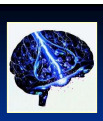

Shake, Rattle and Roll – Understanding Seizure Complexities

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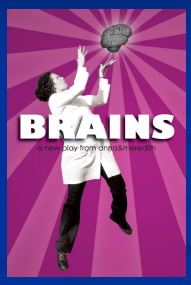
Seizures

- Paroxysmal Depolarization Shift
- Cerebral Dysrhythmia
- Recurrence may be common

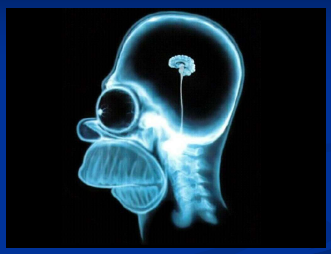


Synonomous Terms

- Seizure
- Ictus
- Convulsion
- Fit

Seizure Pathophysiology

- Focus
- Discharge
- Termination
- Kindling
- Mirror focus



Pathophysiology of Seizures

- Normal brain function
  - Normal brain cells use electrical and chemical signals to communicate with each other
  - These can be both excitatory and inhibitory
    - Kept in fine balance
  - Balance shift toward excitatory or away from inhibitory = SEIZURES

Seizures vs. Episodes ?

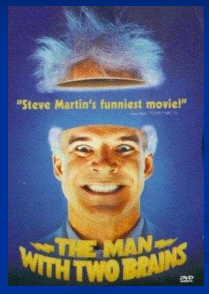
- Seizure components
  - Aura (Pre-ictal phase)
  - Ictus (Seizure activity)
  - Post - ictal period
- Physical examination
- Neurologic examination
- Owner history

Episodes

- Vestibular (Central vs. Peripheral)
- Syncope (Cardiac origin)
- Pain
- Intoxication
- Musculoskeletal disease
- Vascular accident

Classification of Seizures

- Generalized
  - Grand mal
  - Major Motor
- Partial
  - Focal motor
  - Psychomotor



Generalized Seizures

- Pre-ictal period
  - Duration
  - Behavior
- Ictus
  - Tonic – clonic phases (Muscle rigidity >> rhythmic paddling)
  - Change in consciousness / mood or behavior changes
  - Purposeless limb movements
  - Generalized motor dysfunction
  - Disturbance of autonomic nervous system – Urination, defecation, salivation
  - Alteration of sensation – hearing, visual, olfactory changes

Generalized Seizures

- Post-ictal period
  - Behavior changes
  - Visual changes
  - Intellect and / or gait changes
  - Duration from seconds to days

Partial Motor or Focal Motor Seizures

- Usually an acquired cause
- Activity of a local seizure focus in an area producing motor activity
- Movements are restricted to one side or part of the body, face or limb
- Change in consciousness is inconsistent
- Involuntary movement of the extremities, head, facial / ear twitching, salivation and/or temperature elevation
- Can spread

Psychomotor Seizures

- Complex Partial Seizures
- Temporal/limbic lobe origin
- Complex Motor Signs / Paroxysmal episodes of abnormal behavior
  - Fly biting
  - Tail chasing
  - Floor licking / Vocalizing / Vomiting
  - Regurgitation / salivation / dysphagia

Seizure Patterns

- Isolated
  - May occur once a month or singly
- Clusters
  - Random vs. Sequence
- Status epilepticus

Seizure Classification

- Structural
  - Neoplasia
  - Infectious / Inflammatory
  - Vascular
  - Traumatic
- Functional (Metabolic)
  - Hepatic disease
  - Renal disease

Seizure Classification

- Hypoglycemia
- Toxicity
- Electrolyte disturbances
- Endocrine

- Cryptogenic (Idiopathic)
- Must determine if intra vs. extracranial in origin

Seizure Etiology

- Degenerative – Storage diseases
- Anomalous (vascular/malformation)
- Metabolic
- Neoplastic / Nutritional
- Infectious / Inflammatory / Immune
- Traumatic / Toxin
- Cryptogenic / Idiopathic / Primary
- Seizures are a manifestation of a disease , not the disease itself
- Origin is the forebrain

Adult or Late Onset

- Intracranial causes
  - Acquired, progressive
  - Neoplastic , past or present Infectious , Inflammatory
  - Acquired , non-progressive
  - Vascular
  - Traumatic
- Extracranial causes
  - Metabolic
  - Endocrine

Juvenile Onset

- Cryptogenic
- Intracranial causes
  - Infectious / Inflammatory
  - Malformation / Degenerative
- Extracranial causes
  - Portosystemic shunt
  - Microvascular dysplasia
  - Toxicity

Primary Epilepsy

- Cryptogenic causes
- Genetic factors ?
- Breed predisposition
- Normal neurologic exam
- Normal interictal period
- Stereotypical episodes
- Normal blood work

Epilepsy

- Refers to repeated seizures over time where no underlying cause is identified
- Reactive epilepsy
  - Secondary to electrolyte disturbance or hypoglycemia
- Symptomatic epilepsy
  - Structural change
  - Brain tumor, vascular accident
- Cryptogenic or primary epilepsy
  - Cause is suspected but not identified

Diagnostics

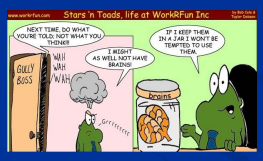
- Dependent upon findings and history
- CBC / Biochemical profile / UA
- Bile acids / Blood Ammonia
- Microfilaria check / fecal
- FeLV/FIV/Toxo/Crypto/Tick Serology
- Coagulation profile
- Chest +/- abdominal radiographs

Diagnostics

- Endocrine screening especially thyroid panel
- Insulin level
- Toxicology screen (Lead,strychnine)
- Diagnostic imaging
  - Cardiac / abdominal ultrasound
- Blood pressure / ECG

Neurodiagnostics

- Dependent upon history, signalment and examination findings
- Skull radiographs
- CT scan
- MRI
- CSF analysis
- Indications ?



Therapy

- Indications to begin an anticonvulsant
  - Seizure frequency > once per month
  - Status epilepticus or sequence clusters
  - Owner concern over recurrent episodes
- Client education is vital
  - Eradication of seizures is not the expected goal
  - Seizures are treatable, not curable
  - Life time therapy possible
  - Realistic expectations

Strategies - Limitations

- Toxicity
- Tolerance
- Inappropriate pharmacokinetics
- Expense

Pharmacokinetics

- Optimal drug should have the following properties:
  - Complete bioavailability
  - Available in a parenteral formulation
  - Elimination half-life suitable for daily or twice daily dosing
  - No enzyme induction
  - No other interactions with other drugs
  - Obviously, these drugs are hard, if not impossible, to come by

New AED Strategies

- Designed to improve quality of life of the patient
  - Choices based upon tolerability and cost
  - Tolerability must take into account:
    - High quality of life for both owner and patient
  - Cost must take into account:
    - Number of visits
    - Blood tests
    - Emergencies

Monotherapy vs. Polypharmacy

- Monotherapy approaches
  - Still the recommendation on new onset epilepsy
  - Use of a single AED advantages:
    - No drug interactions
    - More predictable pharmacokinetic and pharmacodynamic properties
    - Less potential adverse effects
    - Less expensive

Monotherapy Drugs

- Phenobarbital and Bromide
  - Most commonly used
    - Proven efficacy
    - Relatively well-tolerated
    - Dosed once to twice a day
    - Can be loaded as a parenteral form
    - Variable expense

Therapy

- **Phenobarbital**
  - Still the drug of choice
  - Acts at a site related to the GABA receptor/chloride ionophore to increase Cl- channel opening time in the presence of GABA
  - Diminishes the excitatory action of decarboxylic amino acids
  - Suppresses sustained repetitive firing of neurons at high concentrations
  - Broad spectrum, safety and efficacy
  - Variable expense
  - Efficacy complicated by microsomal enzyme induction in the liver
  - Drug concentration can decrease by 50% over the first 3-6 mo. of treatment

Phenobarbital

- **Formulations**
  - ¼, ½ and 1 grain tablets = 16.2 mg, 32.4 mg, 64.8 mg, 97.2 mg or 15, 30, 60 and 100 mg tablets
  - Side effects : PU / PD / PP
  - Acclimation in 7-14 days
  - Serum half-life: 36-48 hours
  - Maintenance dose : 2.5 mg/kg BID
  - Loading dose: 12-16 mg/kg divided over 4 doses
  - IV loading dose: Total mg IV = (Body wt (kg)) X (0.9 L/kg) X (15 ug/mL)
  - Therapeutic range: 15-35 ug/ml

Phenobarbital

- Frequency of dosing
  - 2.5 mg/kg BID
  - BID due to longer elimination half-life
  - More owner compliance when BID
  - Cost for 64.8 mg tablets #60: $44.34

Phenobarbital Monitoring

- Timing
  - In most dogs, the timing of blood sampling has no effect on clinical decision making
  - Recommendation is to retrieve trough level 1 hour prior to the next dose
- Sample handling
  - Serum separator tubes contraindicated
  - Can falsely lower levels

Pheno level interpretation

- Therapeutic range: 15-35 ug/ml when used alone
- When used with KBr: 9-36 ug/ml
  - Most times < 20 ug/ml
- Goal is to use lowest dose to control seizures
- Can be affected by other drugs

Phenobarbital Side Effects

- Polyphagia / polydipsia / polyuria
- Weight gain
- Elevated ALT / ALP
- Bone marrow suppression
- Increased peripheral metabolism of thyroid hormone / adrenal effects
- Hepatotoxicity

Phenobarbital Side Effects

- Continually elevated ALT / ALP
- Elevated serum bile acids
- Toxicity noted at levels > 40 ug/ml
- Recurrently seizuring animals may become refractory to valium when administered

Indications for other therapy

- Increased bile acids or blood ammonia
- Development of ataxia
- Phenobarbital levels > 40 ug/ml and refractory seizures
- Intolerance of medication due to side effects

Potassium Bromide (KBr)

- Drug of choice as an adjunctive therapy
- Good choice as a primary therapy
- Mechanism of action not completely understood, but most likely due to membrane hyperpolarization due to Br
- Different salt forms (Na,K)

Bromide Monotherapy

- Useful in dogs with:
  - Hepatic disease (shunts / microvascular dysplasia / toxic hepatopathy)
  - Transitioning relatively well-controlled chronic PB treated dogs to a non-metabolized AED

KBr

- Pharmacokinetics not well established in the canine
- Half-life is 25-46 days (Pheno is 24-48 hrs)
- Steady state not achieved for 2-3 months
- Rate of elimination dependent upon sodium administration / renal function

KBr

- Dose:
  - Loading - 100 mg/kg BID for 2 days or 50 mg/kg BID for 4 days
  - Maintenance – 30 mg/kg SID or 15 mg/kg BID
- Formulations
  - Liquid or capsule
- BID dosing used to avoid vomiting
- Compounded or KBroVet brand

KBr

- Therapeutic monitoring
  - Blood levels 1 month after beginning therapy
  - Therapeutic range: 1-3 mg/ml (1000-3000 ug/dl)
  - Dosages will need to be adjusted accordingly
  - Dietary salt intake can affect elimination

KBr Side Effects

- Sedation, ataxia
  - Saline diuresis
  - Decrease dosage, then increase in smaller increments (0.5 mg/ml)
- Falsely increased serum Cl- levels
- Dermatologic reactions (rare)
- GI disturbances
- Bronchitis in the feline
- Megaesophagus / pancreatitis in the canine – incidence

Benefits of KBr

- Can decrease the amount of phenobarbital used
- Animals with hepatopathies
- Inexpensive
- No hepatoxicities, renally excreted

Other Monotherapy drugs with potential

- Clorazepate (clorazepate disodium)
  - Enhances GABA activity in the brain
  - Available in regular and sustained release forms
  - Active metabolite is nordiazepam after oral dosing
  - Hepatic metabolism / serum half-life is 4-6 hours
  - Dose : 1-2 mg/kg PO BID
  - Formulations: 3.75, 7.5 and 15 mg tablets (human)
  - Can use for 3 days following a cluster of seizures
  - Therapeutic range: 100-400 ng/ml of nordiazepam

Other Anticonvulsants

- Levetiracetam (Keppra)
  - Used for focal and generalized seizures in humans now common in the dog
  - Mechanism of action – binds to synaptic vesicle glycoprotein SV2A and inhibits presynaptic calcium channels
  - Oral administration approaches 100% bioavailability in the canine; serum half-life of 3-4 hours in the dog; 70% excreted unchanged in the urine
  - Dose: 20 mg/kg PO TID, extremely safe, minimal sedation, 20 mg/kg XR (Extended Release) BID
  - Formulations: 250, 500, 750 mg and 100 mg/ml solution, injectable 100 mg/ml; 500 and 750 mg extended release tablets
  - Generic and brand name
  - Cost of therapy in a 25 kg dog/month: $30.18 or $43.34 (XR)

Other Anticonvulsants

- Zonisamide (Zonegran)
  - Sulfonamide-based anticonvulsant approved for use in humans
  - Treatment of focal and generalized seizures with minimal side-effects
  - Suspected mechanism of action: blocking of T-type calcium/ voltage-gated sodium channels in the brain
  - Microsomal enzyme metabolism; half-life is 15 hours (dog)
  - Dose: 10 mg/kg BID (in dogs not receiving phenobarbital, 5 mg/kg)
  - Formulations: 25, 50 and 100 mg capsules - generic
  - High margin of safety in the dog – therapeutic range of 20-30 ug/ml
  - Cost of one month therapy in a 25 kg dog: $33.70

Other Anticonvulsants

- Topiramate (Topamax)
  - Exact mechanism of action unknown but multimodal
  - In the canine, rapidly absorbed after oral dosing
  - Bioavailability between 30 and 60%
  - Half-life ranges for 2-4 hours
  - Side effects: GI signs, anorexia, dizziness
  - Dosing:
    - Dogs: As an add-on to phenobarbital: 2 mg/kg PO BID for first 2 weeks, then 5 mg/kg PO BID X 2 months and can increase to 10 mg/kg BID
    - Cats: 2.4 – 5 mg/kg (12.5 – 25 mg/cat PO)
    - 25, 50, 100 and 200 mg tablets - $23.06/month 25 kg dog

Changing drug dosages

- In general:
  - Current Dose/Current Level = Desired Dose/Desired level
  - "X" is equal to the desired dose
  - Solve for the "X" to get the desired dose
- Rough estimate of necessary increase
- Phenobarbital levels 2-3 weeks after change of therapy
- Other anticonvulsants variable due to half-life

Polypharmacy Approaches

- Combining AEDs is now a viable option
- Many new AEDs have novel or complementary mechanisms of action to stop or slow spread of epileptic foci

Polypharmacy Approaches

- Should be considered when:
  - Seizures are not controlled at maximal tolerance of a single drug
  - Adverse effects reduce the quality of life of the patient
  - Severe consequences of epileptic seizures occur (ie. status epilepticus)

Polypharmacy Approaches

- Most reasonable combinations in veterinary medicine:
  - Bromide with PB
  - Followed by BR with any of the new AEDs
  - Combinations of BR + Keppra, and BR + Zonisamide or Topiramate
    - Provide multi-mechanistic approaches
    - No drug interactions
    - Minimal adverse effects

Polypharmacy Approaches

- Drawbacks
  - Added expense of several dollars a day, although now the generic forms are allowing more use
  - Variability in patient response
  - Owner compliance with multiple drugs being used

Polypharmacy Approaches

- In general:
  - Best approach is to "go low, go slow" when titrating in a secong AED
  - Allow gradual adaptation
  - Observe for adverse side effects
  - Goal is to achieve better seizure control with a lower dose and fewer adverse effects

When Anticonvulsants Fail

- Owner compliance problem
- Intoxications
- Incorrect diagnosis
- Important to discuss that seizures are a treatable, but not curable condition
- Seizure frequency is unpredictable
- Breed predilections

Part 2: Acute Seizure Management

- Emergency
  - Status epilepticus or clusters
  - Establish and treat underlying cause
  - Pretreatment bloodwork
  - Treat hyperthermia
  - ABC's of emergency medicine
  - Refer to the Steps of acute seizure management on your handout

Status Epilpeticus or Cluster Seizures

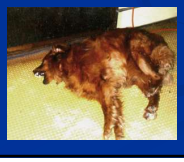
- Step1:
  - Stabilize patient and initiate drug therapy
    - Airway
    - Fluid choices
    - Diazepam, Midazolam or Lorazepam bolus IV or rectal (diazepam)
    - Longer acting anticonvulsant (Phenobarbital) IV or IM
      - Loading dose (total mg): 25 (dog) or 15 (cat) ug/ml) X (0.8 L/kg) X BW (kg) Administer @ 100 mg/min
      - OR can use 12-16 mg/kg total dose over 24 hours (can divide into 4 doses)
      - Keppra – IV, SQ or IM at 20 mg/kg

Emergency Management

- Diazepam (Valium)
  - Drug of choice
  - IV or per rectal use
    - Intravenous / per rectum dose: 0.25-0.5 mg/kg
      - Small dog, cat: 2.5-5 mg total
      - Medium: 5-7.5 mg
      - Large: 7.5-10 mg
- Midazolam (Ativan)
  - IV or intranasal use
  - Dose: 0.2 mg/kg IV or intranasal
  - Use in liver compromised patients

Emergency Treatment

- Can repeat twice
- If this therapy is unsuccessful, then consider other drugs to include Phenobarbital, Propofol, Levetiracetam



Status epilepticus or Cluster seizures

- Step 2: Institute maintenance therapy
  - Institute maintenance Phenobarbital, Keppra or KBr
  - Drugs can begin PO or IV
  - Can give KBr IV, but is technically challenging
  - If seizures continue, then go to Step 3

Status epilepticus or Cluster seizures

- Step 3: Treat recurrent seizures
  - Begin Diazepam (DZ) at 0.3 mg/kg/hr in 0.9%NaCl (if not on KBr) or 0.45% NaCl + 2.5% dextrose (on KBr) total fluid rate of 60 ml/kg/day
  - If seizures stop: Decrease DZ by 25% every 6 hours
  - If seizures continue (<3): Increase DZ infusion up to 0.5 mg/kg/hr
  - If seizures continue (>3): Administer ONE of the following anesthetic protocols:

Drugs for status epilepticus

- Diazepam 0.2 -0.5 mg/kg/hr diluted in 0.9% NaCl or 0.45% NaCl + 2.5% dextrose (avoid LRS)
- Phenobarbital 3-16 mg/hr CRI plus loading
- Propofol: 2-8 mg/kg followed by an infusion of 8-12 mg/kg/hr (0.4-0.8 mg/kg/min); if premedicated, 0.115-0.3 mg/kg/min) can be utilized
- Thiamine: 50-100 mg IM (dogs) / 10-50 mg (cats)
- Levetiracetam 20 mg/kg IM, SQ or IV

Special Considerations

- Seizures in the pediatric patient
  - Pathophysiology
    - Human neonatal seizures are often subtle and fragmentary
    - Classified using EEG and video monitoring
  - Can seizures cause brain damage to the immature brain ?
    - More resistant to damage than adult brain
    - Glycolytic flux accelerated in neonate brain
    - Maintenance of cerebral high-energy phosphates

Etiology of pediatric seizures

- Most are symptomatic
  - Degenerative / Anomalous
    - Hydrocephalus
    - Storage disease – rare
  - Metabolic
    - Hypoxemia – respiratory / CV compromise
    - Hypercapnea
    - Decreased blood pressure

Etiology of pediatric seizures

- Hypoglycemia
- Hepatopathy
  - PSS / Microvascular dysplasia (MVD)
- Inflammatory
  - Canine distemper virus (CDV)
- Traumatic
- Toxicity
- Epilepsy – breed predilection

Management of the pediatric patient

- Goals
  - Minimize seizures with limited side effects
- Considerations
  - Lower albumin concentration
  - Larger % total body water
  - Lower amount of body fat
  - Decreased hepatic metabolism and renal excretion

Special Considerations for Management

- Dosage reductions or prolonged intervals for drugs that are highly protein bound
- Hepatic induction by phenobarbital and other drugs
- Hepatic enzyme activity equivalent to mature dog by 5-8 weeks of age
- Glomerular filtration / tubular function by 21/2 months of age
- Remember to adjust for body weight

Feline Seizures

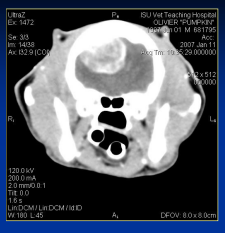
- Idiopathic epilepsy is less common in the feline patient, but does exist
- Most feline seizures are caused by underlying past or present structural forebrain disease
  - Infectious
  - Vascular
  - Neoplasia
  - Traumatic
  - Metabolic

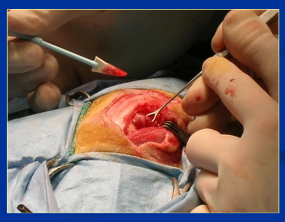
Feline Seizures

- The diagnostic plan should take into account:
  - Signalment
  - History
  - Physical examination
  - Neurologic examination
    - Lateralizing signs
    - Diffuse signs

Diagnosis of Feline Seizures

- Special considerations
  - FeLV / FIV / Toxoplasma / Cryptococcosis status
  - Hyperthyroidism
  - Diabetes mellitus
- CBC / Complete panel / UA / T4
- Blood pressure
- Chest radiograph
- Abdominal ultrasound
- Imaging – MRI, CT scan
- CSF analysis





Treatment of Feline Seizures

- Status epilepticus
  - Diazepam intravenously or per rectally
- Maintenance anticonvulsants
  - Phenobarbital is the drug of choice
  - Levetiracetam is becoming more popular
    - 20-30 mg/kg TID
    - May want to begin at BID instead of TID dosing
  - Zonisamide 5-10 mg/kg PO BID
  - Avoid oral diazepam
    - Hepatic necrosis
  - Potassium bromide
    - Coughing and respiratory signs

Seizures in the Geriatric Patient

- Must take into account underlying system abnormalities
  - Cardiovascular
  - Renal
  - Hepatic
- Diagnostics are contingent upon:
  - Physical and neurologic exam findings
  - Increased likelihood of primary intracranial disease – neoplasia / vascular

Geriatric Seizure Management

- Suggested diagnostics
  - CBC / Serum chemistry / UA / thyroid panel
  - Chest +/- abdominal radiographs
  - Blood pressure
  - If above normal, consider neurodiagnostics to include:
    - CT Scan
    - MRI
    - CSF analysis

Treatment options for the geriatric seizure patient

- Things to consider:
  - Underlying liver and kidney function
  - Acclimation to the drug and owner lifestyle
  - Phenobarbital may be better tolerated than KBr due to side effects
  - Levetiracetam is gaining popularity
  - Interactions with other drugs that the pet is taking for concurrent diseases

How about Diets ?

- Purina Pro Plan Neuro Care

- Medium chain triglycerides
- Research on the efficacy
- Expense

Dietary Management

- **Dietary therapy: a new approach to managing dogs with epilepsy?**
- While high-fat, low-carbohydrate diets utilizing long-chain triglycerides have been used and studied in children, this type of diet has yet to be shown to significantly improve seizure control in dogs. Fortunately, dogs can metabolize medium-chain triglycerides (MCTs) to produce ketones,[18] and experts believe that dietary MCTs may also have direct antiseizure effects via blocking the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors in the brain.[19]
- **Epilepsy study examines the effects of test diet with MCT oil on seizures**
- Neurologic researchers at the Royal Veterinary College (RVC), in partnership with Purina, recently investigated the potential role of diet in the nutritional management of dogs whose seizures were not being well controlled with AEDs. While achieving complete remission was not considered realistic for many patients, the goal was to reduce seizure frequency in epileptic dogs on chronic AED therapy.

Dietary Management

- A total of 21 dogs with idiopathic epilepsy that had experienced at least 3 seizures in the 3 months prior to enrollment completed a 6-month, randomized, placebo-controlled, double-blinded crossover study at the RVC. The study demonstrated for the first time that a test diet with MCT oil can have positive effects on reduction of seizure frequency when fed as an adjunct to veterinary therapy.[18] Dogs in the 2 groups were fed either a test diet containing MCT oil or a placebo diet for a period of 3 months—then switched to the other diet. In the study, the following results were noted:
- 71% of dogs showed a reduction in seizure frequency
- 48% of dogs showed a 50% or greater reduction in seizure frequency
- 14% of dogs achieved complete seizure freedom
- **Diet helps nutritionally manage dogs with epilepsy as an adjunct to veterinary therapy**
- The results of this study inspired Purina to develop the Purina® Pro Plan® Veterinary Diets NC NeuroCare™ diet, which is formulated with MCT oil to help nutritionally manage dogs with epilepsy that are also being administered AEDs. The diet is enhanced with a unique blend of nutrients—eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), arginine, antioxidants, and B vitamins, as well as MCT oil—to promote cognitive health and help nutritionally manage dogs with cognitive dysfunction syndrome.

What about CBD ?

- What is the evidence ?

CBD

- Cannabidiol (CBD) is an extract of the cannabis plant (marijuana). Unlike the major active ingredient of the plant, delta-9-tetrahydrocannabinol (THC), CBD does not cause "high" sensations. Instead, it is associated with pain relief and is the main ingredient in many cannabis pet products. Anecdotal evidence suggests that CBD may also offer a treatment alternative for several illnesses, including canine epilepsy, but no in-depth studies have verified these claims.
- The AKC Canine Health Foundation (AKCCHF) recently announced a major clinical trial to study CBD as a treatment for drug-resistant epilepsy in dogs. We talked with Dr. Diane Brown, the chief executive officer of the AKC Canine Health Foundation, and Dr. Stephanie McGrath, veterinary neurologist at Colorado State University and the principal investigator for the AKCCHF research project, to find out more.
- AKCCHF's Breakthrough Clinical Trial
- The AKCCHF's CBD study could be the first published, large-scale study to examine the effects of CBD on seizure activity in dogs. "This clinical trial is important for several reasons," Dr. McGrath shared. "Generally speaking, the science supporting CBD use in veterinary medicine is lacking. There is abundant anecdotal evidence, but very few, if any, well-executed research studies. Regarding the epilepsy study specifically, it is important work because we are constantly searching for an effective anticonvulsant drug to treat epilepsy in dogs. The drugs we currently have available frequently cause intolerable side effects or do not work well enough to control the seizures. Therefore, if CBD does prove to be an effective anticonvulsant, this would affect thousands of dogs worldwide."
-

CBD

- She explained, "The study is testing CBD on dogs with epilepsy in a controlled research setting. The dogs enrolled in the study are randomly assigned to receive either a placebo or the CBD oil for 12 weeks and then, after a 4-week washout period, receive the opposite drug for an additional 12 weeks. The researchers and the owners are blinded as to which drug is given in each half of the study."
- The study will also explore any possible side effects associated with CBD. According to Dr. McGrath, the researchers examine the dogs in the study every four weeks, perform regular blood work, and provide the owners with weekly questionnaires.
- Why Studies Matter
- Without studies and regulations, many of the CBD products on the market are untested and unregulated. When asked if pet owners should be wary of these products, Dr. McGrath said, "Yes, the lack of regulation is of great concern. Not knowing the exact constituents and quantities of those constituents in a particular product is scary, especially with the knowledge that at certain doses, THC can be toxic to dogs. Hopefully, this market will change in the future."
- AKCCHF Epilepsy Initiative

Questions ?

Part 3 : Case Studies

How do I treat ?

Case 1: Chico

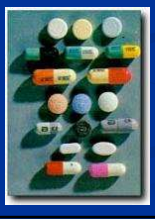
- Chico
- 2 year old MC Labrador retriever
- Presents with seizures that are occurring once a month
- Normal interictal period and normal neurologic exam

Chico: Diagnostic plan

- What do I start with ?
  - CBC
  - Serum Chemistry
  - Urinalysis
  - Bile acids - Pre and Post
  - Thyroid testing

Chico: Treatment plan

- What are our options ?
- Would you even start an anticonvulsant ?
- What drugs would you choose ?



Chico: Treatment plan

- Begin KBr at a dose of 100 mg/kg BID for 2 days as a loading dose and then 15 mg/kg BID as a maintenance dose
- Recheck KBr levels in one month
- Advise owners to watch for vomiting, severe lethargy or ataxia
- Pros
- Cons

Case 2: Ebony

- Signalment
  - 4 year old FS German Shepherd, 35 kg
  - Presents with cluster seizures occurring every 2 weeks for 3 months
  - Has been on phenobarbital at a dose of 1 grain BID since the seizures began
  - No antecedent history of seizures or behavior changes
  - Normal physical and neurologic examinations

Ebony: Diagnostic plan

- CBC
- Serum chemistry
- UA
- Pre and post bile acids
- Thyroid testing – how about this ?
- What else would you do ?

Ebony: Treatment plan

- Phenobarbital level is 14 ug/ml
- Increase Phenobarbital to 100 mg PO BID
- Add in KBr at a dose of 100 mg/kg BID for 2 days then maintenance at a dose of 15 mg/kg BID
- Recheck blood levels in 1 month
- If both within the normal range and no seizures we can either keep the meds at the current doses or attempt to decrease the phenobarbital by 1/3 every 2 weeks until totally off of the drug, stay on the KBr indefinitely
- Keppra ?

Case 3: Max

- Signalment
  - 5 year old MC Beagle
- Seizures since 1 year of age
- Non-progressive
- Normal interictal period and neurologic exams
- On phenobarbital at a dose of 3 mg/kg BID
- Still seizuring every 3 weeks

Max: Diagnostic and Therapeutic Plan

- CBC / Chem / UA
- Bile acids: Pre – 40 & Post - 76
- Serum phenobarbital level: 35 ug/ml
- Options ?

Case 4: Alex

- Signalment
  - 3 year old FS Labrador cross
  - Currently on Phenobarbital and KBr at therapeutic levels for seizures that began 2 years ago
  - Still having break through seizures every 3-4 weeks
  - Normal interictal period and neurologic examination

Alex: Diagnostic and Treatment Plan

- What are my options ?
  - Bloodwork
  - Consider imaging with CT or more specifically MRI
  - CSF analysis
- Add in Keppra or Zonisamide as the next steps
- Consider altered hypoallergenic diet
- Acupuncture

Case 5: Emma

- Signalment
  - 1 year old FS Yorkshire terrier
- History:
  - Seizures and behavior changes, intermittent blindness occurring after eating or sometimes not associated with eating
- PE & NE:
  - Within normal limits

Emma: Diagnostic plan

- Where do we go from here and what are the options ?
  - CBC, serum chemistry, UA
  - Pre and post bile acids
    - Pre: 200
    - Post: 350

Emma: Therapeutic Plan

- How are we going to treat ?
  - Diagnosed with PSS via ultrasound
  - Placed on Keppra prior to shunt ligation at the recommended dose 1 month before surgery
  - Taken to surgery and the shunt was ligated and a liver biopsy was taken and revealed MVD
  - Indefinitely will stay on Keppra

Case 6: Buddy

- Signalment
  - 9 year old MC Mixed breed
- Presents with an acute onset of seizures and progressive behavior changes for 1 month
- Neurologic examination localizes to the left forebrain

Buddy: Diagnostics

- Bloodwork
  - What would you perform ?
- Ancillary diagnostics
  - Blood pressure
  - Thyroid testing
    - Free T4 by equilibrium dialysis and TSH levels
  - Radiographs of the chest
  - Abdominal ultrasound

Buddy: Therapeutic Plan

- Antihypertensives
  - Enalapril
  - Amlodipine
- Thyroid supplementation
  - Synthroid or Levothyroxine
  - Dose: 0.1 mg/ 10 pounds

Case 7: Henri

- Signalment
  - 2 year old MC DSH
- Histroy of a URI and severe pyrexia as a kitten
- Presents with multiple seizures over the last month
- Normal interictal period
- Normal physical and neurologic exams

Henri: Diagnostics

- CBC, serum chemistry, UA
- Pre and post bile acids
- FeLV/ FIV Toxoplasma IgG and IgM titers
- Anything else ?

Henri: Therapeutic plan

- What anticonvulsant would you choose ?

Questions ?