IDIOPATHIC EPILEPSY (IE)

Classic case: 3-year-old Beagle; History of two seizures in past month. He is otherwise normal on exam.

**Presentation:**
- **Signalment**
  - **Dogs 1-5 years old**, slightly more common in males
  - **Any dog breed**, but inherited in beagle, Belgian Tervuren, keeshond, dachshund, Labrador retriever, golden retriever, Shetland sheepdog, Irish wolfhound, Viszla, Bernese mountain dog and probably more
  - Cat, idiopathic epilepsy (IE) less common than dogs
  - Horses
    - **Arabian foals**
    - Adult horses do **not** usually have seizures due to IE
- **History** - Need detailed, accurate Hx. IE has many, many rule outs
  - One or more seizures, usually about a month apart
  - Generalized tonic-clonic – duration of 30 seconds to 3 minutes
    - Loss of consciousness
    - Sustained contraction of all muscles
    - Paddling limb motions or rhythmic muscle contractions (esp limbs, masticatory muscles)
    - Usually urinary and fecal incontinence
  - Generalized mild seizures affecting only the face and jaws
- **Clinical presentation**
  - **Patients are usually normal when presented in clinic**
  - May have temporary neurologic deficits if present w/in 24 hours of a seizure
    - Ataxia, abnormal behavior, cortical blindness, hemiparesis
    - If these sx continue more than 24 hours after a seizure – consider differentials below
  - Normal fundic examination – if abnormal, consider differentials listed below

**DDX: VITTAMIN D** acronym:
- **Vascular** (stroke, coagulopathy)
- **Inflammatory** (encephalitis)
- **Toxic** (lead, metaldehyde, organophosphate)
- **Trauma**
- **Anomalous** (hydrocephalus, lissencephaly)
- **Metabolic** (hepatic encephalopathy, hypocalcemia, hypoglycemia)
- **Idiopathic** (epilepsy)
- **Neoplasia**
- **Nutritional** (thiamine deficiency)
- **Degenerative** (lysosomal storage disease)
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Test(s) of choice: Diagnosis is based on exclusion of other causes of seizures

- **Basic work-up**
  - **Bloodwork** to rule out metabolic or toxic cause of seizures
  - **Bile acids** to rule out hepatic encephalopathy
  - If normal physical and neurologic examination and typical signalment,
    - Presumptive diagnosis of epilepsy can be made at this point.
    - If deterioration or failure to respond to medication, pursue more advanced testing

- **Advanced testing**
  - **MRI or CT of brain** to rule out structural brain disease (e.g., brain tumor)
  - **Cerebrospinal fluid analysis** to rule out encephalitis
  - Electroencephalography to confirm seizure activity

- **Monitoring**
  - **Monitor anticonvulsant blood levels** (DO NOT USE SERUM SEPARATOR TUBES)
    - 2-4 weeks after starting meds or changing dosage (3 months for potassium bromide)
    - Every 6-12 months
    - If there is poor seizure control
    - If concerned with anticonvulsant toxicity
  - **Monitor bile acids** every 6-12 months if using meds that can be hepatotoxic (ie: phenobarbital)

Rx of choice:

- **Acute treatment to halt seizure activity**
  - **Benzodiazepines**: Intravenous diazepam, midazolam, lorazepam (if necessary, diazepam may be given rectally and midazolam may be administered intramuscularly or intranasally)
    - Very short half-life; will need concurrent maintenance anticonvulsant if seizures recur
    - If not effective after 3 doses, give propofol IV to stop seizure then continuous infusion
  - **Digital ocular pressure** – vagal stimulation
  - If temporarily effective but seizures reoccur
    - Benzodiazepine continuous rate infusion (CRI)
    - Propofol or isoflurane anesthesia
  - After seizure stops
    - Administer oxygen; Place IV catheter
    - Check glucose, calcium, hematocrit, protein
    - Maintain hydration & blood pressure w fluid therapy
    - Monitor temperature and treat >104°F (40°C)
    - Turn at least every 4 hours
    - Express bladder if needed every 8 hours
    - Keep clean, warm dry
    - May require 24-72 hours of heavy sedation
  - **If animal is not already on anticonvulsants**
    - Give parenteral loading dose of Phenobarbital (IV) or levetiracetam (Keppra) (IV or SQ)
    - Then continue with maintenance therapy
  - **If animal is already on anticonvulsants**
    - Draw blood for anticonvulsant levels
    - **Continue anticonvulsants** on schedule (give parenterally if necessary, potassium bromide can be given rectally if necessary)
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Extended version

- **Maintenance therapy to control seizures**
  - **Goals:**
    - Reduce frequency & severity of seizures
    - Maximize quality of life of patient and family
    - Avoid serious side effects.
  - **Risks of seizures versus risks of treatment**
    - Seizures: seizures themselves and emotional effect on family
    - Treatment: Side effects of meds; expense, effort of giving meds BID/TID, monitoring med levels.

- **Phenobarbital**
  - Potent inducer of cytochrome P450
  - **Multiple side effects:** sedation, ataxia, PU/PD, polyphagia
  - Decreases T4, free T4, and increases TSH without clinical signs of hypothyroidism

- **Potassium bromide**
  - Renally excreted, half-life of 24 hours
  - Often administered with phenobarbital, or alone
  - Bromide competes with chloride for renal elimination
    - High chloride diet increases bromide elimination
  - **Do not alter dietary salt**!
  - **Multiple side effects:**
    - Ataxia, sedation, vomiting, PU/PD, polyphagia, hyperactivity,
    - Pruritic rash, pancreatitis, pneumonitis (cats)

- **Levetiracetam** (Keppra)
  - Renal metabolism
  - Half-life of 4 hrs but anticonvulsant effect appears to last longer; available in extended release
  - 100% bioavailability after oral or parenteral dosing
  - **No drug interactions** – can be given with any other anticonvulsant
  - **Very safe** in dogs and cats
  - “Honeymoon effect” – reported in people – excellent control for first several months only

- **Zonisamide**
  - Hepatic metabolism – **give double dose** when administered with phenobarbital because phenobarbital will increase clearance of zonisamide
  - Side effects-high safety margin, transient sedation, ataxia, vomiting, thyroid suppression

- **Felbamate**
  - May be beneficial in dogs refractory to phenobarbital and bromide
  - Side effects: nervousness, hyperexcitability, decr appetite, hepatotoxicity, blood dyscrasia, KCS
    - Monitor CBC every few months

- **Gabapentin**
  - Hepatic metabolism but no enzyme induction
  - Mixed results as add-on anticonvulsant
  - Side effects uncommon: sedation, ataxia, polyphagia, weight gain

- **Pregabalin**
  - Gabapentin analog, effective add-on in some dogs
    - Side effects: sedation, ataxia
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Prognosis:
- Guarded to good
- Can have normal lifespan if well-controlled.

- Animals with repeated emergency episodes of status epilepticus (continuous seizure >5 min) or clusters (several seizures in a 24 hour period) tend to have a shorter lifespan.

- Only 70-75% of dogs will be controlled with phenobarbital and/or potassium bromide
- Larger breed dogs tend to have more difficult to control seizures

Prevention:
- Spay females (estrogen can lower seizure threshold)
- Client education – give meds on time. A missed dose can precipitate a cluster or status epilepticus.
- Do not breed affected dogs

Pearls:
- Goal of treatment is to reduce seizure frequency by 50%
- Less than two seizures every 2-3 months is considered adequate control

- Its an emergency when:
  - More than 3 seizures in 24 hours or
  - A single seizure lasting more than 5 minutes

- Have owner keep diary of seizure activity, meds, med levels, unusual events

- Seizures happen most often at night or when patient is resting or sleeping.
- Can be “provoked” by a visit to the veterinary hospital, groomer, or loud noises.
- Have owner videotape episode if possible-helps ddx from syncope, narcolepsy, etc

- Kindling effect: Seizures themselves seem to increase seizure frequency over time

- Don’t combine or change anticonvulsants unless the therapeutic blood level is achieved with 1st drug
- If need to discontinue an anticonvulsant, do so as gradually as possible
- The number one cause of seizures in a dog over 5 years old is a brain tumor