SEIZURES

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OVERVIEW

- Types of seizures
- Differentials
- Emergency Management and Testing
- Longterm Management and Testing

TYPES OF SEIZURES

- Focal/ partial
- Generalized
- Absence

FOCAL/ PARTIAL SEIZURE VIDEO

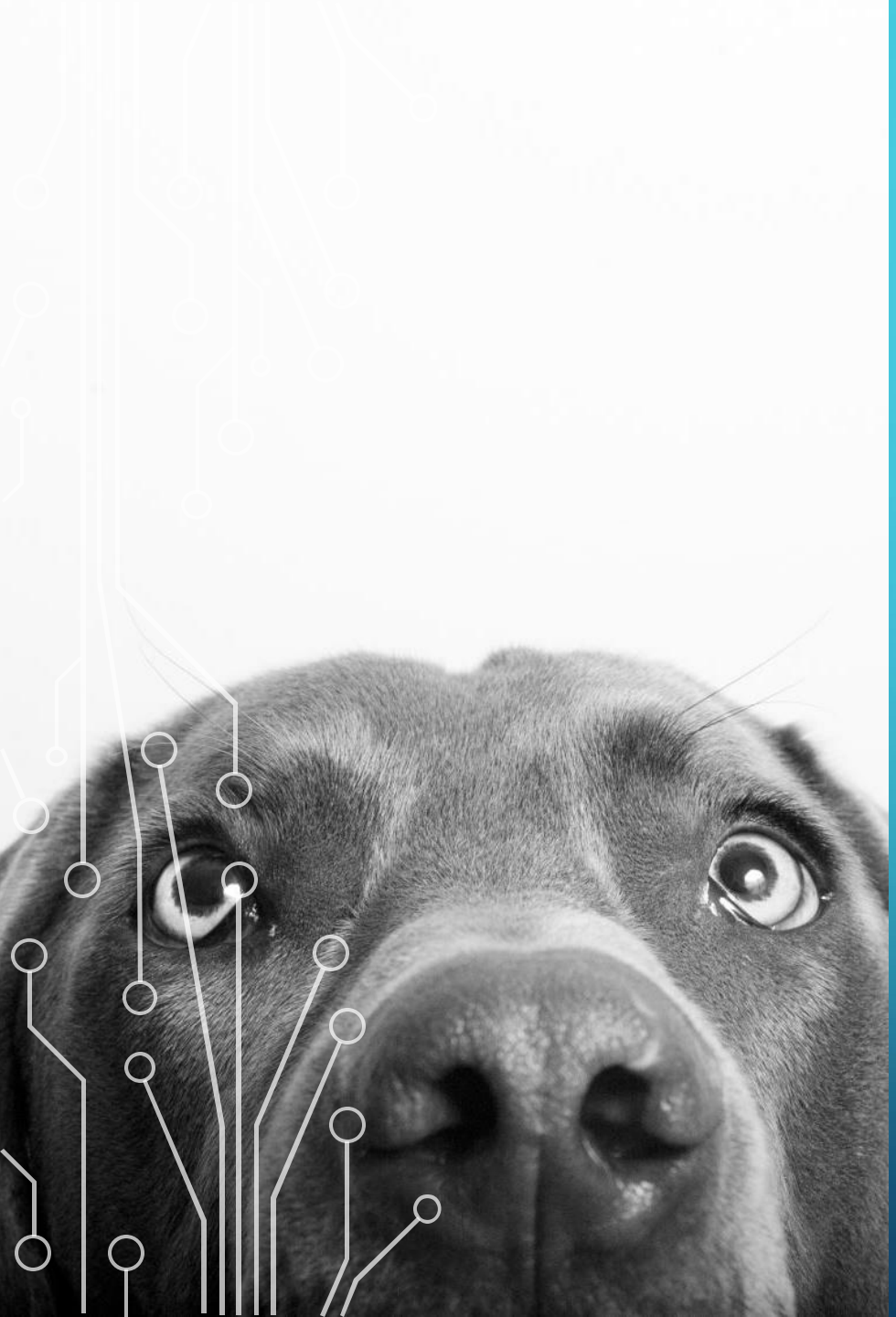
DIFFERENTIALS FOR SEIZURES

- Vascular (ischemic infarct vs. hemorrhage)
- Idiopathic epilepsy
- Toxins/ Trauma
- Anomalous (i.e. hydrocephalus)
- Metabolic (i.e. hepatic encephalopathy, hypoglycemia, etc.)
- Inflammatory (immune- mediated i.e. MUE vs. infectious)
- Neoplasia
- Degenerative (i.e. canine cognitive disorder, lysosomal storage disease)

SEIZURE LOOK-A-LIKES

- Syncopal episodes
- Vestibular episodes
- Paroxysmal dyskinesias (Movement Disorders)

SEIZURE LOOK A LIKE



EMERGENCY TESTING

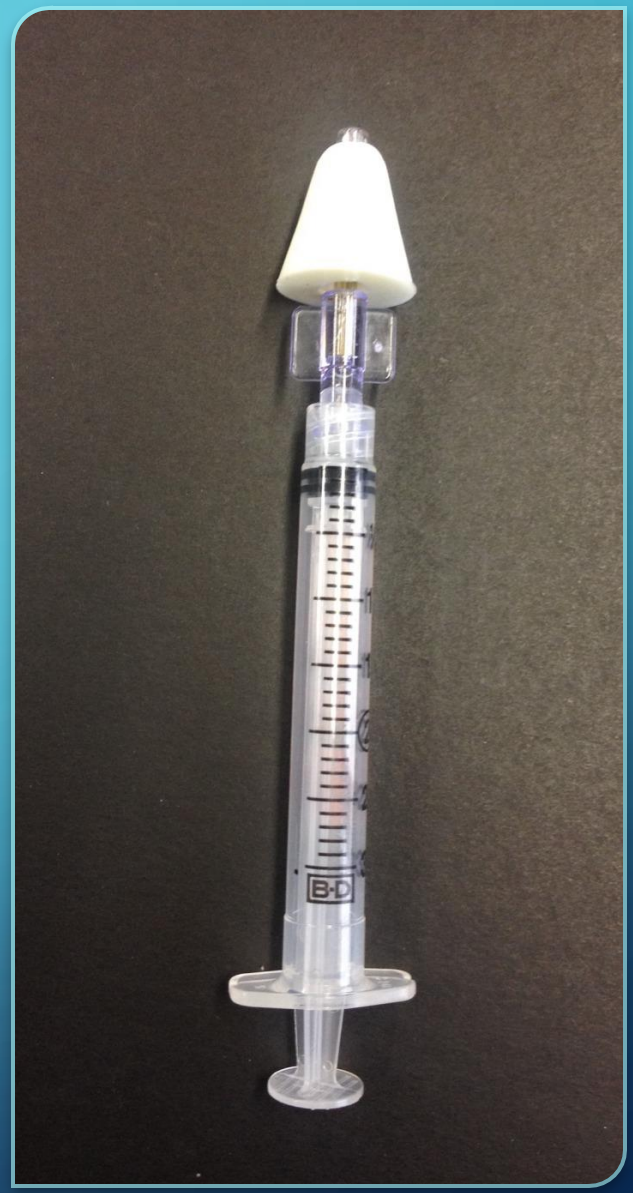
- 3yo Labrador Retriever presents with sudden onset generalized seizures
  - History
  - Physical Exam
  - CBC/ Chemistry/ Electrolytes/ Blood glucose
  - Lesion localization/ Differentials
  - Top Ddx: Idiopathic Epilepsy

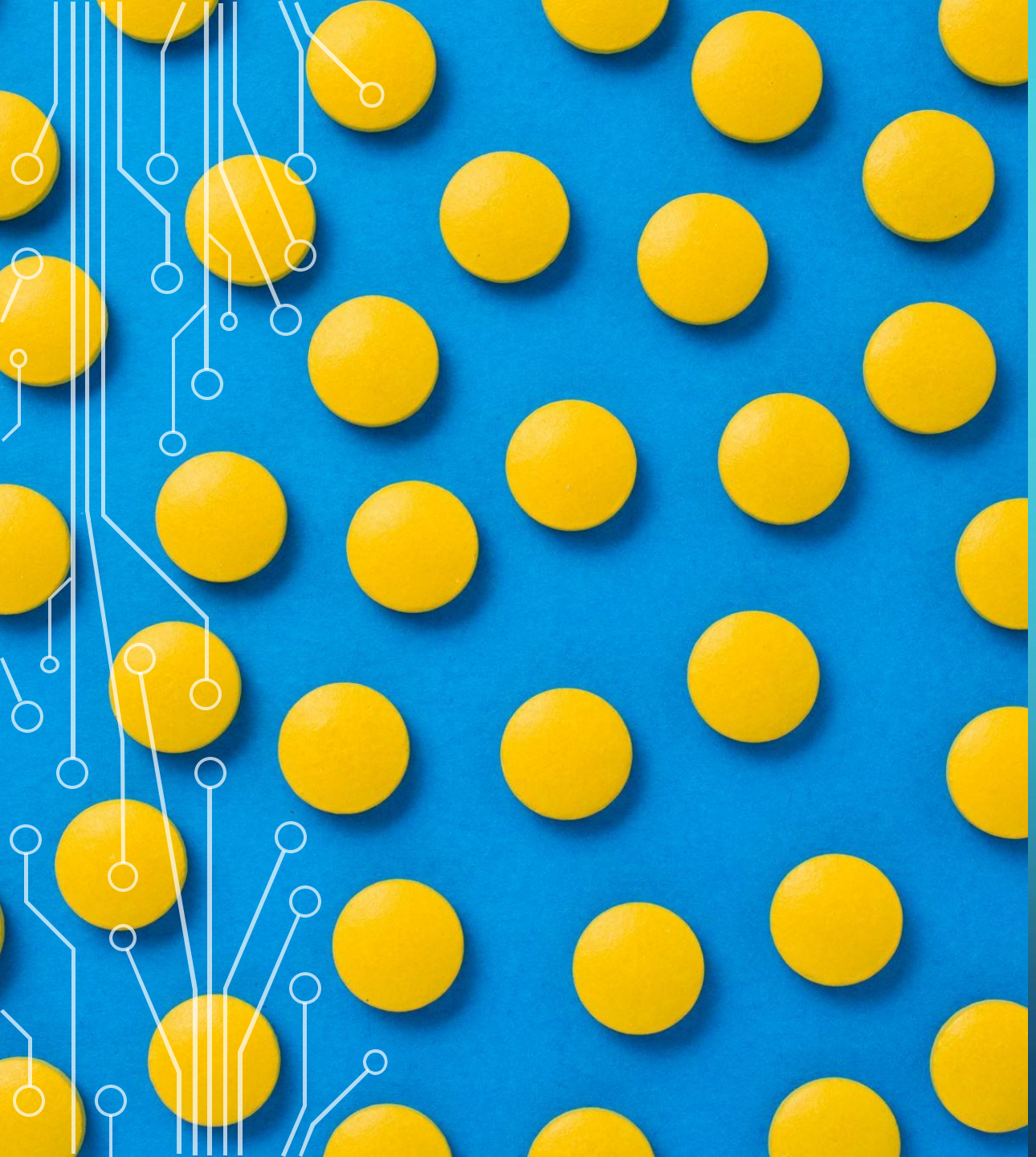
EMERGENCY MEDICATIONS

- Many options with new recommendations often
- Benzodiazepenes
- Ketamine
- IV phenobarbital or levetiracetam
- Propofol/ general anesthesia

BENZODIAZEPENES

- Rectal diazepam – 1mg/kg
- Intranasal midazolam -0.2mg/kg
- IV midazolam or diazepam (0.25mg/kg midazolam – 0.5mg/kg diazepam)
- CRIs
  - 0.25-0.5mg/kg/hr midazolam
  - 0.5-1mg/kg/hr diazepam





KETAMINE

- Bolus- 5mg/kg for refractory status epilepticus; less evidence that it will help a cluster seizure event

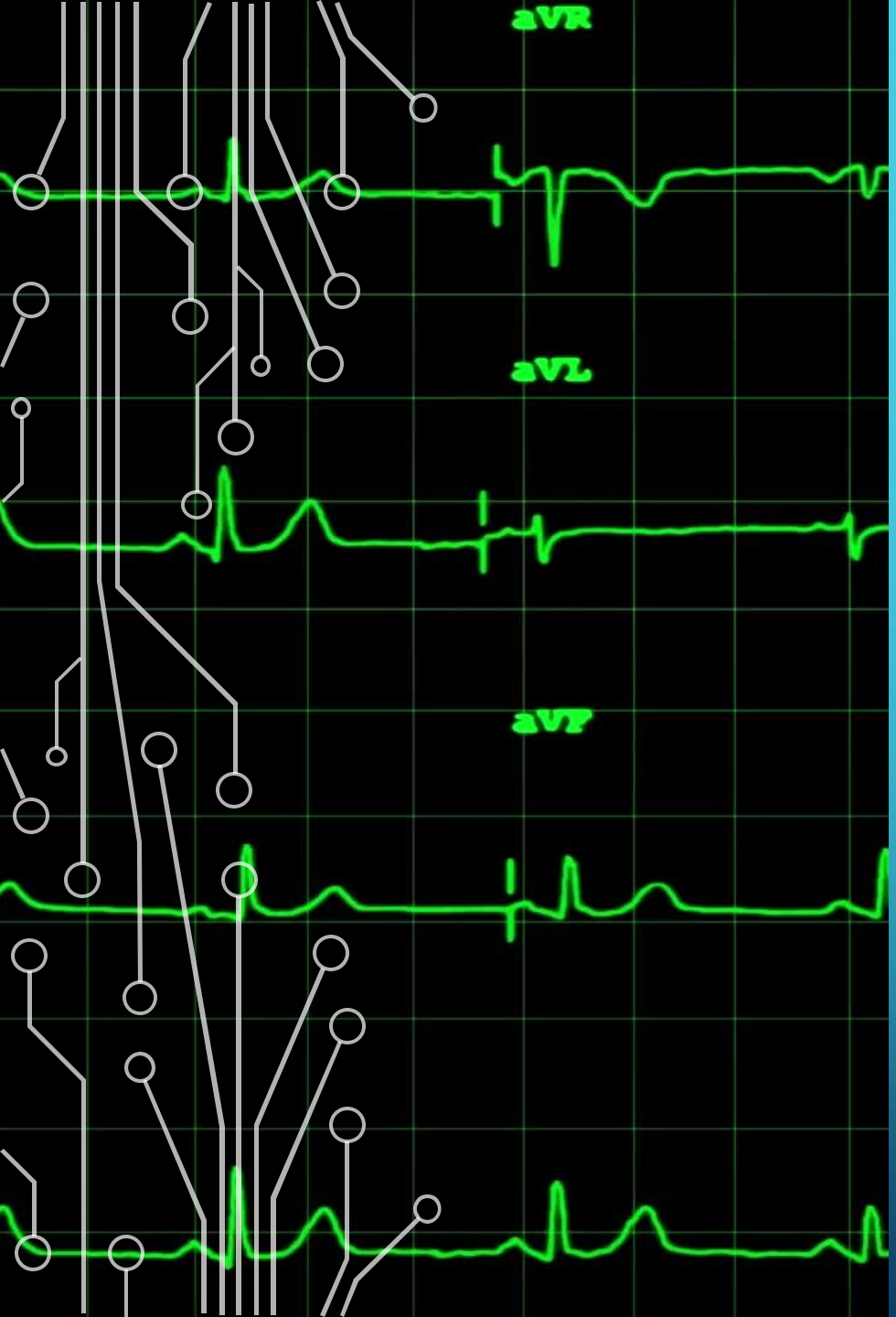
IV PHENOBARBITAL AND LEVETIRACETAM

1

Loading dose: Pheno ~15-20mg/kg total over a ~24 hour period. Generally will aim to give ~3mg/kg IV per dose q ~2-4 hours depending on frequency of seizures → transition to q 12 hour dosing of ~3mg/kg thereafter

2

Loading dose: Levetiracetam ~60mg/kg IV **cost once then transition to minimum of ~30mg/kg PO or IV q 8 hours thereafter



PROPOFOL AND GENERAL ANESTHESIA

- Titration and induction of general anesthesia as you would normally
- Be prepared to intubate
- Propofol CRI may be necessary
- Rare to reach this point

LONGTERM MANAGEMENT AND TESTING

- When to start?
- Medications: Phenobarbital, Potassium bromide (KBr), Levetiracetam (Keppra), Zonisamide
- Goals?
- Adjustments

WHEN SHOULD WE START LONGTERM AEDS?

- Single seizure events occurring more often than once every 8 to 12 weeks
- Cluster seizures (2 or more seizures within a 24 hour period)
- Single status epilepticus event (seizure lasting > 5 minutes w/out self resolution)
- Concerning post- ictal signs (i.e. aggression, respiratory distress, etc.)

PHENOBARBITAL

- Dogs: ~3mg/kg PO q 12 hours; Cats: 7.5mg/CAT (not kg) PO q 12 hours
- ~2-3 weeks until steady state
- Common side effects: PU/PD, polyphagia, sedation/ ataxia for up to ~2 weeks considered normal, ALP elevation
- Rare side effects: Hepatotoxicity, Bone marrow suppression, Pseudolymphoma, Aggression

PHENOBARBITAL

- Before starting: CBC, Chemistry +/- BA
- After starting: ~3-4 weeks repeat CBC, Chemistry & trough pheno level
- Ideal therapeutic range: 100-120umol/L
- Tolerated up to 140umol/L
- Hepatotoxicity over time if sustained >140umol/L

PHENOBARBITAL- ADDITIONAL PEARLS

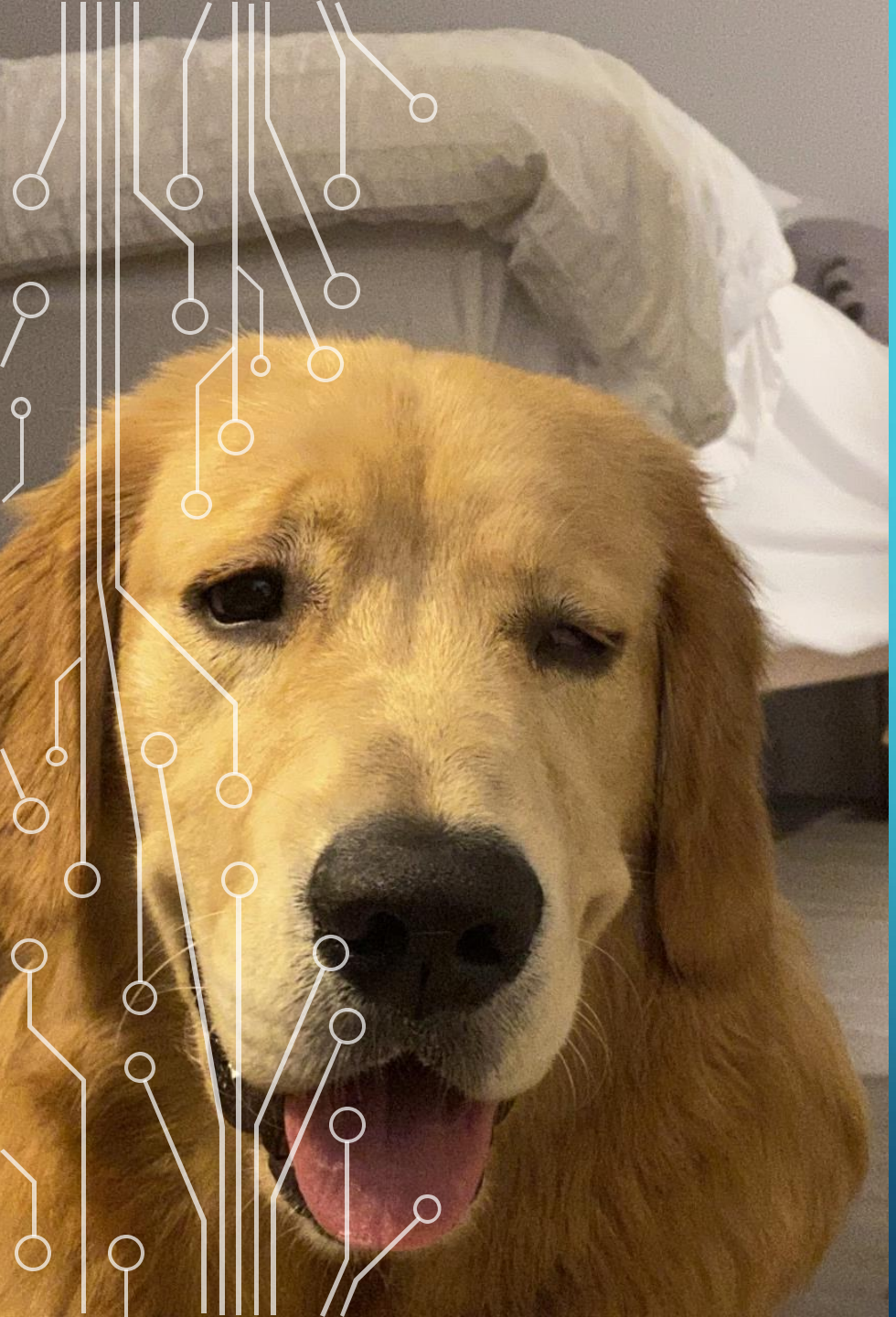
- Trough and peak levels are generally similar- if there is a big difference, split dose to q 8 hour dosing (i.e. 60mg BID becomes ~40mg TID)
- Monitor blood work every 6 to 12 months (sooner if lethargic, poor appetite, etc.) to suggest possible rising pheno level and liver toxicity

POTASSIUM BROMIDE (KBR)

- Dogs ONLY – Typically start at ~30-40mg/kg/day; often divided into q 12 hours
- ~3 MONTHS until steady state
- Common side effects: Sedation, ataxia, lethargy, paresis (especially PL), PU/PD, polyphagia
- Rare side effects: (Pancreatitis)**, Pruritus

POTASSIUM BROMIDE (KBR)

- Can use a loading dose
  - 600 to 1200mg/kg divided over 5 to 7 days
  - Give more often over the course of the day to help avoid GI upset
  - WILL see side effects→ Stop load if becoming unable to get up



KBR

- Before starting: CBC/ Chemistry
- After starting: Bromide level ~3 months later (Time of day does not matter)
- Ideal therapeutic range ~20-35mmol/L
- No real “upper” range vs. pheno; Driven by tolerance to side effects

KBR- ADDITIONAL PEARLS

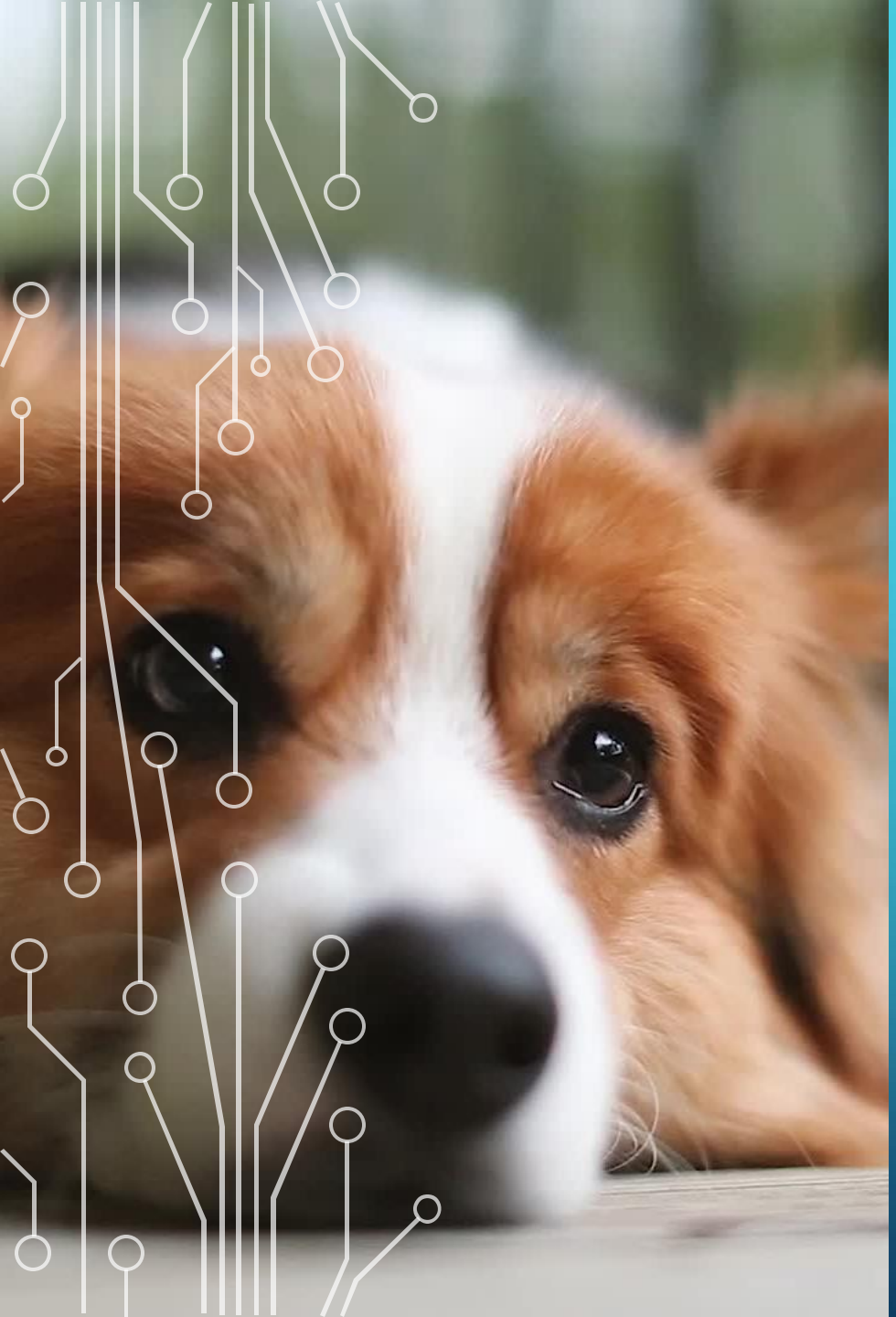
- Consistent diet required
- Swimming/ drinking ocean water also risky re: serum level stability

LEVETIRACETAM (KEPPRA)

- Dogs: 20mg/kg PO q 8 hours MIN; I generally start at 30mg/kg TID
- Cats similar dosing
- Toy breeds and dogs on phenobarbital require proportionately higher doses
- Common side effects: Minimal sedation, ataxia for first couple of days
- Rare side effects: PU/PD, aggression, ongoing lethargy (geriatric more common)

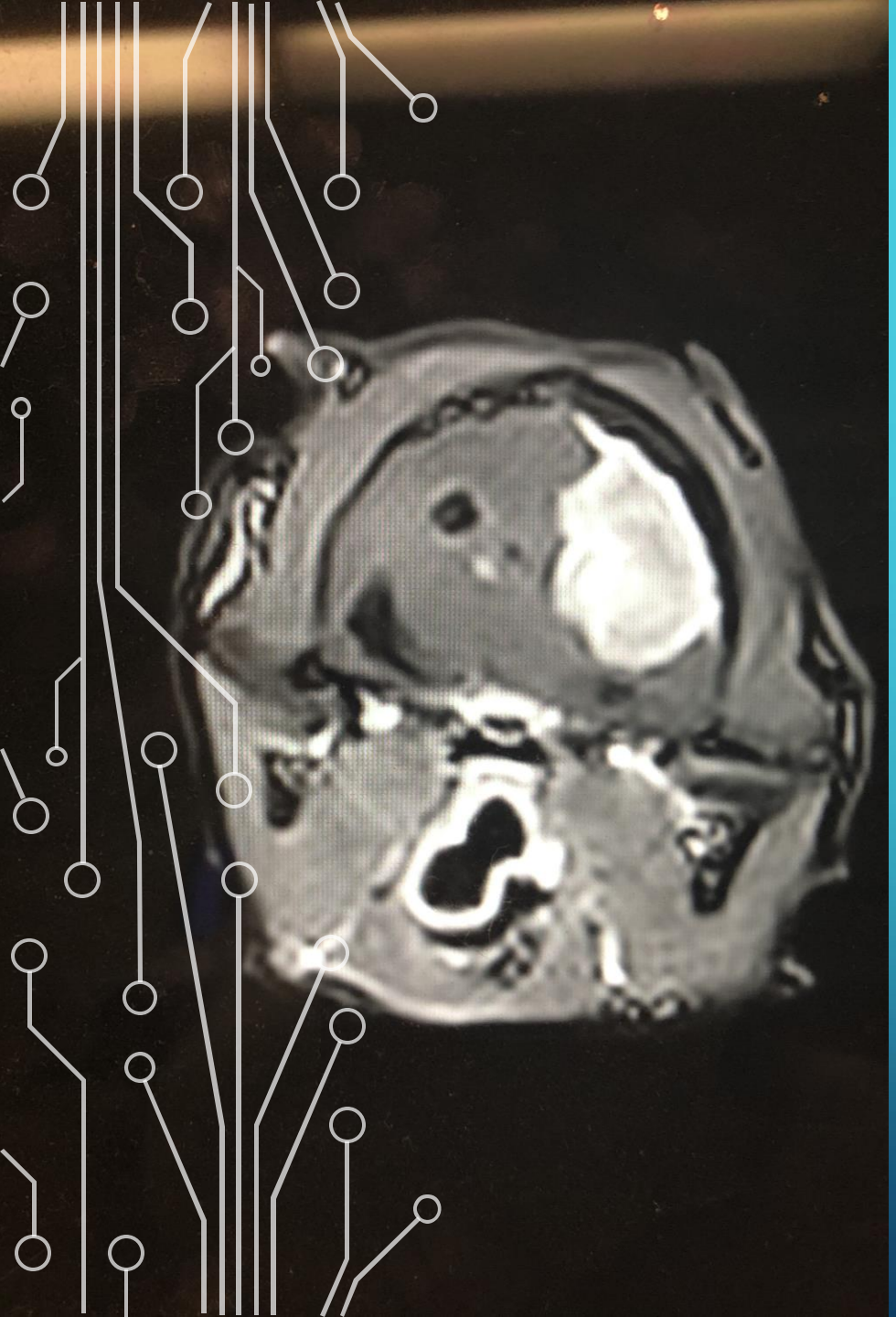
LEVETIRACETAM

- Before starting: CBC/ Chemistry
- After starting: CBC/ Chem q 12 months; Levels not routinely performed
- I will increase the dose gradually up to ~60-70mg/kg PO q 8 hours before I would consider a level vs. consider this medication is not the right choice for seizure control in a patient
- Logistical downsides: XR formulation not available in Canada



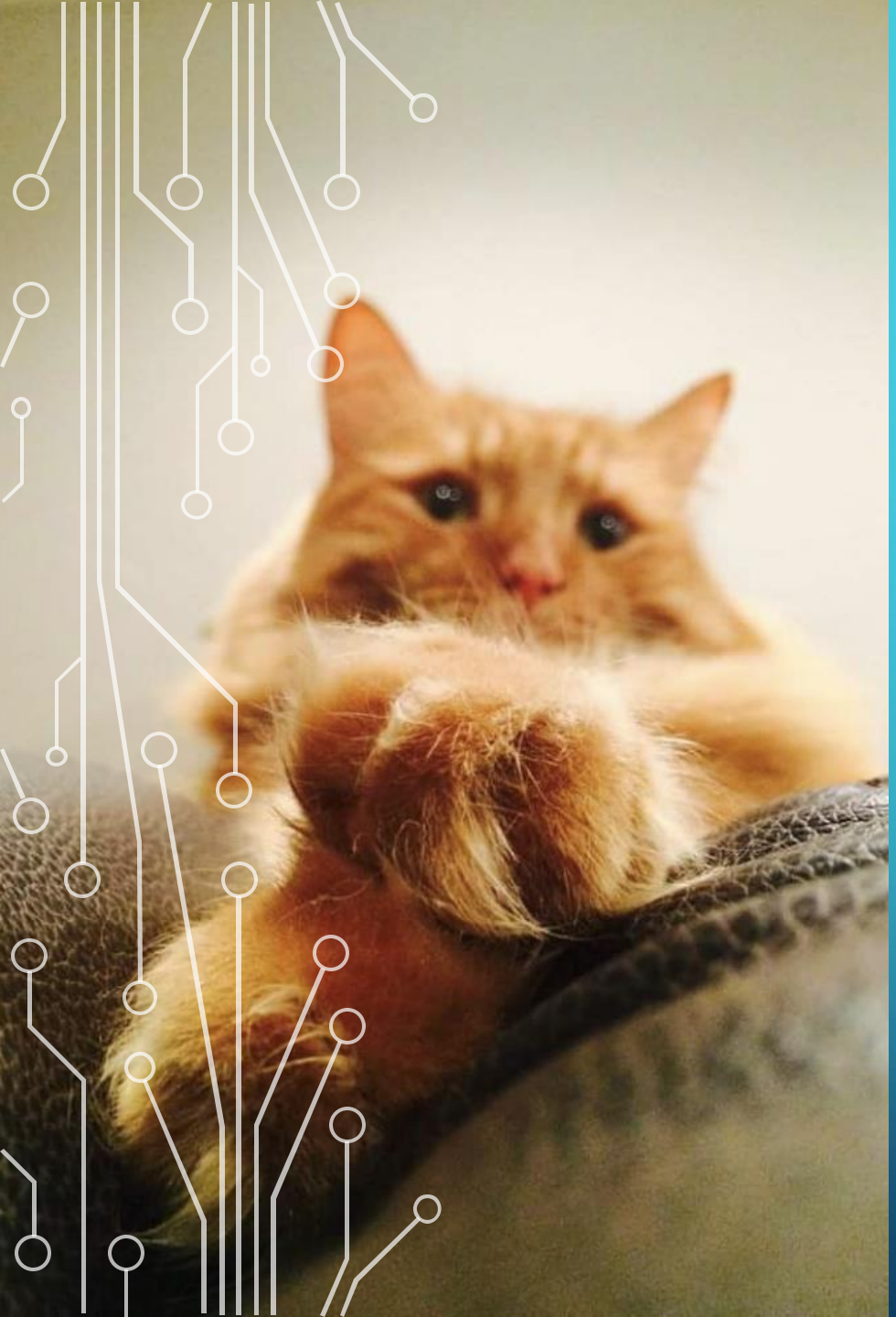
ZONISAMIDE

- Dogs 5-10mg/kg PO q 12 hours; starting at the high end of the range if already on phenobarbital (metabolized faster)
- Cats 3-5mg/kg PO q 24 hours, will increase to q 12 hours if seizures still occurring
- Common side effects: Sedation, lethargy for up to 1 week
- Rare side effects: Idiosyncratic liver toxicity, myelosuppression, renal tubular acidosis (RTA), dermatologic effects (similar to sulpha abx), anorexia



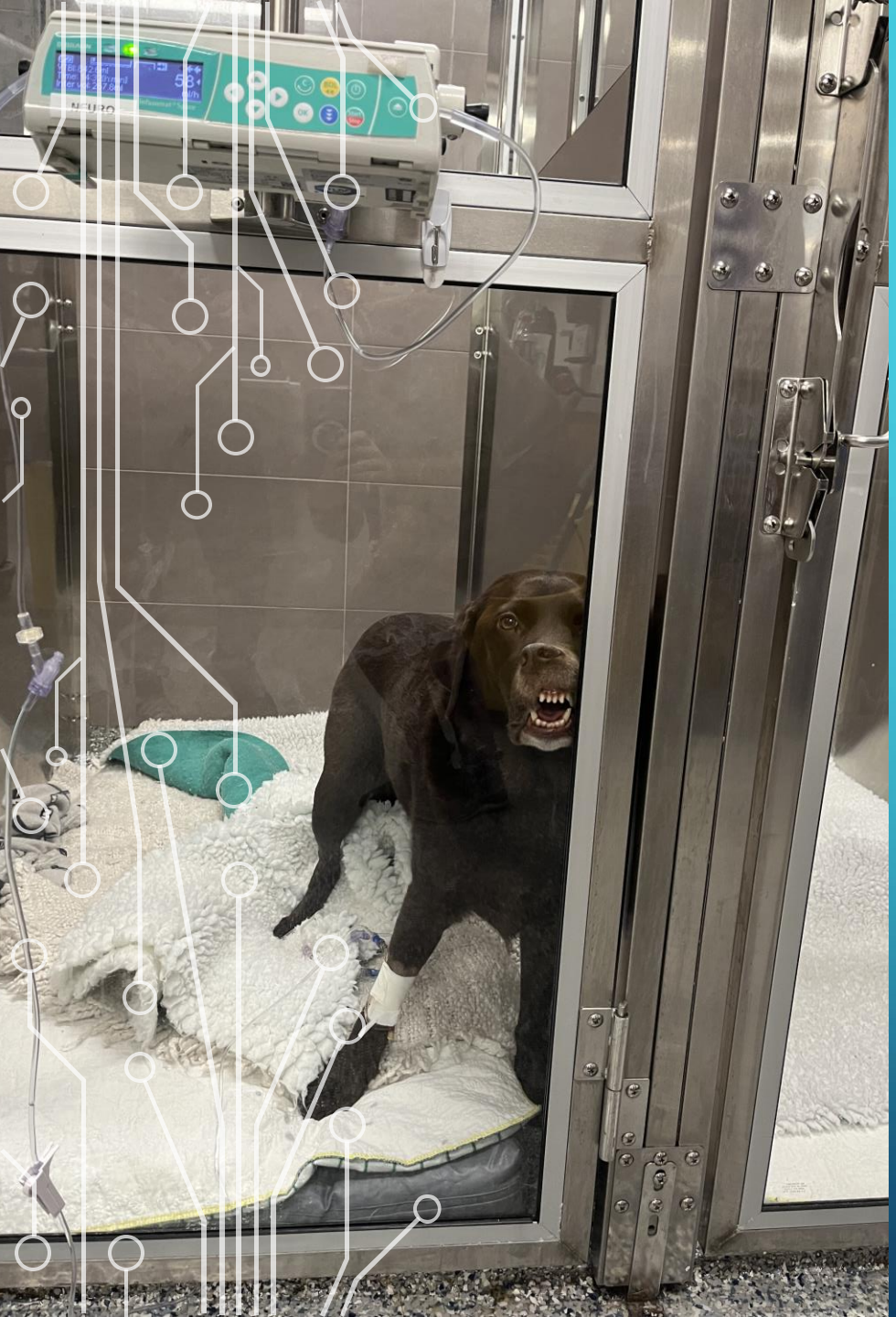
ZONISAMIDE

- Before starting: CBC, chemistry
- After starting: CBC/ Chem 4 weeks later; Levels not routinely performed
- Reference range for levels stolen from human medicine (not specific to dogs/ cats to expect seizure control at those levels)
- Max dose generally ~15mg/kg q 12 hours for dogs/ 5mg/kg q 12 hours for cats
- Logistical Downsides: Compounding pharmacies only in Canada



CLUSTER BUSTERS

- Rectal diazepam
- Intranasal midazolam
- Oral clonazepam
  - 0.5mg/kg q 8 hours Day 1, ~0.25mg/kg q 8 hours Day 2, ~0.1mg/kg q 8 hours Day 3
- Keppra for ~3 days
- Extra doses of maintenance AEDs



GOALS OF AEDS

- Reducing seizures to being less than 5 minutes individually, minimal clusters, no more often than 1 seizure every 8 to 12 weeks
- Reduce the “kindling” effect
- Reduce costs of emergency hospitalization for severe seizures
- Balance between QOL and seizure frequency

ADJUSTMENTS

- When the seizures are happening more often than our goal of 8 to 12 weeks
- Generally try & maximize the seizure control from 1 AED before adding a 2nd
- If seizure control is poor, I am adding a 2nd AED before I am thinking about tapering or stopping the 1st AED; Drugs can be synergistic with each other

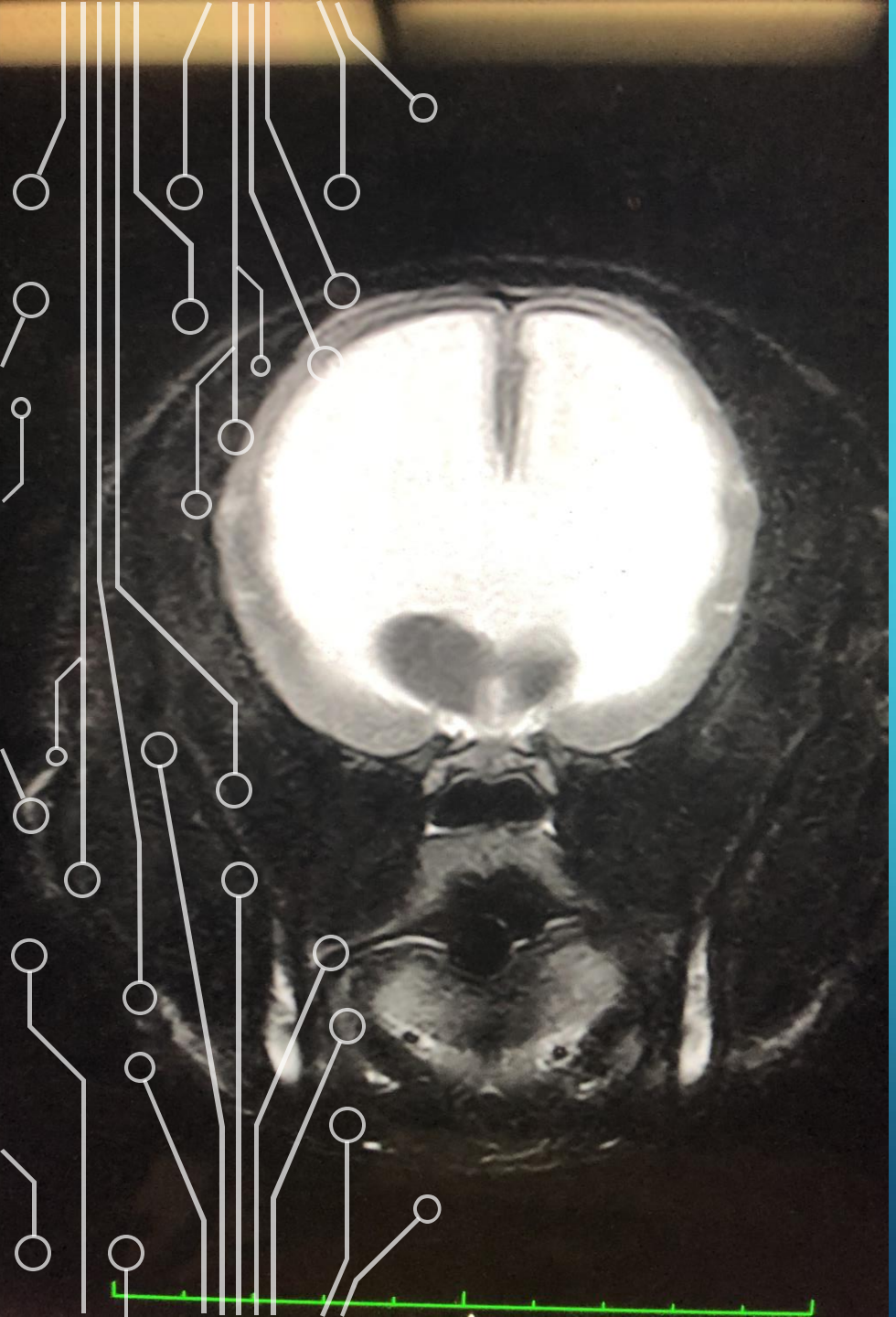
CASE EXAMPLES

- Case 1: Dog with seizures every 6 weeks, Wt=30kg and receives 90mg q12hr of pheno, no current concerns with AED side effects
- Pheno level 6 months ago= 95umol/L & seizures every 12 weeks at that time
- Repeat trough level today= 70umol/L (mechanism?)
- How do we maximize the pheno for this patient?

PHENOBARBITAL DOSE CALCULATIONS

- Current level: 70umol/L → Target level: 120umol/L
- Current dose 90mg q 12 → Target dose:?
- (Target level – Current level)/Current level = 50/70 =~0.71
- Therefore, you are going to want to raise the current dose by 71% to reach a blood level of ~120umol/L
- 90mg x1.71= 153.9, which in effect means 150mg q 12 hours

Remember to check a new pheno level in ~3-4 weeks to make sure not in toxic range



CASE EXAMPLES

- Case 2: Dog with seizures every 6 weeks, Wt=30kg and receives 90mg q12hr of pheno, no current concerns with AED side effects
- Pheno level 6 months ago= 120umol/L & seizures every 12 weeks at that time
- Repeat trough level today: 118umol/L
- Pheno is already maximized, time to add a 2nd AED

CASE EXAMPLES

- Case 3: 8yo Border Collie that has been on phenobarbital for 5 years
  - Seizures used to happen every 8 to 12 weeks; It has been 20 weeks since the last one
  - Owners initially happy with improved seizure control but have noted slow on walks, “a bit drunk”, appetite a bit off when used to be voracious
  - CBC/ Chemistry shows ALP of 3014U/L, ALT 500U/L, elevated GGT
  - Phenobarbital level 1 year ago was 125umol/L; now it is 180umol/L
  - Bile Acids are mildly elevated (pre – 20, post - 30)
  - Current phenobarbital dose is 75mg PO q 12 hours

IDEAL WORK UP

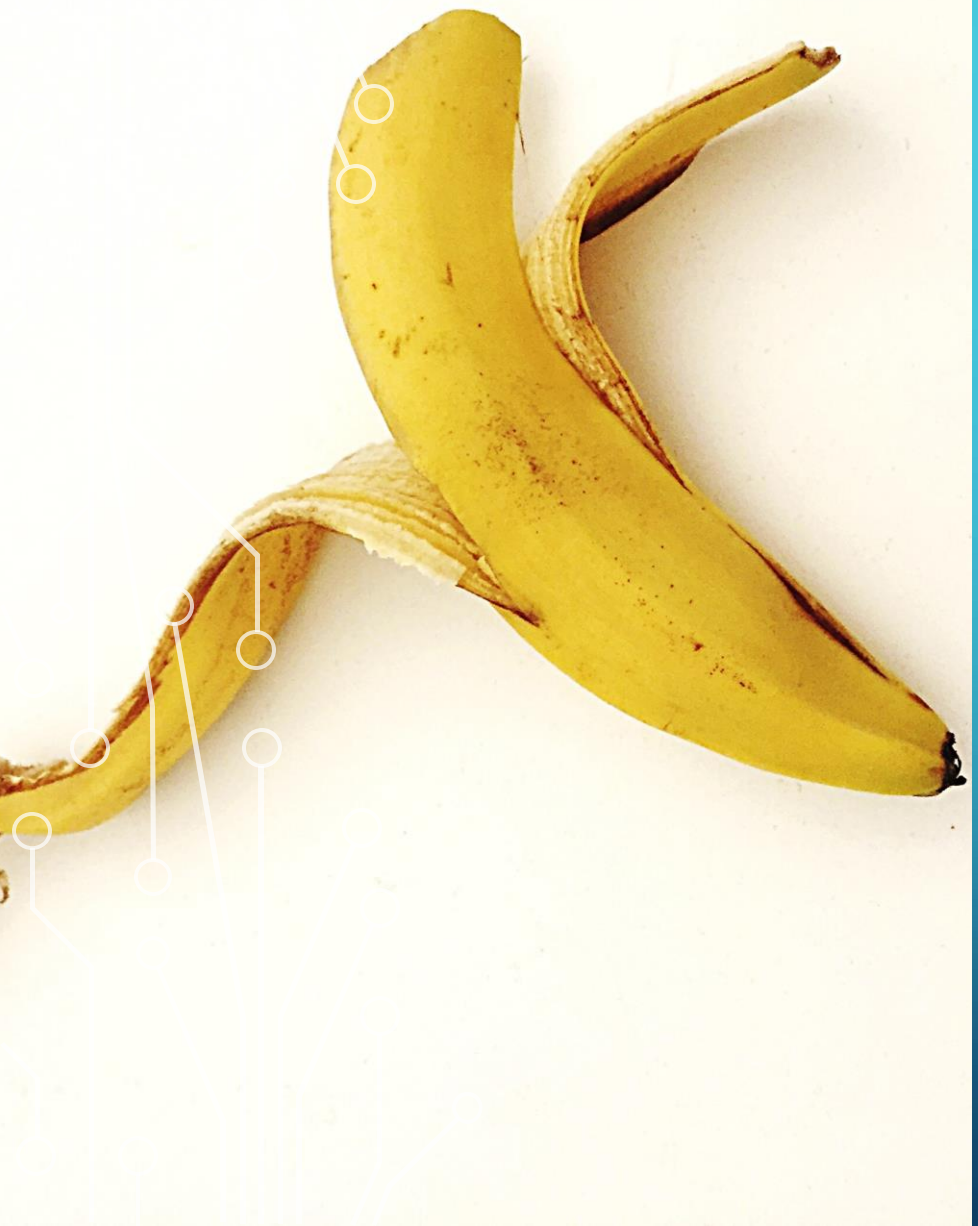
- Bile Acids can help you determine how upset the liver is over time
- Elevated phenobarbital is a “cheap bile acids” so the liver is likely a bit dysfunctional right now but may not be caused by the phenobarbital
- AUS to help r/o other causes of hepatopathy

NEXT STEPS FOR AED:

- Need to decrease the phenobarbital level back down to safe range; may or may not be able to stay on phenobarbital
- First step: 180 → 100umol/L serum level target is a ~44% decrease in level
- Decrease dose by similar percentage = 45mg PO BID (technically 42mg)
- Imperative to recheck Chemistry, phenobarbital level +/- bile acids in 3 weeks
- Start 2nd AED (levetiracetam or KBr), liver support medication in meantime

FOLLOW UP

- Scenario 1: Phenobarbital level now at 102umol/L and liver enzymes improving; Response: Recheck Chem/ pheno level in 2-3 months; sooner PRN
- Scenario 2: Phenobarbital level remains above >140umol/L, which means liver more unhappy than initial impression→ QUICKLY taper and stop phenobarbital within ~2-4 weeks; Start a 3rd AED (Risk of withdrawal seizures); Recheck values again once off phenobarbital for ~1 month



CASE EXAMPLES

- Case 4: 2 yo FS Cockapoo has been on phenobarbital for 1 year
- Had 2-3 “seizures” prior to being on phenobarbital within a 24 hour period but owners thought maybe she could have eaten something “off” at that time
- Seizure- free since she has been on Phenobarbital

TAPERING/ DISCONTINUING MEDS

- After ~1 year seizure-free it is an option to try and get off AED(s)
- However, important to move slowly to avoid withdrawal seizures
- Also, there is a risk that the seizures return and do not go back to being well controlled despite restarting the previous medication
- For phenobarbital: taper no more than 25% of the original dose once every 4 weeks until done (~4-5 months); If seizures return then pause the taper vs. increase dose back to previous step

TAPERING/ DISCONTINUING MEDS

- For levetiracetam- shorter acting drug, still a ~25% decrease but can decrease every 2 weeks; eliminate mid- day dose first to get to q 12 hours
- For bromide- will likely stick around for ~2-3 months following the last dose; still recommend not decreasing the dose more often than once every ~3-4 weeks unless dealing with toxicity
- For zonisamide- follow same plan as levetiracetam

QUESTIONS?