mission  
veterinary specialists  
What's in Your Anticonvulsant Arsenal?  
Case Examples in Seizure Management  
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missionvetspecialists.com

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Overview

Approach to chronic seizure management

- Treatment options
  - Selection
  - Monitoring
  - Reaction
  - Cessation
- Case Examples



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Using Anticonvulsant Drugs

- WHEN TO TREAT?
  - GUIDELINES?
  - FREQUENCY
  - CLUSTERS/ STATUS
  - UNDERLYING DISEASE
  - SEVERITY
  - CLIENT
- ADDING A 2<sup>ND</sup> ACD
  - MECHANISM
  - EFFICACY
  - TOLERANCE
- WHAT HAPPENS WITH #1?



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Using Anticonvulsant Drugs

- THE IDEAL ACD
  - EFFECTIVE
  - CHEAP
  - SAFE/LOW SE PROFILE
  - CONVENIENT
  - QUICK ONSET
  - MONITORING
  - MOA



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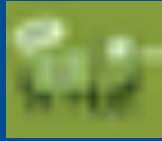
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## Using Anticonvulsant Drugs – THE OPTIONS

### Old school

Phenobarbital  
Potassium bromide



### New school

Levetiracetam  
Zonisamide  
Gabapentin/pregabalin



## Phenobarbital (PB) - Increases Inhibition



- METABOLISM = HEPATIC
- t1/2: 40-90h (D)
- t1/2: 40-50h (C)
- SS: 10-15d
- Efficacy (80%)
- D: sedation, ataxia, PU/PD/PP, blood dyscrasias, skin
- C: facial pruritus, edema, TCP, lymphadenopathy
- Thyroid testing
- Enzyme induction
- Level dependent toxicity
- Dosing:
  - Load: 16-20 mg/kg IV
  - Oral: 2-3 mg/kg PO q12\*
- Monitoring:
  - CBC, chemistry, UA, BA, level q 6 months
- Cost for 50# dog: \$55/mo



## Potassium Bromide (KBr) – Inhibition



- Renal excretion
- t1/2 = 24 days
- SS: 3-4 MONTHS
- Efficacy (80% R)
- SE (LEVEL DEPENDENT):
  - Ataxia, PU/PD/PP, vomiting, aggression
- CONTRAINDICATIONS
- CATS? - NO!!!!
- Watch:
  - Salt intake
  - IVF
- Dosing:
  - Load:
    - Maint: 30 mg/kg PO q24
- Monitoring:
  - CBC, chemistry, UA, level q 6-12 months
- Cost for 50# dog: \$15



## Levetiracetam (LEV) – Decrease excitation



- t1/2 = 3-4 hours (D)
- t1/2 = 2.5-3 hours (C)
- SS: 1 day
- Efficacy (65% R)
- Ongoing CNS disease
- Side effect profile
- High oral bioavailability
- HONEYMOON EFFECT
- OK for cats
- PB
- Dosing:
  - 20-60 mg/kg PO or IVq8
  - 20-60 mg/kg POq12 XR
    - [500, 750 mg]
- Monitoring:
  - Routine BW, levels?
- Cost for 50# dog: \$58/mo



## Zonisamide (ZON) - BOTH



- SULFA DERIVATIVE
- T1/2 15 HOURS (D)
- 2 X longer in cats (safe)
- SS: 3-4 d (D), 6 d (C)
- SE - mild
- KCS? IMTP, IMHA
- Hepatotoxicity, RTA
- 25, 50, 100 mg capsules
- PB
- Dosing:
  - Start 5-8 mg/kg PO q12
  - Up to 12-14 mg/kg PO q12
- Monitoring:
  - CBC, chemistry, UA q6-12 months
  - Check labs if ill
  - Consider level if on PB
- Cost for 50# dog: \$39 (Costco)



## Gabapentin and Pregabalin - Decrease Excitation



- Elimination - renal and hepatic
- T1/2
- SS: 1 day
- Efficacy: >50% reduction in 50% R patients
- No enzyme induction
- SE: Sedation, ataxia, wt. gain
- Capsules, solution, compound
- Dosing:
- Monitoring:
  - CBC, chemistry q6-12 months
- Safe for cats
- Cost for 50# dog:



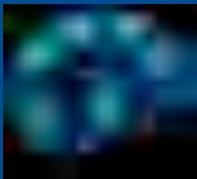
## What if the Drugs Don't Work?

- Guidelines
  - Frequency
  - Side effects
- Communication
  - Compliance
    - Ask direct ??s
  - Rechecks
  - Seizure log
- Monitoring
- React if not working
  - Increase dose if able
  - Add secondary ACDs
  - Know what to do with levels



## Pulse Therapy

- Clusters
- Short t1/2
- Evidence?
- Candidates
  - Levetiracetam
  - Gabapentin
  - Pregabalin
  - Phenytoin
  - Chlorazepate



## Cessation

- ONLY IF RESOLUTION
- NO STRUCTURAL BRAIN DISEASE
- SEIZURE-FREE
- GRADUAL TAPER



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CASE EXAMPLES:  
JESS, ROWAN, BOSS & LITTLE GIRL



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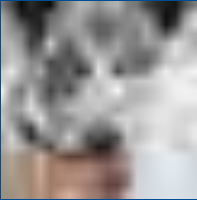
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## JESS – Signalment, history, exam findings

- 3YO FS Catahoula X
- Cluster (2) seizures
- 2 additional in hosp
- Hx healthy, UTD vaccinations, HWP
- Normal PE
- Blind OS, otherwise normal NE



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## Differential Diagnosis & Plan

DDx:  
Inflammatory disease  
Malformation  
Idiopathic epilepsy  
Neoplasia  
Extracranial disease  
Vascular

- Plan:
- CBC, GHP, NH3
  - MRI, CSF
  - +/- serologic testing

- Initial ACD Plan:
- Quick onset, +/- IV



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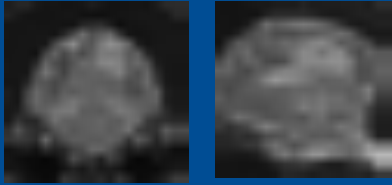
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## JESS – Work up and Management



## JESS – Work up and Management

Rostral

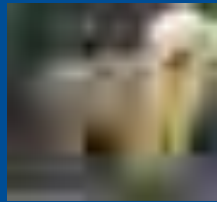


- Take home points:
  - Recommend ER
  - ACD at presentation
  - Adjust accordingly
  - Do a good exam
  - Look for a cause
- Outcome & Management
  - Clinda, doxy, pred
    - Serology → Neosporosis
  - Clindamycin, TMS, LEV
  - Sight returned then lost
  - Control
  - Cessation?



## ROWAN – Signalment and History

- 2 YO MN GoldenDoodle
- 4 mo Hx seizures
  - Cluster (6) 1<sup>st</sup> month
    - Tx PB 30 days
  - No seizures until 3 mo later
  - Cluster (6), back on PB
  - 2 weeks later clusters (6) 3 days in a row
  - PB level 16 ug/mL
- Hx healthy, UTD vaccines and HWP
- Normal PE
- NE: ataxia (PV) and dull mentation (36 h)



## Differential Diagnosis & Plan

DDX:

Malformation  
Inflammatory disease  
Idiopathic epilepsy  
Neoplasia  
Extracranial disease

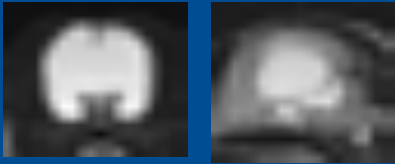
Plan:

- CBC, GHP, NH3
- MRI, CSF
- +/- Serology
- Initial ACD Plan:
  - Quick onset/IV
  - Orals?



## ROWAN - Work up

- MRI findings



Serologic testing – Neospora positive, low



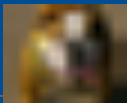
## ROWAN – Take-home Points & Management

- Take-home points:
  - ACD at presentation!
  - Look for a cause & treat it
  - Don't forget malformations in older pets
  - Additional seizures
    - Adjust accordingly
- Ongoing management
  - Meds: prednisone, omeprazole, clindamycin (30d)
  - Seizures
    - Single 2 weeks later (missed dose, no changes)
    - 2 weeks later – PB level 21ug/mL
    - 2 weeks later had singles 3 days in a row (o stopped pred)
    - Increase PB, restarted prednisone



## BOSS – Signalment and History

- 8YO M English Bulldog
- Hx 1-2 seizures/month
  - 1.5 years, no reports
- Oral PB (1.5 mg/kg q12h)
  - no levels
- Found outside in SE (1hr)
- Hyperthermia 107
- Clusters before presentation
- Massive vomiting
- PE: hyperthermia (105)
- Hypotension
- Recumbent and unresponsive
- NE: responsive miosis  
OU, intact reflexes



## Differential Diagnosis & Plan

- |                      |                           |
|----------------------|---------------------------|
| DDX:                 | • CBC, GHP, PT/PTT, BP    |
| Idiopathic epilepsy  | • THX rads                |
| Malformation         | • Imaging if not improved |
| Extracranial disease | • IVF (LRS and colloid)   |
| Vascular             | • Mannitol, 1g/kg         |
| Trauma               | • LEV IV                  |
| Neoplasia            | • PB IV, INCREASE PO 25%  |
| Inflammatory disease | – Why both?               |



## BOSS – Management

Exam, frequency and med changes over next 48 h:

- **Friday-Saturday**
  - Clinical improvement, walking but demented, vocal
  - 4 overnight – LEV dose incr to 40, 50 mg/kg PO q8, PB/LEV IV
  - None throughout day but profoundly abnormal
  - POC BW, BP, continue IVF, LEV, PB
- **Sunday**
  - Clinical improvement, not normal
  - 2 overnight – add ZON 6 mg/kg PO q12
  - Eating well, DC IVF



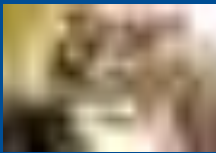
## BOSS – Outcome & Take-home Points

- **Monday- None!**
- **Outcome:**
  - Recheck 6 weeks
    - LEV → LEV XR
    - PB level – 17.6 ug/mL
  - No changes until 3 mo recheck, then discuss
  - 2 seizures in 7 months (both med related)
- **Take-home points:**
  - Know when to adjust
    - Frequency
    - Half-lives
  - Acceptable deficits
  - Side effects
  - Stay the course!
  - Stay involved!



## Little Girl - Signalment and History

- 5 YO FS DSH
- First event - Dec 2012
- Monthly
- Normal per O
- PB - 8.1 mg POq12
  - 2/2013: 10.9 ug/mL
- April 2013 - clusters of focal and gen. seizures
- PB 5 mg/kg IV; Midaz CRI



## Differential Diagnosis & Plan

- |                      |                            |
|----------------------|----------------------------|
| DDX:                 | • Sedated NE               |
| Idiopathic epilepsy  | • CBC, GHP, BP - NSF       |
| Malformation         | • FeLV/FIV, Toxo - NP      |
| Extracranial disease | • MRI/CSF - NP             |
| Vascular             | • Wean off of CRI over 24h |
| Trauma               | • Increase PB dose         |
| Neoplasia            | • Exam normalized          |
| Inflammatory disease |                            |



## Ongoing Management

None from April - Dec  
12/2013: 45.1 ug/mL, dose reduction: 3/4 1 PO q12

2 seizures Jan - June 2014 (compliance)  
6/2014: 18.1 ug/mL, no changes

Cluster in June - increase dose back to 1/1 PO q12  
7/2014: 46.2 ug/mL, 11 am, 3/4 1 PM

Seizures every 3 weeks (cluster, not reported)  
10/2014 Start LEV q12h (rec q8)

Feb 2015 - Cluster, start LEV q8, reduce PB to 3/4 1  
PO q12  
2/2015 and 10/2015: Level <37ug/mL, no change

Control from 2/2015-7/2016!

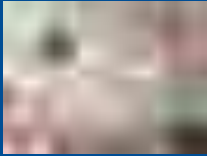
7/2016: 51.1ug/dL, Dose reduction to 1/2 1 PO q12  
Clusters return 1 week later, increase back to last  
dose, liver function

- Important points:
  - Compliance
  - Monitoring
  - Limited options for cats
  - Cats can have IE too



## Keys to Success

- INVESTIGATION
- EARLY TREATMENT
- TAKE CONTROL
- CLIENT EDUCATION
- DRUG SELECTION
- OPTIMIZATION
  - DOSING
  - EXHAUST FIRST DRUG
- OPTIONS
  - DON'T GIVE UP!



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