Presents a LIVE Web-Seminar

**Acute Management of Seizure Disorders**

With

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June 9th 2010
2000hrs AEST/2200hrs NZT
ACUTE MANAGEMENT OF SEIZURE DISORDERS
Dr Terry King BVSc MACVSc
Veteducation Web-Seminar Series 2010

SEIZURES and SEIZURE DISORDERS

Seizures
- Status epilepticus protocol
- CSF analysis
- Some neurological cases

Seizures
Status epilepticus protocol
- ABCD’s
- Stop the seizures
- Maintain homeostasis
- Monitor
- Diagnostics

Possible Complications of Status Epilepticus
- Acid-base imbalances
- Brain herniation
- Cardiac arrhythmias
- Compromised respiratory function
- Hyperglycaemia
- Hyperthermia
- Hypoglycaemia
- Myoglobinuria
- Neurogenic pulmonary oedema
- Permanent brain damage
- Renal failure
- Rhabdomyolysis

Status Epilepticus Protocol
ABCD’s
- Secure a patent airway
- Oxygen Therapy ~ flow by
- Intubation ~ ↓ aspiration

Status Epilepticus Protocol
ABCD’s
- Breathing
  - Mucous membrane colour
- Circulation
  - IV catheterisation
  - Pre-treatment blood samples

Status Epilepticus Protocol
ABCD’s
- Comatosed
  - Intubate & oxygenate
- Semi-comatosed
  - Anaesthetise, ventilation & Oxygenate

* Conscious & Respiratory insufficiency
  - Anaesthetise & ventilate
* Conscious & ventilating properly
  - Oxygenate

Stop the Seizures (1)
- Diazepam bolus 0.5-1.0mg/kg IV
- Peak Effect ~ Five minutes
- Therapeutic Levels ~ 20minutes
- Repeat twice more if necessary

Stop the Seizure (2)
- Diazepam CRI
  - 0.5-1.0mg/kg/hr
  - Can often reduce to 0.1mg/kg/hr
  - Dextrose 2.5% in saline @ maintenance rates

Stop the Seizure (3)
- Diazepam rectally ~ via tomcat catheter
- Therapeutic levels ~ 20-30minutes
- Dose ~ 0.5-1.0mg/kg

Stop the Seizure (4)
- Diazepam intranasally ~ soft catheter
- Peak Levels ~ 10minutes
- Volume?

Stop the Seizures (5)
- Diazepam relatives
- Midazolam IV or IM,
- Peak Effect ~ 15minutes post IM
- Quick, safe, reliable
- Expensive
- Lorazepam, Clonazepam

Stop the Seizures (6)
- Hypoglycaemia (?)
- Dextrose 50% 1ml/kg IV over 10-15minutes
- Repeat blood glucose level
- High demands ~ toy breed, paediatrics, vigorous exercise prior to seizure vs. Large breed middle aged/diabetics on insulin
Stop the Seizure (7)
- Hypocalcaemia (?)
- Calcium gluconate 10% IV slowly to effect
- 0.2ml/kg aliquots
- Total dose 4ml/kg
- Usually lactating bitch

Stop the Seizure (8)
- Phenobarbitone
- Refractory to diazepam
- Better than pentobarbitone (stop manifestations of seizure but not anticonvulsant)

Stop the Seizure (9)
- Phenobarbitone loading dose ~ 12-16mg/kg IV (65-100 umol/L blood level)
- Only if not already on phenobarbitone (PO)
- Phenobarbitone boluses
  - 2-4mg/kg IV, IM every 20minutes until seizures controlled
  - Maintenance dose every eight hours

Stop the Seizures (10)
Status Epilepticus
- Thiopentone 2-4mg/kg boluses
- Pentobarbitone 12-24mg/kg slow IV
- Propofol 1-2mg/kg bolus IV then CRI 0.1mg/kg/min
- Lignocaine?

Summary
- Diazepam boluses
- Phenobarbitone q20minutes
- Propofol CRI

Maintain Homeostasis (1)
- Monitor vital signs
- ABCD’s
- Administer appropriate fluids & electrolytes (acidosis)
- Thiamine (Vit B1) in cats 2mg/kg IM

Maintain Homeostasis (2)
- Hyperthermia
  - cold packs, moist towels, fan, methylated spirit
  - Aim for T = 39.5°C
  - If T > 41°C assume cerebral oedema
  - Mannitol 2.2g/kg IV +/- Dexamethasone 1mg/kg IV

Investigate Extracranial Causes(1)
- Hepatic encephalopathy
- Uraemic encephalopathy
- Electrolyte disturbances
  - Ca↓, K↑, Na↓↑, PO₄↓, Mg↓
  - alkalosis, osmolarity disorders

Investigate Extracranial Causes(2)
- B1, T4
- Hyperlipidaemia
- Polycythaemia

Investigate Extracranial Causes(3)
Toxicities
- Lead
- OP, OC, Metaldehyde
- 1080
- Salt
- Mushrooms

Monitor
- Airway patency
- Ventilation (SpO2, ETCO2, colour)
- Perfusion (colour, T*, Blood pressure, pulses)
- Electrolytes, PCV/TP
- Mentation (↑ ICP signs)
- Neurogenic Pulmonary Oedema

Investigate Intracranial Disorder
- Inflammatory
- Parasites
- Congenital/Inherited
- Vascular
- Trauma
- Neoplasia
- Idiopathic
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**STATUS EPILEPTICUS**

SIX MOST FREQUENTLY ASKED QUESTIONS IN THE MANAGEMENT OF THE REFRACTORY SEIZURING SMALL ANIMAL PATIENT.

**STATUS EPILEPTICUS**
- Recurrent seizures without complete normalisation of neurochemical and physiological homeostasis in the brain between seizures (without intervening periods of consciousness).
- Continuous seizure activity for ≥ 30 minutes, or ≥ 2 seizures without full recovery of consciousness between the attacks.
- People 5-10 minutes maximum.

**STATUS EPILEPTICUS**
- Life threatening neurologic emergency characterised by prolonged seizure activity.
- In general, there has been no definitive evidence connecting status epilepticus to any specific aetiology.

**STATUS EPILEPTICUS**
- Prompt recognition and treatment of seizures is important because prolonged or frequently repeated generalised seizures may lead to permanent brain injury.

“If appropriate recovery is delayed, status epilepticus can cause permanent sequelae or death”  ..........

Thus

“…… any child who presents actively convulsing should be assumed to have status epilepticus”.

Haafix, A.
Paediatric Emergency Care 1999; 15(2) : 119-129

**STATUS EPILEPTICUS**
Seizures may occur as a result of:
1. Substrate deprivation
   - Oxygen
   - Glucose
   - Sodium (maintains electrochemical property of neurones)
2. Synaptic dysfunction
   - Toxins
   - Metabolic encephalopathy’s
   - Infections inflammations
3. Brain injury
   - Trauma (acute and delayed)
   - Neoplasms
   - Vascular anomaly
4. Primary generalised epilepsy
   - Disturbance is probably related to neurotransmitter and synaptic dysfunction

The longer SE persists:
- The lower is the likelihood of spontaneous cessation
- The harder to control
- The higher the risk of M & M

Treatment for most seizures needs to be instituted after >5 mins of seizure activity

**STATUS EPILEPTICUS**

HUMANS
Mortality
Adults  15 – 22%
Children  3 – 15%

Fountain, NB
Epilepsia 2000 ; 41 Supp 2 : 523-530

**STATUS EPILEPTICUS**
Q.1 WHY STOP THE SEIZURES?
- Uncontrolled seizures lead to irreversible neuronal injury.
- Complications include acidosis, brain herniation, cardiac arrhythmias, compromised respiratory function, hyperglycaemia, hypoxia, hypotension, hyperthermia, hypothermia, myoglobinuria, DIC, neurogenic pulmonary oedema, renal failure, rhabdomyolysis, permanent brain damage.
STATUS EPILEPTICUS
Respiratory
Hypoxia and Hypercarbia
• ↓ ventilation (chest rigidity from muscle spasm)
• Hypermetabolism (↑ O2 consumption, ↑ CO2 production)
• Poor handling of secretions
• Neurogenic pulmonary oedema as a rare complication; likely occurs as a consequence of marked increase of pulmonary vascular pressure during SE

Johnstone, SC
Postictal pulmonary oedema requires pulmonary vascular pressure increases. Epilepsia 1996; 37(5) 428-432

STATUS EPILEPTICUS
HYPOXIA
• Hypoxia/anorexia markedly increase the risk of mortality in SE
• Seizures without hypoxia are much less dangerous than seizures and hypoxia

Towne, AR
Epilepsia 1994 : 35(1):27-34

STATUS EPILEPTICUS
ACIDOSIS
• Respiratory
• Lactic
  o Impaired tissue oxygenation
  o Increased E expenditure

STATUS EPILEPTICUS
HAEMODYNAMICS
• Sympathetic overdrive → within 30 – 60 minutes exhaustion (hypotension and hypoperfusion)
  o Massive catecholamine/Autonomic discharge
  o Hypertension
  o Tachycardia
  o High CVP

CEREBRAL BLOOD FLOW
Cerebral O2 Requirement

Hyperdynamic Phase
• CBF meets cerebral O2 requirement
Exhaustion Phase
• CBF drops as hypotension sets in
• Autoregulation exhausted
• Neuronal damage ensues

GLUCOSE
Hyperdynamic Phase
• hyperglycaemia
Exhaustion Phase
• hypoglycaemia develops
• Hypoglycaemia appears earlier in presence of hypoxia
• Neuronal damage ensues

HYPERPYREXIA
May develop in protracted SE and aggravate possible mismatch of cerebral metabolic requirement and substitute delivery

GOALS OF TREATMENT
• Stop the seizures
• Protect the brain from further damage (↓ ICP by ↓ cerebral oedema by providing the care to support neuronal metabolic activity)
• Allow full recovery from the SE episode

STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

Complications:
• Autonomic changes - ↑BP, ↑HR, ↑T’, arrhythmias, vomiting; ↑BG (sympathetic stimulation, catecholamines, glucagon release)
• Indirect – rhabdomyolysis with myoglobinuria & ARF, pulmonary oedema, aspiration pneumonitis.
• Prolonged S.E. → metabolic decompensation with ↓BP, ↓HR, hypoxaemia, ↓BG, acidosis, ↑K”, cerebral oedema (loss of cerebral auto regulation), irreversible organ failure (renal, cardiac, hepatic) from circulatory collapse, organ hypoperfusion and energy depletion.
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STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

“Seizure induced rhabdomyolysis accompanied by acute renal failure in a young dog”.
Spangler WL, Muggli FM JAVMA 1978 May 15; 172 (10) 1190-4

STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

• Physical exertion → necrosis of skeletal muscle → ↑ myoglobs → severe impairment of renal function
• Anoxia (↓ breathing during seizures) → brain damage.

STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

Conclusions:
• Primary treatment to alleviate the intense seizure activity
• Subsequent screening for renal disease and corollary supportive treatment is appropriate.

STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

59% of Idiopathic Epilepsy patients have ≥ 1 S.E. episode during the course of the disease.
Saito M, JAVMA 2001; 219: 618-623

Risk of developing S.E. is higher for 2' epilepsy.
Platt SR, JSAP 2002; 43: 151-3

31% of human S.E. patients developed Refractory S.E.
Mayer SA, Arch Neurol 59: 205 2062

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?

Diazepam
• Effective rectally, nasally, IV
• Rectally:
  o ~ 1mg/kg at onset of seizures
  o ~ 2mg/kg if receiving phenobarbitone


STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

“Kindling” process – one seizure leads to intensification of subsequent seizures.

The longer you wait with anticonvulsant, the more anticonvulsant you will need to stop SE.
Most common mistake is ineffective dose.

Studies in human epilepsies demonstrate that patients who have a greater number of seizures prior to initiation of treatment are more likely to have refractory epilepsy.

STATUS EPILEPTICUS
Q.1 WHY STOP THE SEIZURES (S.E.)?

“Kindling” process – one seizure leads to intensification of subsequent seizures.

Dogs with Idiopathic Epilepsy in which therapy was initiated early in the course of the disease (based on total number of seizures) responded better to treatment compared to dogs in which treatment was delayed.
Heynold Y et al, JSAP 1997; 38:7-14
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STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Diazepam

“The use of diazepam per rectum at home for the acute management of cluster seizures in dogs”
Podell J. JVIM 1995, 9(2); 68-74

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Diazepam:

11 dogs over 18 months (Idiopathic Epilepsy), all on phenobarbitone and 10 also on KBr.
Diazepam 0.5mg/kg PR when 1’ seizure occurred and when a 2’ or 3’ seizure occurred within 24 hours.
Results:
↓ no. of seizure events
↓ no. of clusters
↓ no. of seizures per cluster
↓ no. of isolated seizure events

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Midazolam:

Not effective rectally (gets very low system bioavailability rectally)
IV 0.1-0.5 mg/kg bolus
0.1-0.5 mg/kg/hr CRI
Angelini G et al, Crit.Care Med. 2001; 17(4) 863-880

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Midazolam:

Water soluble; no problems with adhering to plastics; no problems with calcium containing solutions
Becomes lipid soluble @ physiologic pH and readily crosses B.B.B.
Shorter ½ life more rapid onset of action and steeper dose-response curve
No problem with tolerance?

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Midazolam vs Propofol
Midazolam + Propofol

Midazolam: Better maintenance of sedation, amnesia, lower cost
Propofol: More CV depression (especially during induction), less respiratory depression
Weinbroum AA et al, Int.Care Med. 1997; 23(12) 1258-63

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Lorazepam:

Long acting benzodiazepine that interacts with a high degree of infinity for the GABA receptor complex
0.2mg/kg IV vs diazepam (0.5mg/kg) had no significant difference in median seizure-free interval, precent seizure free, or number of dogs in seizures were initially controlled

0.2 – 0.5 mg/kg/hr compares favourably with diazepam (0.5-1.0 mg/kg/hr CRI)
Coates J, IVECCS 2002

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?

“Development of tolerance to be anticonvulsant effect of diazepam in dogs”

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?

Diazepam PO + IV → convulsive threshold for pentetrazole despite ↑ concentration of diazepam and its active metabolites (hence a functional tolerance)

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?

Desmethyldiazepam IV and chlorazepate PO (converted by gastric acid to desmethyldiazepam) did not produce tolerance
Clinically (tolerance → ↑ seizures) and chemically (lessened effect of drug on spiking activity in ECG)

STATUS EPILEPTICUS
Q.2 WHAT WORKS IN S.E.?
Methocarbamol, Guaifenesin, Pancuronium, Vecuronium

Muscle relaxants prevent tonic-clonic movements, however do not prevent seizure activity
Results have shown irreversible cerebral damage in animals with curariisation and ongoing seizure activity
**STATUS EPILEPTICUS**

**Q.2 WHAT WORKS IN S.E.?**

- n-m blocking agents may abolish tonic-clonic movements and may facilitate ventilation and other measures but have no effect on abnormal neuronal activity; need EEG monitoring to assess the effectiveness of anticonvulsant therapy.


**STATUS EPILEPTICUS**

**Q.2 WHAT WORKS IN S.E.?**

**Propofol**

- "Propofol for treatment of refractory seizures in dogs (12) and a cat (1) with intracranial disorders”
  Steffan F, JSAP 2000; 41(11) 496-9

  - Boluses of 2-8 mg/kg
  - All were on medication (diazepam ±, phenobarbitone, ± pentobarbitone)
  - 1 died; 10/11 controlled

**STATUS EPILEPTICUS**

**Q.2 WHAT WORKS IN S.E.?**

**Propofol**

1. Barbiturates and benzodiazepines like effects on GABA-A receptor and can suppress CNS metabolic activity
2. ↓ cerebral O2 consumption
3. ↓ ICP
4. Potent antiepileptic convulsant properties
5. Hypotension is most common side effect
6. Rare Mburia in long standing CRI

**STATUS EPILEPTICUS**

**Q.2 WHAT WORKS IN S.E.?**

**Propofol**

± Midazolam

Pappagallo S, Minerva Anaesth. 1993; 59(9) 441-6
Beyer R, JSAP 1996; 37(7) 317-21
Beller JP, Br.J.Anaes 1998; 61(5) 583-8

- "Use of propofol to manage seizure activity after surgical treatment of portosystemic shunts”.
  Heldmann E, Holt DE et al JSAP 1999; 40(12) 590-4

**STATUS EPILEPTICUS**

**Q.2 WHAT WORKS IN S.E.?**

**Propofol**

- 4 cats and 1 dog
- 1-3.5 mg/kg bolus and 10-25 mcg/kg/min CRI⇒ good control in all cases, however, good neurological outcome in only 2/5 cases.

- 12-16 mg/kg if naïve
- 2-6 mg/kg if already on phenobarb

± Phenobarbitone (takes 15-30 minutes to exert effect)

- 0.2-1.0 mg/kg/hr

**STATUS EPILEPTICUS**

**Q.3 TREATMENT ALGORHYTHM**

If seizures persistent, general anaesthetic?

- Pentobarbitone
  - 2 mg/kg to effect then CRI 1-5 mg/kg/hr
  - or
  - Propofol
  - 3-6mg/kg to effect then CRI 8-12 mg/kg/hr
  - or
  - 100 – 200 mcg/kg/min
  - or
  - ± Midazolam
  - 0.15 mg/kg bolus then CRI of 1-10 mcg/kg/min
  - or
  - Isoflurane
  - 2% MAC if poor liver function

Monitor for hypoventilation; may require mechanical support

**STATUS EPILEPTICUS**

**Q.3 TREATMENT ALGORHYTHM**

- Once stabilised, maintenance AED therapy is started
- Phenobarbitone IV/IM until PO medication can be started

**STATUS EPILEPTICUS**

**Q.4 WHAT’S COMING FOR S.E.?**

Standard drugs in use:

- Diazepam’s etc. often ineffective in halting seizures
- Barbiturates
- Propofol

Disadvantage is sedation ⇒ often need intubation
STATUS EPILEPTICUS
Q.4 WHAT’S COMING FOR S.E.?
Phenytoin (humans)
• Most important drug in management of S.E.
• Injectable and oral: low cost
• Can cause cardiac arrhythmias (need ECG monitoring) and contraindicated if 2’ or 3’ heart block
• May cause ↓ BP
• Largely protein bound, hence toxicity more likely if hypoproteinaemia
• Precipitates in glucose containing solutions
• Sloughs occur if goes perivascularly


STATUS EPILEPTICUS
Q.4 WHAT’S COMING FOR S.E.?
Fosphenytoin
• A phosphate ester of phenytoin but not a problem previously and less cardiac arrhythmias effects.
• Effective IV & IM in people
• Minimal sedation
• Well tolerated IV in dogs and reaches levels consistent with those thought to be therapeutic in people
• Dose and efficiency presently being determined, including CRI management.

Dewey CW et al, JAAHA 2004; 40:285

STATUS EPILEPTICUS
Q.4 WHAT’S COMING FOR S.E.?
Levetiracetam (LEV)
• No sedation
• Well tolerated IV in dogs
• Does not undergo hepatic metabolism, so may be a useful drug for seizure management in post-operative PSS’s?
• Good potential for CRI management

Dewey CW et al, JAAHA 2004; 40:285

STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
• Primarily epilepsy probably uncommon (7-60% depending on the study) and hence should suspect the presence of an underlying cause of seizures in the cat
• Extracranial causes
  • metabolic (liver disease, hyper T4, hypo G, electrolyte disturbances, polycythaemia, anaemia)
  • Nutritional disorders (thiamine)
  • Toxins (OP’s, heavy metals, ethylene glycol)

Center SA et al, JAVMA 1996; 209: 618-625

STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
• Oral diazepam and fulminant liver failure
  • Idiosyncratic reaction to 5-7days p/o diazepam (generic brand)

Boothe DM et al, JAVMA 2002; 221: 1131-5
STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
S.E. treatment similar to dogs
• Diazepam is eliminated slowly, hence may be sufficient
• Diazepam +/- phenobarbitone can induce profound sedation; hypothermia and bladder paresis are common sequelae
STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
“The effects of consecutive day propofol anaesthesia on feline red blood cells”
STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
• 6 cats given G.A. (6 mg/kg) then CRI 200-300 mcg/kg/min for 30 minutes S/D/10 days but average 6 days (none > 7 days) in investigation of the potential of propofol to induce oxidative injury (in the form of Heinz bodies) to feline RBC’s
• No haemolysis detected in any cat
• ≥ 3 days, significant ↑ in mean % Heinz bodies
STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
Recovery time significantly ↑ after 2’ consecutive day
• 5/6 developed malaise, anorexia, diarrhoea
• 2/6 developed facial oedema
• All signs resolved without treatment 24-48 hours after propofol
STATUS EPILEPTICUS
Q.5 WHAT ABOUT CATS?
PROGNOSIS
• Underlying cause
• Lot of cats develop clusters or S.E. at onset of seizures and may require aggressive AED therapy from the onset; however, severity of seizures at onset NOT a good predictor of outcome.
STATUS EPILEPTICUS
Q.6 TIPS FOR CLINICAL MANAGEMENT OF S.E.?
Diazepam
• Adheres to plastic
• Inactivated by light
• 0.9% NaCl and P148 don’t microprecipitate diazepam
• Rubber catheter or teat cannula for rectal administration (pharmacokinetics of suppository forms have not been studied in dogs)
STATUS EPILEPTICUS
Q.6 TIPS FOR CLINICAL MANAGEMENT OF S.E.?
IV Solutions
• Animals on bromide (KBr) should be given 0.45& NaCl and 2 ½% Dextrose as the additional chloride in 0.9% NaCl will result in increased excretion of bromide and hence a drop in serum concentrations.
• In general, don’t use glucose containing solutions unless hypoglycaemia is documented – hyperglycaemia in the face of reduced oxidative phosphorylation in the brain results in CNS lactic acidosis and resultant neuronal necrosis.
STATUS EPILEPTICUS
Q.6 TIPS FOR CLINICAL MANAGEMENT OF S.E.?
Phenobarbitone
• Give slowly (if IV) to avoid CV and respiratory depression from combined effects of diazepam and phenobarb
STATUS EPILEPTICUS
Q.6 TIPS FOR CLINICAL MANAGEMENT OF S.E.?
Deteriorating CNS
• If suspicion of an underlying intracranial mass, give mannitol (1 mg/kg) IV over 15 minutes for treatment of underlying cerebral oedema
• Corticosteroids usually withheld until a diagnosis is obtained or if there is evidence of underlying cerebral herniation (dexamethasone NaPO4 0.25-1.0 mg/kg IV)
STATUS EPILEPTICUS
Q.6 TIPS FOR CLINICAL MANAGEMENT OF S.E.?

Corticosteroids
- Indicated if hypoglycaemia is resistant to glucose administration or is associated with signs of adrenal insufficiency.
- Hydrocortisone (5-15 mg/kg IV)
  Failure to respond to a parenteral glucose administration should prompt consideration of other causes of hypoglycaemia – sepsis, toxin, insulinoma, hepatic failure, adrenal insufficiency.

Corticosteroids
To target the primary disease and help seizure control, give 0.25 mg/kg Dexamethasone IV bolus to:

a) reduce peri-tumoural cerebral inflammation in case of cerebral tumour.

b) antagonise insulin effects at the cellular level and enhance hepatic glycogenolysis in the occurrence of an insulin secreting tumour.

STATUS EPILEPTICUS
Q.6 TIPS FOR CLINICAL MANAGEMENT OF S.E.?

Glucose
- Give 100-200 mg/kg (1-4 ml/kg of 10% dextrose) IV if hypoglycaemia.
- Thiamine I/M should precede glucose administration as it is essential as a coenzyme in glucose utilisation in the brain (aerobic glycolytic metabolism).
- 10-100mg I/M in kitty’s.

Thank you.
CAUSES OF SEIZURES

EXTRACRANIAL

Systemic Metabolic Diseases
- Hepatic encephalopathy
- Uraemic encaphalopathy
- Hypoxia
- Hyperthermia
- Hypoglycaemia
  ➤ diabetes
  ➤ starvation
    (pups, kittens)
  ➤ insulinoma
- Hypocalcaemia
- Hyperkalaemia
- Hyponatraemia
- Hypernatraemia
- Hypophasphataemia
- Hypomagnesaemia
- Hypothyroidism
- Thiamine deficiency
- Hyperlipidaemia
- Hyperlipoproteinaemia
- Acid/base imbalanes (esp alkalosis)
- Osmolalitv disorders
- Polycythaemia
- Hyperviscosity syndrome

Toxicities
- Lead
- Organophosphates
- Metaldehyde (snail bait)
- Pyrethrin (cats)
- Ethylene glycol
- Strychnine
- Arsenic

Other toxins include:
- fluoroacetate (1080)
- salt
- salicylate (aspirin)
- bromethalin (rodenticides)
- organocarbamate
- chlorinated hydrocarbons
- theobromines (chocolate)
- blue-green algae
- motor oil and grease
- gasoline/kerosene
- paradichlorobenzene
  (mothballs)
- dipyridyl compounds
  (paraquat)
- rhododendron
- roquefortine
  (mouldy cheese)

INTRACRANIAL

Inflammatory Disorders
- Canine distemper virus
- Rabies
- Fungal encephalitis
- Bacterial encephalitis
- Rickettsial meningoencephalitis
- Psudorabies
- Granulomatous meningoencephalitis
- Pug dog encephalitis
- Feline infectious peritonitis
- Feline immunodeficiency virus
- Polioencephalomyelitis

Parasites
- Aberrant migration of Cuterebra or Dirofilaria
- Fleas
- Hookworm
- Cryptococcus
- Toxoplasmosis

Congenital or Inherited Disorders
- Hydrocephalus
- Portosystemic shunt
- Lissencephaly
- Primary epilepsy
- Lysosomol storage diseases

Vascular Disorders
- Feline ischaemic encephalopathy
- Ischaemia (stroke)

Trauma
- Severe head trauma
- Cerebral hypoxia/anoxia

Neoplasia
- Primary brain tumors (meningiomas, glial cell tumor)
- Metastatic brain tumor

Idiopathic conditions
- Feline hyperaesthesia syndrome
- Springer Spaniel rage syndrome
- Idiopathic Epilepsy
**DIAGRAM ONE - Emergency protocol for status epilepticus**

1. **Generalised Tonic-Clonic Status Epilepticus**
   - A diabetic animal on insulin Therapy
   - A young animal or toy breed
   - An animal that was vigorously

2. **History**
   - **or**
   - **or**

3. **Any other patient**

4. **Lactating Bitch**

5. **Diabetes Animus on Insulin Therapy**
   - Administer 50% dextrose Solution at 2 mL/kg intravenously

6. **History**

7. **Any other patient**

8. **Lactating Bitch**

9. **Collect blood ASAP for: CBC, TP, BUN, glucose and Ca**

10. **Diazepam 0.5 mg/kg IV/PR**

11. **Wait 20-60 seconds**

12. **Seizures persist**

13. **More than 1-2 mg/kg Diazepam given?**
   - **No**
   - **Yes**

14. **Wait 15-30 minutes?**

15. **Seizures persist?**

16. **Start Phenobarbital load 2mg/kg IM/IV**

17. **Repeated twice?**
   - **No**
   - **Yes**

18. **Go to refractory status protocol**

19. (i) Consider the cause
    (ii) Assess the need for maintenance of anticonvulsant treatment
DIAGRAM TWO – Emergency protocol for refractory status epilepticus

Seizures persist despite treatment with diazepam and phenobarbital

Options are:
(i) Additional low-dose boluses of diazepam
(ii) Continuous IV diazepam infusion 0.1 mg/kg/hour in 2.5% dextrose/0.9% sodium chloride drip at maintenance rate
(iii) No further treatment except to optimize Phenobarbital serum level

Medical team and owner decide to use aggressive treatment

Consider:
(i) Intubation/ventilation
(ii) Arterial line for blood gas evaluation
(iii) Urethral catheter
(iv) Continuous electrocardiogram

Consider cause and institute maintenance therapy

Propofol bolus (2-8 mg/kg IV) followed by constant rate infusion (0.1-0.6 mg/kg/min IV)

Seizures stop

Phenobarbital infusion maximum 24 mg/kg/day

IV pentobarbital
(i) 3-15 mg/kg to effect
(ii) Dopamine to maintain blood

Significant hypotension/bradycardia

IV dopamine infusion 2-10 g/kg/min and/or IV dobutamine 2-10 g/kg/min

Seizures stop

Severe decreased blood pressure

IV pentobarbital infusion 1 mg/kg/hour up to 6 hours

Poor prognosis consider:
(i) Isoflurane anaesthesia
(ii) Propofol infusion 0.1-0.6 mg/kg/minute
(iii) IV mannitol 1g/kg bolus
(iv) IV furosemide 0.7 mg/kg
Appendix A: Diagnostic approach to status epilepticus:

1. Ask to owner:
   - Age?
   - Duration of the seizure?
   - Previous seizure history?
   - Current anticonvulsant therapy?
   - Current insulin therapy?
   - Recent trauma?
   - Exposure to a toxin?

2. Stop the seizures:
   - Give 5-35 mg Diazepam IV (Valium: 0.5-1.0 mg/kg). Generally diazepam maintains a therapeutic blood level for only about 20 minutes.
   - Should a second or third dose of diazepam be needed or if the dog or cat does not have a maintenance level of Phenobarbital from previous anticonvulsant therapy, commence PHENOBRABTIAL with the FIRST LOADING DOSE ONLY given at a dosage of 12-16 mg/kg IV to achieve a 65-100 umol/L blood level immediately.
   - After first treatment continue Phenobarbital at a dosage of 2-4 mg/kg every 20 minutes IM or IV IF NEEDED until seizure control is achieved. It take at least 20 minutes from IV Phenobarbital administration for the drug to have an anticonvulsant effect.
   - Should the dog have a maintenance level of Phenobarbital on admission, then avoid the loading dose, and begin 24 mg/kg Phenobarbital IV every 20 minutes until seizure control is achieved. Upon achieving control maintenance phenobarbital is given every 8-12 hours.
   - If Phenobarbital does not stop the seizure within 20 minutes or less give PENTOBARBITAL to effect (18-24 mg/kg or less IV). Since phenobarbital and diazepam potentiate the effect of pentobarbital, GIVE THE PENTOBARBITAL VERY SLOWLY OVER SEVERAL MINUTES. (Note - pentobarbital IS NOT an anticonvulsant, and will stop only the overt manifestations of seizures!)
   - Avoid phenothiazine tranquillisers as the may potentiate seizures

3. Assure the animal is breathing once the seizure is stopped. Intubate and ventilate if necessary.


5. Give 25% DEXTORSE (8mL/kg) IV if indicated. Also if indicated give CALCIUM GLUCONATE IV SLOWLY (4 mL/kg of 10% solution)

6. If body temperature is > 41 degrees C, cool with cold water. Stop the cold water as soon as rectal temperature begins to decline or hypothermia may result. Whole body submersion is the most effective cooling method.

7. If body temperature > 41 degrees C, assume cerebral oedema is present and may be causing cortical necrosis. Five 2.2 grams/kg of 20% MANNITOL IV and lmg/kg dexamethasone Na P04 IV. Reduce dexamethasone dose by 50% every 6 hours for 24 hours. Then continue 0.2 mg/kg/day dexamethasone only if needed.
8. Should the animal be unconscious for a prolonged period, or should the PCV and TS indicate the development of dehydration, place an IV catheter and give IV fluids SLOWLY. Do not over hydrate as this will worsen cerebral oedema.

9. Start oral anticonvulsant medication as soon as possible. In most cases oral phenobarbital is indicated.

10. Animals that have had lengthy episodes of status epilepticus (30 minutes or longer) may require days or weeks to return to normal function. Permanent neurologic deficits occasionally result from severe episodes of status epilepticus, however these should not be assumed to be induced by hypoxia and/or hyperthermia unless other causes are eliminated.

11. As soon as animal is stable, commence workup for a cause of the seizures.
Seizuring Patient

Minimum Data Base

1. Patient Profile
   - Age, breed, sex, species
2. History
   - Vaccination - what, when and by whom
   - Environment
   - Age at onset of seizures
   - Frequency and course of seizures
   - Description of seizure
     - General vs. partial
     - Duration
     - Post ictal signs
     - Any preictal signs
     - Any preictal signs
     - Time of day (relation to food, sleep and stimuli)
     - Previous or present illness or injury (trauma with period of stupor or coma, encephalitis, neonatal hypoxia)
     - Behavioural changes
3. Complete physical exam
   - Musculoskeletal
     - Size and shape of skull
     - Evidence or trauma or muscle atrophy
   - Cardiovascular
     - Mm colour
     - Arrhythmias or murmurs
   - Respiratory
   - Hepatic
   - Urinary system
   - Fundoscopic exam - evidence of neoplasia?
4. Complete neuro exam
   - Localising lesions indicate acquired intracranial disease
   - Note time of last seizure. If in last 24-48 hours and abnormal exam, repeat in 24 hours.

Minimum Data Base (cont’d)

5. Clinical Pathology
   - Blood
     - CT/ACTT
     - WCC
     - RCC
     - RBC morphology
     - Cytology (inclusions)
   - Biochemistry
     - 24 hour fasting glucose
     - Calcium
     - Urea/creatinine
     - ALT/ALP
     - AST/CK
     - Sodium
     - Potassium
     - Ammonia tolerance test
     - Pre and post prandial bile acids
   - Urine
     - Specific gravity
     - Glucose/ketones
     - Bilirubin/urobilinogen
     - Crystals in sediment
     - Fungi in sediment
   - Other tests as indicated
     - Lead
     - Serology
     - Culture
     - Serum cholinesterase
     - Thyroid function
   - Chest xray - met check - may choose not to treat if find tumours.

Positive findings
- Metabolic
- Developmental
- Toxic
- Traumatic

Suggestive findings
- Metabolic toxic
- Rule out with specific tests

Complete Data Base
- CT or MRI
- CSF after rule out extracranial causes
- Skull radiographs
- EEG

Abnormal neuro and any age

Normal neuro > 5-7 yr old

If poor control and serum levels are adequate
- Treat with anticonvulsants

Negative findings
- Assume idiopathic
- Repeat evaluation at intervals or as status changes
- Treat with anticonvulsants
**Anticonvulsant Therapy: A Review**

**Phenobarbital**

Half Life:-
- Dog: 47-74 hours
- Cat: 34-43 hours
- Will decrease with time (induces hepatic enzymes)

Steady state - 5 half lives

Mechanism of action:-
- Increase Cl- inside cells
- Stops Ca++ dependent neurotransmitter release
- Suppresses focal seizure discharges
- Decreases neuronal excitability
- Increases AP threshold to electrical stimulus

Metabolism:-
- Hepatic
- Ideally check bile acids BEFORE starting medication

Side effects:-
- Sedation, PU/PD, restlessness
- May alter metabolism of other drugs, T4
- Liver toxicity

Dose:-
- Initial 2-4 mg/kg PO bid

Monitoring:-
- Serum levels in 2 weeks from commencement
- Then every 2-3 months depending on clinical signs

**KBr (Potassium bromide)**

Half Life:-
- Dog: 25 days
- Cat - approx. 10 days

Steady state - 5 half lives (ie. Dogs 4 months, cats 5 weeks)

Mechanism of action:-
- Unknown
- Hyperpolarizes neurons
- Alters Cl- channels

Metabolism:-
- Not hepatic
- Excreted in urine

Side effects:-
- Ataxia ****
- Pancreatitis (rare)

Dose:-
- Initial 20 mg/kg PO bid
- If need to achieve steady state levels faster, use 100 mg/kg PO bid for 2 days then 20 mg/kg PO bid
- If adding KBr onto phenobarb therapy, do not reduce phenobarb does until reach close to therapeutic levels of KBr

Monitoring:-
- Serum levels in 4 weeks from commencement
- Then every 2-6 months depending on clinical signs

**Diazepam**

Half Life:-
- Dog: < 4 hours

Steady state - 5 half lives

Mechanism of action:-
- Facilitates binding of GABA

Metabolism:-
- Hepatic
- Tolerance occurs within one week of dosing

Side effects:-
- Sedation, drowsiness, lethargy

Dose:-
- Initial 1-2 mg/kg PO bid-tid (cats only)

Monitoring:-
- Clinical signs

**Primidone**

Half Life:-
- Dog: 10-14 hours

Steady state - 5 half lives

Mechanism of action:-
- As for phenobarbital

Metabolism:-
- Hepatic
- Oxidized to phenobarbital (64%) and PEMA (34%)

Side effects:-
- Sedation, drowsiness, lethargy
- Hepatotoxicity (with duration of treatment > 6 months)
- Toxic to cats
**Dose:**
- 10-15 mg/kg PO bid

**Monitoring:**
- Serum levels of Phenobarbital

### Phenytoin

**Half Life:**
- Dog: 4 hours
- Cat: 24-108 hours

**Steady state:** 5 half lives

**Mechanism of action:**
- Interferes with Na+ conduction

**Metabolism:**
- Hepatic

**Side effects:**
- Anorexia, ataxia, sedation
- Hepatotoxicity, coagulation defects
- Toxic to cats

**Dose:**
- 35-50 mg/kg PO tid

**Monitoring:**
- Serum levels of phenytoin

### Felbamate

**Half Life:**
- Not accurately known

**Steady state:** 5 half lives

**Mechanism of action:**
- Acts on NMDA receptor
- Increases seizure threshold

**Metabolism:**
- Hepatic

**Side effects:**
- Hepatotoxicity
- Anorexia, weight loss, nausea, ataxia

**Dose:**
- 200 mg PO tid for dogs less than 10kg
- 400 mg tid for dogs more than 10kg (max 1200mg PO tid)

**Monitoring:**
- Clinical signs

### Gabapentin

**Half Life:**
- Dog: unknown (humans 5-9 hours)

**Steady state:** 5 half lives

**Mechanism of action:**
- Not known

**Metabolism:**
- None, excreted unchanged

**Side effects:**
- Sedation, GI upset, nystagmus, tremors, nausea

**Dose:**
- 100 mg/kg PO tid (up to max of 900mg PO tid)

**Monitoring:**
- Clinical signs

### Lamotrigine

**Half Life:**
- Dog: unknown

**Steady state:** 5 half lives

**Mechanism of action:**
- Stabilises pre-synaptic neuronal membranes by blocking Na++ channels

**Metabolism:**
- Hepatic

**Side effects:**
- Ataxia and nausea

**Dose:**
- 2-5 mg/kg PO divided bid

**Monitoring:**
- Clinical signs
Home Care for the Seizure Patient

Enjoy life with your pet - live with epilepsy and not for it. With appropriate treatment, most animals have more good days than bad and most epileptics live relatively normal lives. However, even the best controlled pets will still have some seizures, and the aim of treatment is to keep these to a tolerable level.

There is no need to restrict your pet's exercise or to go out of your way to reduce the level of excitement in your pet's life - a seizure patient is no more likely to experience an episode with excitement than is a "normal" animal. In fact, seizures have been reported to occur most commonly when animals are relaxed and quiet, and many owners report that their pet was sleeping peacefully when the episode began.

Control Tips

For the best possible control of a seizure patient, it is important that a fairly strict treatment regime is followed at home. If more than one person will be involved in giving the daily treatment, it may be easiest to buy a pillbox with individual compartments for each day of the week. It's then easy to see at a glance whether the necessary treatments have been given. Keep a close watch on the amount of medication left and be sure to order more well ahead of the required time to avoid missing doses. Animals receiving medication to control seizures become dependent on that medication, so missing a dose will often precipitate seizure activity.

If your pet vomits immediately after you've given their medication, wait for about 1 hour then give another dose. If vomiting continues, contact your vet so that alternative means of medication can be given and the problem treated. If at any stage you're unsure of whether to give another dose after your pet has vomited, please call for advice.

If you're going away and need to leave your pet in the care of friends or at boarding kennels, be sure to leave clear instructions for the carer with regards to medication requirements. It's also a good idea to leave your vet's contact details with the carer, and to inform your vet of the arrangements you've made should any problems arise.

Monitoring

Your vet will need to monitor the drug levels in your pet's blood on a regular basis, to ensure these values are within the appropriate therapeutic range. These tests also mean that accurate records of effective dosing regimes can be kept and referred to if changes to medication become necessary at any time. Blood tests are usually done just prior to the pet's normal dosing time, so that the lowest effective levels of the drug can be measured - your vet will advise you of the best time to make the appointment. They may ask that you don't feed your pet before the tests, in order to get a more accurate result.
Be Prepared

Start thinking now about what to do if your pet has a seizure at home. Decide on one place to keep any medications your vet may have given for this situation (e.g. valium) and ensure everyone involved in the animal's care knows where they are kept and how to give them. Look around the dog's environment and think of possible areas you may want to shut off so that your pet can't injure themselves during seizure or post-ictal activity - this can include stairways, swimming pools, terraced gardens etc. If you have other pets at home it is important to keep them away from your pet during seizures as they may become confused and aggressive towards the seizing animal.

Possible Drug Side Effects

Most animals experience very few side effects, and if they do occur, the effects are usually mild and far outweighed by the risk of ongoing seizures if treatment is withheld.

Some animals may become lethargic and want to sleep more due to the sedative effect of the medications used to control seizure activity. Changes in gait may also be seen, with general coordination affected so that animals appear to stumble and weave while walking. If the changes observed are mild, it is often best to wait this adjustment period out. Most animals develop tolerance to the drugs in about 1 week, so that signs will gradually disappear. When animals are more severely affected, it may be necessary to adjust the dose of medication to minimise these side effects - however, always talk to your vet before making any changes to your pet's medication.

The opposite behavioural changes have also been reported as a side effect of seizure medications - these include restlessness, pacing and agitation. Again, a change in dosage may need to be discussed with your vet to alleviate these signs.

Some animals will experience an increase in thirst and appetite due to their medication - ensure your pet has access to appropriate areas for urination when required, and monitor their weight regularly so that any adjustments to diet may be made before obesity becomes a problem. Always ensure your pet receives a high quality, balanced diet.

More serious side effects are uncommon, but can include liver and bone marrow damage. Annual blood tests are usually performed to monitor your pet's health during treatment, but in some cases your vet may recommend more frequent checks.

What to do when seizures occur

Don't panic - most seizures are very brief. Many animals experience an aura or prodrome prior to full seizure activity - this is usually seen as a recognisable change in behaviour. Patients may be upset or anxious, they may seek attention or withdraw and hide. In some cases these signs may go unnoticed and the owner will have no indication of an impending episode.

Watch your pet carefully and make sure they are safe from self trauma and are not at risk of falling from furniture or stairs. Seizuring animals will not swallow their tongue, but may "chomp" involuntarily - keep your hands away from their mouth during this period to avoid being bitten accidentally.

If you have been prescribed diazepam for your pet, administer this as per your vet's instructions. If an oral form has been given, ensure the animal is awake enough to swallow this and aware enough not to bite you.
Time the seizure and if possible, write a description of your pet's behaviour before, during and after the seizure. Note the date seizures occur, and take these records with you for your pet's next check up - this helps to determine whether treatment goals are being met.

If seizures last for longer than 10 minutes, or the patient suffers more than 3 seizures in one day, seek immediate veterinary attention for your pet - there is a serious risk of brain damage within 30 minutes if seizure activity is allowed to continue.

Try to distinguish post-ictal behaviour from seizures. After seizure activity has ceased, animals may enter a post-ictal phase manifested by varying signs such as apparent blindness and bumping into objects, a ravenous appetite, and in some cases, uncharacteristic aggression. These signs may last for a few hours and sometimes up to 1 or 2 days or more. It is important to ensure that children are warned not to try and hug their pet to comfort it during this time, particularly when aggressive behaviour is displayed.

It's usually best to leave your pet alone in a quiet place where it's unlikely to be able to injure itself or others, until it recovers from the post-ictal signs.

If the post-ictal signs are very prolonged or severe, and your pet is at risk of self injury or becomes very aggressive, arrange a consultation with your vet as soon as possible.

**Summary**

- Be prepared:  
  - set place for medications  
  - safe environment
- Watch for signs of seizure - may show behavioural change
- When seizure occurs:
  - note time  
  - secure safe environment for pet  
  - ensure own safety -+ don't get bitten  
  - administer drugs as per vet instructions  
  - write description of what occurred, date, time and length of seizure  
  - keep in quiet place until recovers from post-ictal signs (hours -+ 2 days)
- If seizure lasts > 10 min or patient suffers >3 in one day seek immediate veterinary attention
- If post-ictal signs prolonged or severe - arrange a vet consult as soon as possible.