated similarly in terms of attempts to suppress seizure activity.

5. Start therapy when one or more of the following occurs:
    a. An identifiable structural cause is present
    b. Status epilepticus has occurred
    c. Two or more isolated seizures occur in a 4 to 6 week period (to prevent kindling or a "mirror" focus from developing)
    d. Two or more cluster seizure occur within an 8 week period
    e. The first seizure occurs within 1 week of head trauma

C. Anticonvulsantants: For all anticonvulsants, steady state blood levels will take 3 to 5 half lives to be attained. At that point blood levels of drugs should be measured to be sure you are in the "therapeutic range" for the drug in question. Dosing intervals need to be at least 1/3 of the half-life to maintain reasonable blood levels and not have wide fluctuations throughout the day, i.e., phenobarbital at t ½ @ 37 hrs = dose approximately every 12.33 hrs (BID).

1. Phenobarbital-First drug of choice for single therapy (t ½ = 37-73 hrs)
    a. Depresses seizure initiation (elevates threshold-hyperpolarization)
    b. Rapid onset of action, effective for status epilipticus
    c. Good for cats
    d. Primary side effect = PU/PD, sedation, and ataxia, rare hyperactivity is observed. Hepatotoxicity may occur in 5 to 20%.
    e. **2.5** to 6 mg/kg **BID** to TID-dogs, 3 to 5 mg/kg/day, divided BID for cats. 1/8, 1/4, 1/2 gr tabs (1 gr = 65 mg), elixir = 4 mg/ml
    f. May be increased to 10 to 15 mg/kg/day and rarely, 20 mg/kg to control seizures in some dogs. **Liver toxicity** may develop at these higher dosages characterized by > ALT and ALP, rare jaundice and ascites. Monitor biochemistry @ 6 mo intervals. Serum concentrations of pheno > 35 to 40 μg/ml seem to be associated with increased risk of hepatic failure.
    g. Controlled drug
    h. Therapeutic Serum concentrations = 15-35 μ/ml, in dogs and 10 to 30 μ/ml in cats are attained after 2 to 3 weeks of therapy.
2. Primidone (mylepsin) 50 mg or 250 mg tabs (rarely used today)
    a. 25% metab to phenobarb, most of its therapeutic effects are due to phenobarbital activity.
    b. Toxic to cats(heavy sedation), hepatotoxic in some dogs, chronic inflammation, and cirrhosis after long-term administration. If toxicity to primidone occurs, may switch to phenobarbital. **5 mg of primidone = 1 mg phenobarbital.**
    c. Side effects (sedation, ataxia, PU, PD, PP, aggression, rare hypocalcemia, macrocytic anemia, hepatotoxicity is more common than with phenobarbital)
    d. Dose - **15** to 30 mg/kg TID, initially, up to a maximum of 50 to 70 mg/kg. Side effects may cause owner non-compliance.
    e. Blood levels continue to increase for at least 30 days
3. Phenytoin (Dilantin-DPH)-**Poor choice** for dogs or cats
    a. Inhibits seizure spread
    b. 10-55 mg/kg TID -QID usual starting dosage range
    c. Side effects minimal, ataxia, PU, PD, polyphagia, hepatic enzyme changes (alk phos)

d. 4-10 days for CSF concentration to peak and therefore have anti-seizure activity

e. Blood levels can be measured, 10-15 micrograms/ml

f. Minimal toxicity, also **least effective** antiepileptic drug (< 2% improve on phenytoin alone).

g.Available as 30, 100, 250 mg capsules and pediatric elixir (30 mg/5 ml)

h.**Toxic to cats at high dosages.** 1 to 2 mg/kg/SID may be tried in refractory feline seizures; usually combined with diazepam phenobarbital.

4. DPH + phenobarb - 1/4 + 1/2 gr pheno added to 100 mg cap DPH. Not controlled.

5. Diazepam - Valium

a. Usually restricted to status epilepticus, or acute seizure control in dogs, but is a **good first choice drug in cats**.

b. Sedation variable

c. Rapid effect, brief control

d. Dose 1-4 mg/kg divided qid/os. IV = **5**-30 mg bolus

e. May be used in combination with other drugs 5 & 10 mg tabs

f. In cats, 0.5 to 1.0 mg/kg, divided BID to TID

6. Glucocorticoids

a. Primary use is in status epilepticus where organic brain injury is suspected. Dexamethazone is usually used. Dosage = 0.25 mg/kg TID for 2 to 3 days

b. Used in suspected cases of primary neoplasia which are associated with seizures. Often use prednisone long-term, starting at 2.2 mg/kg/ day, decreasing by 50% at 2 week intervals. Lowest dosage that controls signs is indicated. Most dogs will be maintained on low dosages of alternate day prednisone to prevent clinical signs from reappearing.

c. For dogs with seizures secondary to hydrocephalus. Begin on 0.25 mg/kg of dexamethazone TID and decrease slowly as signs resolve. Some dogs must remain on low dosages of dexamethozone to controls signs.

D. Experimental/non-approved drugs - reserve for problem cases

1. **Potassium bromide-best second choice drug.** Some use it as first line drug

a. Decreased seizure frequency by 58% in dogs refractory to phenobarbital or primidone. Most effective in dogs with generalized tonic-clonic seizures

b. Dosage: 30 to 40 mg/kg orally once daily with food, when combined with phenobarbital, or twice daily if given alone

c. Side effects = sedation

d. Effective serum level: 0.5 to 1.5 mg/ml, in older animals, young animals may tolerate 2.0-3 mg/ml serum concentrations

e. Usually combined with phenobarbital. No pharmaceutical grade currently available. Buy reagent grade chemical from chemical suppliers and put in capsules or dissolve in water at 250 mg/ml. We order from Spectrum Chemical Supply, 14422 S. San Pedro St., Gardena, CA 90248 (1-800-7228786). 500g = $14.75, 2.5 kg = $49.50

f. Long half-life between 16 to 25 **days**. May take 4 to 6 weeks to reach steady state.

g. Can give loading dosages to rapidly attain therapeutic levels. Some use 400 to 600 mg/kg/os in water, divided into **5** doses and administered over **5 days** to rapidly attain serum concentrations. May have powerful sedative effect and/or induce vomiting if too much given at one time. As an emergency control for status epilepticus, can give 100 mg/kg q 4 hrs per rectum with red rubber catheter to a total dosage of 600 mg/kg. Check serum levels at 2 days, 1 month and 4 months.

h. High salt intake decreases serum concentrations (chloride intake augments renal excretion).

2. Felbamate (Felbatol) - Newly released for humans, T ½ = 5-8 hrs!. Some efficacy in dogs with complex partial and generalized seizures. Proposed to inhibit glutamate binding. No controlled studies. 20 mg/kg PO TID initially, up to 100 mg/kg TID. Aplastic anemia and liver toxicity noted in some human patients. Monitor CBC and liver enzymes z6 to 12 weeks.
3. Chlorazepate dipotassium (Tranxene)
    a. Metabolized quickly to nordiazepam, may be valuable as adjunctive therapy, t ½ = 4-6 hrs. Do not develop resistance to anti-seizure activity as with diazepam and clonazepam. May increase serum phenobarbital levels and lead to sedation (monitor pheno at 2 and 4 weeks)
    b. Dosage: 2 mg/kg/PO BID or 0.5-1 mg/kg/PO TID.
    c. Side effects = sedation
    d. Effective serum level = unknown, can measure nordiazepam in blood at 10d, 30 d, and 6 mo.
    e. Long term effects and efficacy = unknown, severe seizures resulted following abrupt drug withdrawal in experimental studies in dogs
4. Gabapentin (Neurotonin): Approved for complex partial seziures in people, t ½ = 3 hrs!.
    a. No confirmed evidence for success in dogs with refractory seizures. Used for partial and generalized seizures. May mimic GABA in the CNS or block glutamate production?. Renally excreted, no measurable metabolites. Few adverse effects except sedation.
    b. 100 to 300 mg/patient PO TID up to 1200 mg/patient TID over 4 weeks
5. Clonazepam (Klonopin)
    a. Long acting benzodiazepine, rapid development of tolerance within weeks of initiation of therapy
    b. Dosage: 0.06-0.2 mg/kg divided TID to QID with phenobarbital, or 0.5 mg/kg BID to TID if given alone
    c. Side effects = sedation
    d. Effective serum level: 0.02-0.08 microgram/ml
6. Mephenytoin
    a. Primary metabolite is nirvanol, may be effective in dogs refractory to phenobarbital or KBr.
    b. Dosage = 10 mg/kg TID

c. Increase dosage to attain serum concentrations of 25 to 40 micrograms/ml. Steady state in 6 days.

d. Side effects = sedation, bone marrow toxicity is common in humans

7. Paramethadion (Paradone)
   a. Licensed for petit mal seizures - man
   b. Dose = 30-50 mg/kg/day divided TID
   c. Some success in large dogs refractory to other therapy, generally half-life is too short to be useful in dogs or cats.
8. Valproate (Depakene) - released - 1978 for petit mal seizures
   a. Dose = 15-200 mg/kg/day divided TID (start at 25 mg/kg)
   b. Hepatotoxicity is a potential problem-monitor patients
   c. Blood levels 500-100 micrograms/ml (man)
   d. Very short half-life, little chance of success
8. Carbamazepine (Tegretol)
   a. Dose 4-10 mg/kg/day divided BID or TID - little efficacy in dogs (Parker), very short half-life.

E. Treatment Protocol

1. Allow seizure pattern to develop if possible (<u>frequency</u>, duration, severity)
2. Start with one drug initially **Pheno**, or **Potassium Bromide**, or diazepam (cats).
3. If poor control increase dosage to max, prior to adding 2nd drug, **monitor via serum concentrations** at trough time, i.e., just before the next dose of medication (may not be critical for phenobarbital if given BID).
4. Add second choice drug and increase dose until control seizures or reach max-tolerated levels.
5. Once controlled, may reduce first drug slowly (by 10-20% at 6 <u>month</u>.intervals.
6. Do <u>not</u> stop drugs abruptly when changing medications!
7. Continue first drug for 2 interictal periods to be sure it is or is not effective and that levels are high enough (**measure**).

F. Treatment failures

1. Medication/Dosage Errors
   a. Improper drug choice
   b. Non-compliance of owners (failure to medicate as instructed
   c. Dosages too low, delayed increases, inadequate increase
   d. Intervals between administration too long, leading to fluctuations in drug levels
   e. Stopping one drug too soon while adding a second
   f. Inappropriately combined drugs
2. Drug-Drug Interactions
   a. Anticonvulsants may interfere with metabolism of newly added drugs, > or < serum concentrations.
   b. Non-anticonvulsants may alter metabolism of anticonvulsant drugs:
      (1) antibiotics
      (2) cardiac drugs
      (3) antirheumatics
      (4) antacids
      (5) theophylline

(6) steroids

3. Drugs lowering seizure threshold
    a. **Phenothiazine** tranquilizers (acepromazine, others)
    b. Anthelmintics (piperazine, mebendazole)
    c. **Metoclopramide**
4. Superimposed diseases alter drug metabolism
    a. Gastroenteritis
    b. Pneumonia
    c. Metabolic abnormalities
5. Diagnostic failures
    a. Extranial causes for seizures not identified (hypoglycemia, hypocalcemia, etc.)
    b. Progressive brain disease is present (tumor)

XI. Management of Status Epilepticus

A. Definition: Continuous seizure activity with either no interictal period or very brief periods of rest followed by a seizure (30 minutes or more in duration)

B. Status epilipeticus can lead to death secondary to hyperthermia, hypoxia, acidosis, and circulatory collapse

C. Treatment regimen

1. STOP THE SEIZURE!
    a. Make sure airway is patent
    b. Check blood glucose immediately-if low give 5 to 50 ml of 50% dextrose I.V.
    c. Draw blood for additional lab work, catheterize a vein
2. Diazepam first, Phenobarbital (IV) second, pentobarbital or propofol, or inhalent anesthetics third. May consider I.V. calcium gluconate 2.5 to 10 cc slowly, prior to Valium. Risk is high (will cause hypercalcemia, likelihood of hypocalcemia being present is low.
3. Diazepam (Valium) - 2 to 30 mg IV bolus
    a. Cats - Small dogs 2.5-5 mg
    b. Medium Sized Dogs - 5 to 15 mg
    c. Giant Breeds - 15 to 30 mg
    d. Several injections of Valium may be necessary to arrest seizure activity initially.
    e. A continuous drip of diazepam in 5% dextrose may be useful if boluses do not stop the seizures. Give 2-5 mg/patient/hour up to 0.5 mg/kg/hour as constant infusion. Often, total dosages of 5 to 20 mg/hour will stop all seizure activity.
4. If after the first hour, Valium must be given frequently, 1 or more times per hour, or an IV infusion does not stop the seizures, go to longer acting drugs.
    a. Go to phenobarbital first, 6-24 mg/kg IV total dosage, given in 3 mg/kg boluses every 15 minutes to effect. Loading dose to achieve serum concentration of 25 μg/ml is : Total mg to give IV = (Body wt kg) x (0.8L/kg) x (25 μg/ml). For 20 kg dog x 0.8L/kg = 16 x 25 μg/ml = 400 mg phenobarbital = 20 mg/kg
    b. Wait 15 min after IV phenobarb for maximal effect. If still seizing, repeat initial dose.

c. If bolus phenobarbital fails, you can also administer this drug as a slow constant infusion. It can be administered with constant rate diazepam, and the two drugs may work better together than either one alone. Be careful of hypotension when you use these agents concurrently

d. Administer at a rate of 3 to 6 mg/hour IV, continue the drip until seizures are controlled or the dog is heavily sedated.

5. After phenobarb, if dog still seizes, give pentobarbital, propofol, or inhalents

a. Pentobarbital - 3 to 15 mg/kg IV to effect

b. Use only after Valium and phenobarbital fail to control repetitive seizures.

c. Give slowly IV, to effect

d. Goal is heavy sedation, not surgical planes of anesthesia.

e. Will usually provide 4 to 8 hrs of seizure free time.

e. Be cautious of over medicating. Suppress overt grand mal activity. Want dogs semi-conscious if possible. Anesthesia recovery closely resembles mild seizure activity.

6. Convert dog to oral medication as soon as possible (usually 12-24 hrs) and use rapidly acting drugs. Phenobarb should be given IM if dog not able to tolerate oral medication, or use KBr rectally vie enema catheter

7. Reverse hyperthermia - Ice baths, be cautious of centrally acting hypothermic drugs (Novin)

D. Begin diagnostic work-up

X. Management of Cluster Seizures at Home

A. Rectal diazepam can halt cluster seizures in patients known to have this problem. It may prevent them from recurrent long hospitalizations.

1. Dispense injectable diazepam for emergency use only.

2. Have the owners administer **0.5** to 1 mg/kg via syringe and a teat canula intrarectally at the first seizure if not on phenobarbital or, 2 mg/kg intrarectally if receiving phenobarbital. Some are using diazepam intranasally at 0.5 mg/kg, half in each nostril (watch for biting). Give a second dosage if a second seizure occurs and a third dosage if a third seizure occurs within 24 hours. If the dog seizures a fourth time, seek veterinary assistance. Do not administer the drug if the dog is excessively sedated, has signs of respiratory depression or any rectal bleeding is noted.

3. Owners must keep the valium secure and keep careful records of its administration.

DRUG PROTOCOL FOR MANAGEMENT OF IDIOPATHIC EPILEPSY IN THE CANINE AND FELINE

I. Patients Currently Receiving No Drugs

A. Start initially on oral phenobarbital

1. Dogs - **2.5**-6 mg/kg, BID
2. Cats - 1 mg/kg, BID
3. Monitor serum phenobarbital concentrations after 14 to 21 days, just befor next dose .
    a. Therapeutic concentrations = 15 to 35 μ/ml
    b. Sample patients after 2-3 wks, 3 months, 6 months, and at 6 month intervals thereafter.
    c. Serum concentrations > 35 micrograms/ml are associated with depression, ataxia, liver disease.

B. If seizures are not controlled after increasing phenobarbital to maximal tolerated concentrations, **add potassium bromide** to the phenobarbital.

1. Dogs - 30 to 40 mg/kg/day, SID. Dosage should start at lower end of recommended range when added to phenobarbital. May have to decrease phenobarbital to reduce toxic side effects (sedation).
2. Cats - No doses established, toxicity = unknown.
3. If seizures are controlled, may slowly decrease phenobarbital dosage by 10-20%/6 mo., until drug is eliminated or seizures recur.
4. Chlorazepate dipotassium (Tranxene)
    a. Metabolized quickly to nordiazepam, may be valuable as adjunctive therapy.
    b. Dosage: 2 mg/kg/PO BID
    c. Side effects = sedation
    d. Effective serum level = unknown
    e. Long term effects and efficacy = unknown
5. If seizures recur as dosages are dropped, go back to last dose of phenobarbital that suppressed seizures.

C. Alternatives when others fail. Unlikely to help significantly?

1. Clonazepam (Klonopin)-If pheno and KBr fail. Dosage: 0.06-0.2 mg/kg/divided TID or QID with phenobarbital, or 1.5 mg/kg divided TID as single drug
2. Felbamate (Felbatol) - Newly released for humans, T ½ = 5-8 hrs!. Some efficacy in dogs with complex partial and generalized seizures. Proposed to inhibit glutamate binding. No controlled studies. 20 mg/kg PO TID initially, up to 100 mg/kg TID. Aplastic anemia and liver toxicity noted in some human patients. Monitor CBC and liver enzymes q 6 to 12 weeks.
3. Chlorazepate dipotassium (Tranxene)-alternative if other drugs fail
    a. Dosage: 2 mg/kg TID
4. Mephenytoin-Alternative if other drugs fail
    a. Dosage: 10 mg/kg TID
5. Valium - Primary use in status epilepticus or feline epilepsy. Also combination drug therapy.
    a. Dogs - 1 to 4 mg/kg/day, divided QID

b. Cats - 1 to 2 mg/cat TID

6. Gabapentin (Neurontin): Most often combined with other antiepileptic drugs 100 to 300 mg/patient PO TID up to 1200 mg/patient TID over 4 weeks for partial or generalized seizures in humans. No dog data as yet.

II. Drugs with Minimal chance of therapeutic success

A. Phenytoin (Dilantin-Parke-Davis)
   1. Dogs - 10 to 55 mg/kg/QID - Erratic absorption, very short half-life.
   2. Cats 1-2 mg/kg/SID, may cause liver failure.
   3. Monitor serum concentrations 7 days after initiating therapy. Sample 4 hrs post administration.
   4. Effective, antiseizure concentration = > 10 micrograms/ml

B. Paramethadione (Paradione)
   1. Dogs - 30 to 50 mg/kg/day, divided TID

C. Valproic acid (Depakene)
   1. 15 to 200 mg/kg/day, divided TID (start at 25 mg/kg)

D. Carbamazepine (Tegretol)
   1. 4-10 mg/kg/day divided BID to TID

SEIZURE INFORMATION SHEET FOR CLIENTS

Your dog has been diagnosed as having a seizure disorder or epilepsy. Seizures, sometimes called convulsions or "fits", can result from many different causes, but are usually manifested by abnormal body movements, loss or disturbance of consciousness, abnormal behavior, involuntary urination or defecation.

While there can be many causes of seizures in dogs, most often treatment will consist of giving medication to help prevent seizures from occurring or to decrease their frequency or severity. It must be stressed that the medications used for the treatment of seizure disorders will not cure seizures, but hopefully will control them. Most dogs will require drug therapy for their entire lives.

The success of the treatment for your dog will depend a great deal upon you. While drugs can control seizures in most dogs, drug therapy will be ineffective if the medication is not given regularly. The importance of developing the habit of routinely medicating your dog cannot be emphasized enough. Occasionally it may be necessary to adjust the dosage of your dog's medication and unless it has been given regularly, it will be very difficult to determine the "correct" dosage. Should you have trouble remembering to give the drug consistantly, the following hints may be helpful. Give the dose at the same time(s) each day. For example, give the morning dose at the same time as the morning "walk" or the evening dose along with the evening feeding, etc. The use of a calendar can also be helpful in remembering whether a dose has been given or not and also it can be used to document any seizures or medication side effects (sedation, lethargy, increased drinking, eating, and urinating) that may occur.

Should your dog have a seizure, the best thing to do is to leave him or her alone. Don't try to restrain the animal during a seizure, as you or the dog may be injured. Keep the dog on the floor or ground and keep away from your pet until the seizure is over. Usually the seizure will last only a minute or so, but if the seizure is prolonged, call the Small Animal Clinic at 625-1919 or, if after hours, call 625-9711.

Should you have any questions about your dog's therapy or this informational sheet, be sure to ask the attending clinician for help.

Seizures in Cats

(See Parent, JM and Quesnel, A: Vet Clin N Amer 26:811, 1996)

Seizures in cats are less frequent and more often due to organic disease of the brain than in dogs, i.e., idiopathic epilepsy is much less common in cats than in dogs as a cause for seizures. The most common type of seizure seen in cats is a complex partial seizure, not a generalized grand mal type as is typical for dogs.

Generalized motor seizures in cats are infrequently seen but tend to be more violent than in dogs. They are non-localizing , generally last from 30 sec to 120 sec. They may throw themselves around a room, develop contusions, bite their tongue and rip off their claws during a violent grand mal convulsion. Severe piloerection is common. Varying periods of post-ictal activity (from hyperactive to sleepy) occur in cats as in dogs and can last from minutes to hours.

Mild generalized motor seizures (non-convulsive) are characterized by decreased awareness, bilaterally symmetrical mild motor activity without recumbency, and have a duration of a few seconds. They may stop activity and sit motionless for a few seconds. Pupillary dilitation, and bilateral facial twitching are common. They may shake their head, joints or body.

Partial seizures are more common in cats and have lateralizing signs preceeding or during the ictus. They may be simple or complex. Partial simple seizures are characterized by normal mentation but lateralized motor activity of a part of the body or the whole body. Partial complex seizures, however, have altered consciousness plus lateralizing signs with or without stereotypical behavioral or motor activities. Cats may exhibit a glazed look and be poorly responsive to commands. Motor signs are associated with unilateral facial twitching which may involve one ear, one eyelid or the whiskers, turning of the head to the side, or movements of the fore or rear limbs on the same side of the body. Owners may feel the cat is hallucinating because they hiss, growl, lick or smack their lips and attack imaginary or real objects, startle for no obvious reason, and run frantically. They may blindly collide with objects. Compulsive behaviors such as circling, self-chewing, and biting are also occasionally seen. They are differentiated from obsessive-compulsive disorders by the coexisting motor activity or progression of signs to a generalized convulsion.

Status epilepticus occurs in cats but is more often non-generalized partial or mild generalized (non-convulsive) in type and may not be recognized as status epilepticus by owners or veterinarians.

Idiopathic epilepsy is rare in cats compared to organic causes for seizures. Inflammatory infectious causes in cats include: Toxoplasmosis, FIP, FeLV, crypttococcosis, and presumed viral meningoencephalitis. However, if seizures occur and the cat has a normal physical and neurological exam, only FIP or viral meningoencephalitis should still be on your differential list.

The most common proposed cause for seizures in a large series of cases was meningoencephalitis of unknown origin (47%). The cause was presumed to be an unidentified virus. Cats generally had a good prognosis with therapy. The second most common cause was feline cerebral infarction (substantiated on MRI). These cats did not have the typical severe, peracute lateralized cerebral cortical dysfunction as was originally reported for this disease. Most of these cats also responded well, in general, to phenobarbital therapy.

The diagnostic approach involves a thorough history and physical exam (including a neurological evaluation). In addition, a CBC, chemistry profile (usually normal), fundic exam, CSF and advanced imaging (CT or MRI) may be indicated. CSF findings for cats with ischemic encephalopathy tend to have mild increases in protein <200 mg/dl) and total WBC of <10, with an increased percent of lymphocytes. Cats with CNS FIP have total protein concentrations of > 200 mg/dl, and total WBC of >100 (primarily neutrophils). They also generally have multifocal neurological abnormalities. In suspected viral disease (non-FIP), the total protein in CSF was < 100 mg/dl and total WBC <50. Cats tended to be less than 4 years old and had focal neurological signs.

Therapeutic approaches to cats involves trying to identify a cause and treat it specifically, if possible. While a diagnosis is being established therapy may be instituted to decrease the severity, frequency and number of seizures. Generally, therapy is indicated for cats that seizure more than once every 6 to 8 weeks, those that cluster seizure, or cats that have a single episode of status epilepticus.

Phenobarbital is the drug of choice for chronic therapy of feline epilepsy. Serum trough levels optimally should be between 23 and 30 μg/ml. Sedation and ataxia are common when serum levels exceed 32 μg/ml. Generally cats are administered 3 to 5 mg/kg/day in divided dosages (BID). Others recommend a starting dosage of 7.5 mg BID. Serum trough levels are measured at 10 to 14 days and dosages adjusted accordingly. Some cats require 15 mg BID to attain therapeutic concentrations. Sedation and ataxia are common during the initial phase of therapy. Cats generally adapt after a week or two to the medication. Polyphagia and weight gain are common, as is seen in dogs on phenobarbital. No hepatotoxicity has been documented, but no long-term studies are available. Isolated observations of possible adverse reactions include facial pruritis, thrombocytopenia and neutropenia with swelling of the feet.

Diazepam is a second choice drug for long-term control of cats with seizure disorders. Starting dosages of 0.5 to 1 mg/kg divided BID or TID are used. Gradually work up to these dosages to reduce the sedation associated with initial administration of diazepam. Acute hepatic necrosis associated with an idiosyncratic toxicity to diazepam has been reported in cats. It is generally fatal. If any pre-existing liver disease is present this drug should not be given. In addition, it is recommended to obtain a biochemical profile within 5 days of initiating therapy to monitor for elevated hepatic enzymes. If an increase from pre-treatment values is seen, diazepam should be stopped immediately.

Status epilepticus in cats is treated initially with intravenous diazepam at 0.5 to 1 mg. You must stop generalized motor activity in grand mal convulsions and stop or

significantly decrease abnormal neurological activity in cats with non-convulsive status epilepticus. A second dose of diazepam should follow the first if seizures are not stopped in 5 to 10 minutes. The bolus therapy is followed by a constant rate infusion of diazepam at 0.5 mg/kg/hour added to the cats maintenance fluids. Once seizures have been controlled for 6 hours the animal is weaned off the drug for a duration equal to the time it took to control the seizures. Some cats need intensive monitoring and IV infusions of diazepam for 2 to 4 days.

Phenobarbital can be added to the diazepam at a dosage of 0.5 to 1 mg/kg/hour. Heavy sedation is often required to stop the seizures. Oral anticonvulsants (phenobarbital) is started as soon as the cat can swallow, or is given intramuscularly if the animal cannot swallow.

The prognosis for cats with seizures is directly related to the underlying cause. For those with FIP or neoplasia, the prognosis is grave. It appears that FeLV, FIV and Toxoplasmosis are relatively rare causes for feline seizures. Idiopathic epilepsy also is a very rare syndrome in the cat. Other causes for seizures may respond well to anticonvulsant therapy but be difficult to stabilize if status epilepticus occurs. However, the prognosis for cats with viral meningoencephalitis or ischemic encephalopathy is unpredictable. If status epilepticus can be managed, many of these cats can ultimately be released on medication and live good quality lives.