

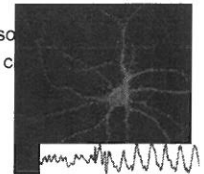
BS, VTS (Neurology)  
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f Veterinary Medicine

- Most common neurological disorder seen in small animal practice.
- Reported incidence - 2.3% of all dogs and 1% of all cats evaluated at veterinary referral hospitals.
- Reported incidence in general population of dogs - 0.5% - 5.7%



- It is estimated that epilepsy affects approximately 5% of the canine population as a whole-in 2014 there were 43,346,000 dogs in the US-approx. 2 million affected
- Epilepsy presents huge challenges to veterinary medical profession, pet owners, patients-and is also an increasing One Medicine topic of discussion
- Enhanced support through research, education, outreach
- Focus of the session will be to discuss
  - Causes
  - Therapies
  - Patient and Client Support

- Clinical manifestation of abnormal, increased neuronal excitability and synchronization
- Transient, paroxysmal disturbance in brain function
  - Sudden onset
  - Spontaneous resolution
- Characteristic EEG changes

[illegible]

- Cerebral cortex
  - Sensory perception
  - Behavior / mentation
- Thalamus
  - Relay center

### Seizure Terminology

- Epilepsy - recurring seizures due to an intracranial cause
- Cluster seizures - > 2 seizures per 24 hours
- Status epilepticus - repeated seizure activity without an intermission
  - continuous seizure activity lasting > 5 minutes
  - 2 or more seizures with incomplete recovery between seizures

### Signs of Forebrain Disease

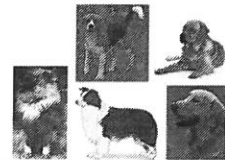
- Altered mentation/behavioral change
- Seizures
- Postural reaction deficits
- Facial hypoesthesia
- Menace deficits
- Circling (tendency) - Ipsilateral
- Relatively normal gait

### Seizure Manifestations

- Prodrome
  - Behavior changes preceding seizure onset
- Ictus - period of seizure activity
  - Alterations of consciousness, behavioral changes, motor activity, autonomic discharge
- Postictal Period
  - Disorientation, behavior changes, ataxia, blindness that can follow seizure activity

### Idiopathic (Genetic) Epilepsy

- No underlying cause other than a presumed genetic predisposition
- Absence of structural brain disease, defect at cellular level
  - Neurologically normal between seizures
- Onset 1-5 years of age



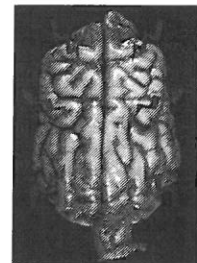
### Differential Diagnosis

- Syncope
- Acute vestibular dysfunction
  - Transient ischemic attack
- Narcolepsy / cataplexy
- REM behavior disorder
- Behavioral disorders
- Movement disorders
  - Idiopathic head tremors



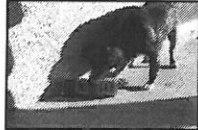
### Generalized Seizure

- Convulsive (tonic-clonic) most common
- Non-convulsive (rare)
- Symmetric signs
  - Motor
- Loss of consciousness
- +/- autonomic signs



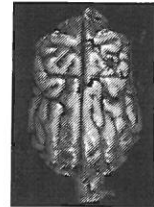
### Reactive Seizures

- Seizures due to extracranial disease
  - Metabolic
  - Toxic
- Not due to intracranial disease – not epilepsy



### Focal Seizure

- Manifestation of localized area of neuronal dysfunction
- Often associated with symptomatic epilepsy
- Can secondarily generalize



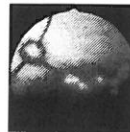
### Cryptogenic Epilepsy

- Suspected to be symptomatic (probable symptomatic epilepsy)
  - Age of onset
  - Presence of neurological deficits
- Nature of underlying cause is as yet unknown



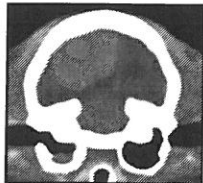
### Physical Findings

- General physical exam
  - Cardiorespiratory disease
  - Evidence of systemic disease
  - Ophthalmologic exam
- Complete neurological exam
  - Mentation, behavior
  - Visual deficits
  - Gait deficits



### Symptomatic (Structural) Epilepsy

- Associated with an identified, structural abnormality of the brain
  - Neoplasia
  - Infection/inflammation
  - Trauma
  - Vascular



### Historical Findings

- Description of episode:
  - Seizure versus other episodic event?
  - Focal or generalized
  - Prodromal or postictal signs
- Pertinent historical information:
  - Age of onset of seizures
  - Vaccination history
  - Past history of trauma, neurologic illness
  - Known exposure to toxins

## Cause of Seizures

Extracranial Causes

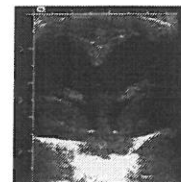
- Metabolic
- Toxic

Intracranial Causes

- Degenerative
- Anomalous
- Neoplastic
- Infectious
- Inflammatory
- Idiopathic
- Trauma
- Vascular

Diagnostic Plan  
< 1 year of age

- Minimum data base
- Serum bile acid tolerance test
- Brain imaging
  - MR, CT
  - Ultrasound
- CSF analysis



## Diagnostic Approach

- Rank likely differential diagnoses based on age, historical data and examination findings.

- < 1 year
- 1-5 years
- > 5 years

Differential Diagnosis  
1-5 years of ageExtracranial

- Metabolic
- Toxic

Intracranial

- **Idiopathic**
- Infectious
- Inflammatory
  - MUE
- Neoplastic
- Trauma
- Vascular

Differential Diagnoses  
< 1 year of ageExtracranial

- Metabolic
  - Liver disease (PSS)
  - Hypoglycemia
- Toxic
  - Lead
  - OPs
  - Others

Intracranial

- Anomalous
  - Hydrocephalus
- Infectious
- Inflammatory
  - Viral (CDV, FIP)
  - Others
- Trauma

Diagnostic Plan  
1-5 years of age

- Minimum data base
- Serum bile acid tolerance test
- Infectious disease testing (if indicated)
- +/- brain imaging
- +/- CSF analysis

### Differential Diagnosis > 5 years of age

#### Extracranial

- Metabolic
  - Liver disease
  - Kidney disease
  - Hypoglycemia
- Toxic

#### Intracranial

- Neoplastic
- Infectious  
Inflammatory
- Vascular
  - Hypertension
  - Infarct / Hemorrhage

### Principles of Treatment

- Treat any identified underlying disease
- Consider antiepileptic therapy when:
  - No specific treatment is possible
  - Diagnosis of idiopathic epilepsy is made
  - As adjunctive, symptomatic therapy

### Diagnostic Plan > 5 years of age

- Minimum data base
- Serum bile acid tolerance level
- Thoracic radiographs
- Blood pressure
- Brain imaging (MR, CT)
- +/- CSF analysis



### General Treatment Recommendations

- Plan on life-long therapy
- Monotherapy is preferred; establish therapeutic levels of drug before adding in a second medication
- Animals can grow refractory to treatment over time - expect dosage adjustments
- Side effects are common



### Diagnostic Approach

- A minimum data base should be performed in every animal, even after a single seizure.
  - CBC
  - Chemistry Profile
  - Urinalysis
  - Bile Acid Tolerance

### When to Initiate Therapy?

- Seizure frequency > 1/month
- Increasing seizure frequency or severity
- Severe postictal signs
- History of clusters or status epilepticus
- Owner preference
- Client education is extremely important when initiating therapy!

### Anticonvulsants: Phenobarbital

- Still first line antiepileptic medication in both dogs and cats
- Acts on inhibitory GABA receptors
- Extensive liver metabolism, induces microsomal enzyme system
  - Drug interactions common



### Zonisamide

- Newer generation human drug (2000)
- Several anticonvulsive properties
  - Blocking of sodium, calcium channels
  - Enhancing GABA
  - Inhibiting glutamate release
- Hepatic metabolism – drug interactions
  - Phenobarbital increases clearance of zonisamide

### Phenobarbital

#### Advantages

- Effective (85%)
- Inexpensive
- Reasonable  $t_{1/2}$  - BID administration
- Serum levels easy to monitor

#### Disadvantages

- Controlled drug
- Side effects
  - PU/PD/polyphagia
  - Sedation
  - Liver toxicity
  - Blood dyscrasias
- Tolerance

### Zonisamide

#### Advantages

- Wide therapeutic index
  - Blood concentrations not routinely performed
- Twice daily administration

#### Disadvantages

- Efficacy unknown
- Metabolized by liver
- Side effects
  - Sedation, ataxia
  - Loss of appetite
  - Hepatotoxicity (rare)
  - Renal tubular acidosis
- Expense - varies

### Phenobarbital: Follow-Up Evaluations

- Serum drug levels 2-3 weeks after initiating treatment or dosage adjustment
  - Timing of sample collection not important in most dogs
- Minimum data base and serum drug levels every 6-12 months while on drug

### Levetiracetam

- Newer generation human drug (1999)
- Unique mechanism of action
  - Modulates neurotransmitter release via binding to presynaptic protein
- No hepatic metabolism, excreted in urine
- Parenteral formulation available

### Levetiracetam

#### Advantages

- Wide therapeutic index
  - Blood concentrations not routinely performed
- Unique mechanism of action
- No liver metabolism

#### Disadvantages

- Efficacy unknown
- Short half life – must be dosed q 8 hours
- Side effects
  - Sedation, ataxia
- Expense - varies

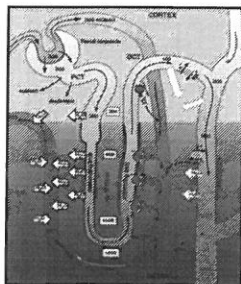
### Bromide in Cats

- Airway disease can occur in up to 40% of cats administered bromide
- Clinical signs – cough, dyspnea
  - Can be fatal if signs severe
- Reversible with drug discontinuation
- Avoid use of bromide in cats!



### Dietary Considerations with Bromide Therapy

- Bromide is excreted by the kidneys
- Competes with chloride for tubular reabsorption



### Potassium Bromide

#### Advantages

- Believed to work synergistically with phenobarbital
- Effective as sole agent (60%)
- No hepatic metabolism
- Once daily administration

#### Disadvantages

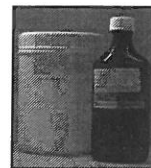
- Not an approved drug
- Long  $t_{1/2}$  (25 days)
- Side effects
  - Sedation, ataxia
  - Polyphagia
  - Vomiting
  - Pancreatitis
  - Bronchitis in cats

### Potassium Bromide Follow-Up Care

- Can give loading dose (400-600 mg/kg) to increase blood levels
- Perform serum levels 3 months after dosage adjustment
- Minimum data base and serum levels every 12 months
  - False elevations of chloride levels common

### Potassium Bromide

- Drug form is not available
  - Chemical grade reagent is compounded
  - Solution, encapsulated, tablets
- Believed to displace chloride at GABA receptor chloride channels
- Not metabolized
  - Excreted unchanged by kidneys



### Home Treatment for Cluster Seizures

#### Rectal Diazepam

- Dose 0.5-1.0 mg/kg PRN
- Must be stored in glass vial until use
  - Inactivated by light, adheres to plastic
- Suppository form available
- Can repeat 3 times in 24 hours



### Management of Status Epilepticus

- Benzodiazepine (diazepam, midazolam)
  - 0.5 mg/kg IV
  - Consider other routes if venous access difficult

#### AND

- Phenobarbital
  - 12-16 mg/kg IV loading dose, divided
  - 2-4 mg/kg if already on drug

#### OR

- Levetiracetam
  - 60 mg/kg IV loading dose



### Home Treatment for Cluster Seizures

#### Other Benzodiazepines

- Midazolam: Intranasal, intramuscular
- Lorazepam: Intranasal

#### Oral Phenobarbital (or other maintenance drug)

- Give 1 additional dose after each seizure
- Should not be given more frequently than every hour, 3 additional doses total

### Management of Status Epilepticus

- Check blood glucose
  - If low, give 0.4 ml/kg of 50% dextrose (diluted to 10%)
- Check body temperature
  - If > 105, cool a few degrees

### Status Epilepticus

- Repeated seizures without intervening periods of consciousness
- Can lead to cerebral necrosis - should be treated as a medical emergency

### Management of Status Epilepticus

- Consider metabolic problem if seizures poorly responsive to antiepileptic drugs
  - Hypoglycemia
  - Hypocalcemia
  - Hepatic encephalopathy



### Management of Status Epilepticus

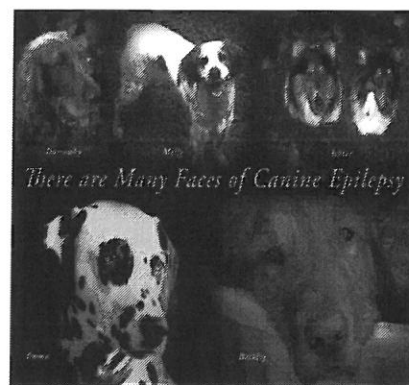
- If antiepileptic drugs ineffective, use anesthetic agent:
  - Pentobarbital
  - Propofol
- Continue on maintenance antiepileptic medications (can be given IV initially)

### Goal of Therapy

- Ideal – seizure freedom
- Practical – reduction of seizures to acceptable level
  - < 1/month
  - No clusters
- Must balance maximizing seizure control with minimizing side effects of drugs
  - Different for each animal

### Comparison of AEDs

Drug	Efficacy	Metabolism	Frequency of Administration	Side Effects
Phenobarbital	~85%	Hepatic	BID	Sedation, ataxia PU/PD/PP Hepatotoxicity Blood dyscrasia
Bromide	~60%	Renal excretion (competes with chloride)	Q 24 hours	Sedation, ataxia PU/PD/PP Vomiting Pancreatitis Bronchitis -cats
Zonisamide	Unknown	Hepatic	BID	Sedation, ataxia Hyporexia
Levetiracetam	Unknown	Renal excretion	TID BID - extended release	Sedation, ataxia

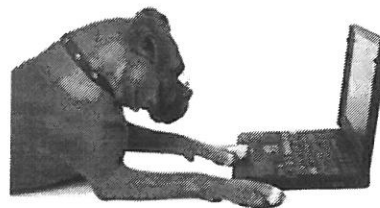


### Monitoring

- Yearly CBC, chemistry profile, urinalysis for animal on any antiepileptic drug
- Serum drug concentrations:
  - Phenobarbital: 2-3 weeks after dosage adjustment, yearly
  - Bromide: 3 months after dosage adjustment, yearly
  - Zonisamide, levetiracetam: Not routine; can be performed in dogs with poor response to drug

### Our Epilepsy Survey begins...

<http://harvest.cals.ncsu.edu/surveybuilder/form.cfm?testid=12936>



### "Signalment" of the Survey

- As of January 2014, more than 228 owners had completed the survey. "Impacts of Epilepsy in Companion Animal Patients"
- Total survey length: 59 questions
- All of the respondents either own or have owned a pet with seizures
- Of those responding, 225 were dog owners
- Three cat owners replied
- Some of the patients and owners participating in the survey have been patients at NCSU-CVM. States and countries represented include US, Canada, Australia, Europe



### Initial Assessment: Survey Condition

- Total 228 respondents: 98.6 % Canine; 1.4% Feline
- 50 % Neutered Male; 43 % Spayed Female
- From the total respondents, 85 % were alive at the time of the survey; 15% deceased
- Out of the 217 respondents, 70% did not have a confirmed cause for seizures in their pet



### Presenting Complaint:

#### Why undertake an impact study?

- Evaluation of Impacts of disease
- Literature search yields minimal research in this area in veterinary medicine, with exception of:  
*"Idiopathic epilepsy in dogs: owners' perspectives on management with phenobarbitone and/or potassium bromide"*  
*Y. Chong, D. J. Melior, T. J. Anderson 2006*
- Comparison to human literature
- As a technician supporting owners facing epilepsy for many years, working directly with veterinary neurologists, professional desire to further understand the disease and impacts of owners and patients as a group (versus individuals)

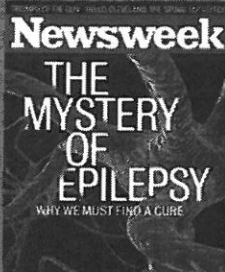


### Physical Findings: "State of the Epileptic"

- Majority of survey respondents give 1-2 Anticonvulsants per day
- Phenobarbital, KBr and Levetiracetam most common
- On average owners spend \$50-75/month for medications (\$ 7% spent over \$200 per month) 2014 Average cost \$227/yr for an unaffected pet
- 21 % of these patients required hospitalization for seizure management
- Even with the above, *more than half* of these cases continue to have more than 4 seizures per month



### "Epilepsy" A Storm in the Brain...2009"



Epilepsy is truly a "One Medicine" Disease

March 22, 2014: National Walk for Epilepsy at Washington DC

NCSU-CVM is uniquely positioned in "One Medicine" CDMT with Neurologists, Neurobiologists and other specialists

Opportunities for volunteers, resources and support

### Quality of life for the Pet & Owner

- Survey includes 11 questions ranking QOL for pet and owner
- Respondents strongly agree that the benefits of caring for a pet with epilepsy far outweigh the cost
- 60 % of Owners reported that owning a pet with epilepsy has helped them to "grow" as a person
- Questions ranked pre-and post medication status
- Also pre-and post seizure status

*Nursing care: Owner to Owner support....  
"It Takes a Village...."*

- Molly's Seizure Study Fund
- Emma's Fund
- Toby's Foundation
- Epi K-9
- Epi Guardian Angel
- And More



*Owner quotes: What are owners searching for?  
(And why they want to help...)*

- "Any research for our pets can help humans also. I have a sister with epilepsy. Neither my husband or I have ever hidden the fact that Mendi is epileptic and encourage anyone with an epileptic dog not to hide it. We take pride in her Agility championships (ATCH 2 and NATCH) and as of 11 she is still running and having fun doing it!"
- "I am a veterinarian. I had no idea how difficult it was to live with a pet that seizures. You cannot understand how difficult until you live it. One Medicine: The Human-Animal Epilepsy Connection"



*Nursing Care: Client and Patient Support*



- Veterinarian
- Veterinary Technician
- Educational materials-Print
- Educational materials-Online
- Client to Client Support

*Owners also want:*

- Clinical study research: Genetics, treatments, nutrition
- Education
- Outreach events
- Support from the *entire* veterinary team



*Veterinary Professional Long-term Care Opportunities:*

- Only 23% of clients received support from technical staff
- Opportunities for all technicians and veterinary professionals
- Recognition of skilled VTS



*Discussion*

- The survey, "Impacts of epilepsy in Companion Animal Patients," has truly been an incredible exercise for me as a technician specialist in the field of veterinary neurology.
- Monitoring the "pulse" of the profession and increasing our understanding as to how we can meet the needs of owners facing epilepsy—a long-term, medically challenging diagnosis



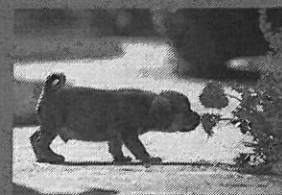
### Long-term care for (and off!) the Pet Caregiver

"They are your friend, your partner, your defender, your dog. You are their life, their love, their leader and in epilepsy, their caregiver. They will be yours, faithful and true, to the last beat of their heart. You owe it to him to be worthy of such devotion" - Unknown



I think our furry family members have the capacity for deep compassion, love, and concern for beings of all types, human and otherwise. I believe it goes beyond human understanding--because what they give comes from a heart that is pure, a spirit that is quietless, and a soul that operates on a level higher than anything close to human. - K & Pippig

### Take time to stop and smell the flowers....



### Pet "caregiver...."



### Survey Completion and Statistical Analysis

- Survey is closed at this time to new enrollees (however Epil Database is open for future projects)
- Statistical Analysis is under development
- Final results and publishing of study findings: Spring/Summer 2014.

### Taking care of the caregiver...

- <http://www.daybydaypetsupport.com/>
- <http://www.pawprintsnetwork.org/>
- <http://timesofindia.indiatimes.com/life-style/relationships/pets/Pet-dog-doesnt-care-if-its-owner-is-nutty/articleshow/7229174.cms>
- Also increasing number of Veterinary Social Workers to help support long-term needs for owners

### In Conclusion:


Overall, this project and the data that has been collected will allow us to:

- Expand our overall of the impacts of epilepsy in veterinary medicine
- Increase our ability to support owners and patients
- Aid us in developing clinical trials that address owner's areas of interest
- Educate in new and novel ways and more as it relates to the "Impacts of Epilepsy in Companion Animal Patients."

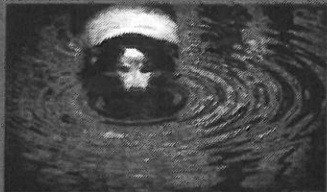
*With Special Thanks to the following:*

- Dr. Karen Munana
- NCAT Fall 2019 Conference Committee
- Epilepsy K-9 Foundation
- Toby's Foundation
- Five Sibes
- Epi Guardian Angel
- Collie Health Foundation
- Willard Moore and Angel Molly


*And to all the epileptic pets and their owners that have helped us learn so much... our hearts have grown through challenge*



*Have a "ripple" effect...*



*Questions?*



*If your dog thinks you're the greatest,  
don't seek a second opinion!*  
*Anonymous*

*Resources for Canine Epilepsy Support*

- <http://cvm.ncsu.edu/epilepsyresearch/>
- [http://www.cvm.ncsu.edu/vhc/c/c/clinical\\_services/neuro/](http://www.cvm.ncsu.edu/vhc/c/c/clinical_services/neuro/)
- <http://www.acvim.org/>
- <http://www.canine-epilepsy.com/>
- <http://www.canine-epilepsy.net/>
- <http://www.tobysfoundation.org/>
- <http://www.canine-epilepsy-guardian-angels.com/>
- <https://www.facebook.com/pages/FiveSibes-Siberian-Husky-K9-News-Reviews/181529415231834>
- <http://www.petliferadio.com/petdocep175.html>