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## **Seizure disorders in dogs (and cats)- Spack Attacks** Georgina Child BVSc DACVIM (Neurology)

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**Seizures, fits or convulsions** are a relatively common disorder in companion animals. More than one in one hundred people have a seizure disorder and the incidence of seizures in dogs it is probably just as high (estimated at 1-5% of all dogs). A seizure is a transitory disturbance of brain function. Seizures may be generalised due to a generalised brain disturbance or seizures may be partial arising from a specific area of the brain. Generalised seizures (tonic /clonic, grand mal type) are characterised by loss of consciousness, muscle rigidity(tonus), involuntary running or paddling movements (clonus), and autonomic abnormalities including salivation, urination and/or defecation. Although generalised seizures are distressing to see, they are usually brief lasting less than 2 minutes. Generalised seizures may be preceded by an aura or period where dogs seem anxious, seek owners or are hyper excitable.

Partial seizures vary in nature depending on the area of brain from which they arise but possible abnormalities seen include involuntary movements, abnormal behaviour, and gastrointestinal signs but animals remain conscious, although mentation may be altered (staring, aggressive, or "not all there"). Partial seizures may last for a longer period of time than generalised seizures and are often more difficult to characterise. Any abnormal movements+/- behaviour that occurs paroxysmally (comes out of the blue) and follows the same pattern each time followed by a return to normal activities may be a partial seizure disorder. Partial seizures may be classified as simple or complex partial seizure disorders. Diagnosis of partial seizures may be difficult and based on recurrence of similar episodes that cannot be explained by another cause. Movement disorders (or dyskinesias) may mimic seizures - are often distinguished by lack of response to anticonvulsant medication. This group of disorders is not well understood in animals but are often familial (or breed associated) and due to a primary CNS disturbance other than seizure activity.

Absence or petit mal seizures -blank staring and reduced muscle tone seen in people- are rarely recognised in dogs.

The post ictal phase is the period immediately after either a generalised or partial seizure. In this phase animals often seem exhausted and sleep or may seem restless, pace constantly, walk in circles, seem disoriented and/or "drunken". Dogs may seem blind or even demented and vocal. They are often thirsty or hungry. Aggression may be seen. The post ictal phase may last from minutes to days and the length may not bear any relationship to the length of the seizure episode. Seizures may occur in clusters with more than one seizure seen in a short period of time.

**Seizures may be the result of abnormalities outside of the brain (extra cranial) or due to a primary brain abnormality (intracranial).** Reactive seizures are due to extra cranial causes such as metabolic disturbance or toxic insult. Metabolic disturbances that can cause seizures include low blood glucose, low blood calcium, high blood potassium, liver disease, kidney failure, thiamine deficiency and hyperlipoproteinemia. Organic aciduria ( inherited metabolic abnormalities) eg L2 hydroxy glutaric aciduria of Staffordshire Bull Terriers may cause seizures. Lead, snail bait (OP and carbamate), strychnine,1080 and brunfelsia (yesterday, today and tomorrow) poisoning can cause seizures in dogs.

**"Symptomatic" seizures** occur as a result of a structural brain abnormality. Brain abnormalities that can cause seizures include congenital brain anomaly (eg hydrocephalus), head trauma,

encephalitis (brain inflammation), brain tumour or cerebrovascular accident (stroke). Seizures may not be seen for weeks, months or years after brain damage occurs. In some instances the underlying cause of the seizures may progress and other neurologic abnormalities are seen (tumour, encephalitis) but in other cases the structural brain abnormality may be static (prior head injury, vascular accident) and recurrent seizures (epilepsy) the only abnormality seen. This form of epilepsy has been called acquired, secondary or symptomatic epilepsy. Partial or generalised seizures may be seen in acquired or secondary epilepsy.

**Idiopathic epilepsy is a seizure disorder where no underlying cause can be established. It is the most common cause of seizures in dogs. It may have a genetic (inherited basis) in many cases. This form of epilepsy is better called genetic or primary epilepsy.** However some cases of idiopathic epilepsy may have a structural cause (for example birth injury) which cannot be confirmed by routine examination as seizures may not be seen for years after a brain injury. This form of epilepsy has also been termed cryptogenic (from the Greek meaning hidden). Idiopathic epilepsy presumed due to genetic abnormality is characterised by generalised seizures. However partial seizure disorders have been recognised in related dogs and some partial seizure disorders may be inherited.

Epilepsy has been shown to be inherited in beagles. Data suggests that it is also inherited in German shepherd dogs, Keeshonds, Belgian (Tervuren) shepherd dogs, dachshunds, Hungarian Vizslas, English springer spaniels, Irish Wolfhounds and collie and Border collie dogs. Several breeds have been reported to have a high incidence of seizure disorders including golden retrievers, Irish setters, Saint Bernard, American Cocker Spaniels, wirehaired fox terriers, Alaskan Malamutes, Siberian Huskies, Welsh springer spaniels, Labrador retrievers, miniature schnauzers, mastiffs, Boxers, CKCSs and poodles. Epilepsy probably has an inherited basis in these breeds. The genetic abnormality associated with epilepsy is not the same in all breeds. Epilepsy may occur in any breed including cross bred dogs and the incidence of epilepsy seems to be constant across breed and cross breed boundaries. One study suggests the high incidence of seizure disorders in certain breeds may reflect the popularity of these breeds. In my practice boxers, Border collies, golden retrievers, spoodles and Maltese terriers are over represented but all are currently popular breeds as family pets. Male dogs have a higher incidence idiopathic epilepsy than females in some breeds. Acquired or secondary epilepsy may be seen in any breed dog of either sex. An increased frequency of seizures may be seen in females during oestrus or pregnancy and it is not uncommon for females to have their first seizure when in season.

Idiopathic(primary) epilepsy is most often recognised in dogs between 1 and 3 years of age however dogs may have their first seizure before 6 months or older than 3 years. Acquired epilepsy and reactive seizures may be seen in dogs of any age. Dogs that have their first seizure at less than 5 years of age are most likely to have idiopathic(primary) epilepsy. Dogs that have their first seizure at greater than 7 years of age are much more likely (50%) to have acquired cause which is more likely to have a progressive aetiology (for example brain tumour).

Genetic or inherited epilepsy is less common in cats but does occur. Acquired epilepsy (eg secondary to head trauma) is seen and cats may have a higher incidence of encephalitis and cerebrovascular abnormalities resulting in seizures than dogs.

**All animals that have had even one seizure should have a thorough physical and neurologic examination.**

Collapse due to cardiac disease can be confused with a seizure and evidence of heart or lung abnormality may be found on exam. A neurologic examination is most important to determine whether any other neurologic abnormalities are present in addition to seizures. **It is important that a neurologic exam be performed when the dog is not sedated or in a post ictal state as many animals show transient neurologic abnormalities for minutes or hours (even days) after a seizure.** Animals with idiopathic (primary) epilepsy will usually show no neurologic abnormalities between seizures.

Animals with metabolic disease, toxin ingestion or a progressive brain disease causing seizures

such as encephalitis or brain tumour will usually have neurologic abnormalities on examination. Some dogs with metabolic disease or brain tumours may have a normal neurologic examination between seizures for some time after seizures are first seen.

**A complete blood count and biochemistry profile should be performed in all animals to investigate possible metabolic or extra cranial causes of seizures.** In animals less than 1 year of age or any animals with other abnormalities suggestive of hepatic encephalopathy, a liver function test (fasted and post prandial total bile acids or an ammonia tolerance test) should also be performed. Porto- systemic shunts are more common in some breeds including Maltese terriers, Australian cattle dogs, miniature schnauzers, miniature poodles and Yorkshire terriers. Porto- systemic shunts are also seen in cats where ptyalism is a prominent clinical finding. Seizures as the only presenting neurologic abnormality are rare in animals with hepatic encephalopathy. A 24 hour fasting blood glucose determination should be made in all dogs over 3 years of age to check for hypoglycaemia associated with pancreatic tumour (insulinoma). Miniature schnauzers should be checked for hyperlipoproteinemia on a 24 hour fasted blood sample. Inherited metabolic diseases may cause seizures in some breeds (eg L-2-hydroxyglutaric aciduria in Staffordshire Bull terriers). Genetic testing is available for some of these conditions.

Most toxins causing seizures also result in other neurologic abnormalities and cause a sudden onset of severe clinical signs but lead poisoning can result in recurrent seizures and any dog or cat with access to lead sources should have a blood lead determination.

**If metabolic and toxic causes of seizures have been ruled out the decision to do further diagnostic tests depends on neurologic examination findings and the animals age.**

**Any dog or cat of any age with seizures and abnormalities on neurologic exam that are progressive (getting worse) is likely to have a progressive intracranial disease** such as encephalitis, tumour or neurodegenerative disorder. Further tests such as brain imaging (CT or MRI scan) and/or CSF analysis should be considered.

**In cats of any age**, with no neurologic abnormalities on neurologic exam, infectious causes of seizures should still be considered and investigation for FIP, cryptococcal and toxoplasmal infection may be warranted.

**Dogs with a normal neurologic exam and recurrent seizures that are less than 5 years of age and no metabolic abnormalities are most likely to have primary epilepsy (if generalised seizures) or acquired epilepsy (if partial seizures).** No further diagnostic tests are usually recommended unless the dog goes on to show neurologic abnormalities between seizures suggesting a progressive aetiology.

**Dogs that are less than one year of age at the onset of seizures** may have a higher incidence of brain malformation as a possible cause of seizures and further investigation (brain imaging) may be warranted. Seizures in dogs less than 12 months of age may be associated with neurodegenerative disorders, inherited metabolic disorders (eg organic aciduria) and have also been seen young dogs (generally less than 6 months of age) with a heavy parasitic burden.

**Dogs that are 5-7 years of age when seizures are first seen with a normal neurologic exam and no metabolic abnormalities are most likely to have an acquired cause. Some of these dogs will have a progressive cause such as brain tumour.** Further diagnostic testing (MRI) should be offered early or these dogs should be monitored closely and if seizures increase in frequency or more importantly if neurologic signs are seen between seizures further diagnostic tests should be considered.

**Dogs that are 7 years of age or older when seizures are first seen with a normal neurologic exam and no metabolic abnormalities have at least a 50% probability of an underlying progressive intracranial disease such as a tumour .** If metabolic causes are ruled out brain imaging should be considered.

**In cats older than 5 years of age** (and more especially older than 10 years) intracranial tumour and cerebrovascular disease secondary to hypertension (renal disease, hyperthyroidism) should also be considered.

**If an underlying cause of seizures is found specific treatment should be given.**

If idiopathic (primary or acquired) epilepsy is diagnosed the decision on whether or not to start treatment with anticonvulsant medication depends on seizure frequency and severity. Animals that seizure infrequently (less than 1 seizure every 4-6 weeks) do not require medication unless seizures are long, are accompanied by intolerable behaviour changes, or seizures are distressing to the owner.

**Dogs that seizure more frequently than 1 seizure a month and/ or have seizures in clusters (more than 2 seizures in 24 hours) and/or have ever had an episode of status epilepticus (continuous seizuring) and/or have prolonged seizures (> 3-5 mins) should be treated with anti convulsant medication.**

It has been suggested that the more seizures an animal has the more likely it is to seizure again as if the brain becomes 'wired' to seizure more easily. Early institution of anticonvulsant therapy has been suggested as a way of achieving better seizure control. However starting therapy after a single seizure may result in unnecessary treatment of dogs that would have seized very infrequently and there have been no studies to show that early treatment prevents the development of refractory seizures. Seizures are generally not life threatening however misadventure associated with seizure may result in death (falls in swimming pool and drowns) and status epilepticus (state of continuous seizures or repeated seizuring without recovery between seizures) is a medical emergency as prolonged hypoxia and hyperthermia are life threatening. Some breeds have a known tendency to the development of cluster seizures, increased risk of status epilepticus and pharmacoresistance to anticonvulsant medication especially large breeds (G.Shepherds, Golden retrievers, Labrador retrievers, Boxers), Border Collies and Australian Shepherds.

Anticonvulsant medication is a long term and often lifetime commitment. Medication needs to be given every day at regular intervals and all medications have significant side effects. The most effective anticonvulsant in dogs is **phenobarbitone**. Starting dose of phenobarbitone is 2-4mg/kg q12hours (dogs) and 2mg/kg q12 hours for cats. Animals may be dozey and ataxic for first 10-14 days but generally become tolerant to the sedative effects of the drug after this time. Occasionally dogs will become hyperactive and excessively vocal -this effect also subsides generally with continued treatment. It takes 2 weeks for phenobarbitone to reach a steady serum level. A serum phenobarbitone level of >150umol/L may be required to manage seizures in some animals. A phenobarbitone level of >170umol/L is more likely to be hepatotoxic. The phenobarb dose given should be determined by the level of seizure control and persistent side effects (sedation). If seizures are not managed at a lower dose a higher dose may achieve better control) **and for dogs receiving a higher mg/kg dose (>5-6mg/kg q12 hours) serum blood levels should be monitored.** Individual dose requirements vary considerably. **The therapeutic level of a drug is a guide only –some dogs will be poorly controlled at a serum drug level at the lower end of the therapeutic range and better controlled with a higher blood level.** The upper end of the therapeutic range is the most useful guide as it determines the likelihood of hepatotoxicity. If an animals seizures are well controlled and the blood level is lower than the therapeutic range there is probably no need to increase the phenobarb dose. For many dogs the dose of phenobarbitone given is limited by the side effects especially persistent sedation and polyphagia.

**Primidone (Mysoline)** is metabolised predominantly to phenobarbitone (some PEMA and primidone) and its effectiveness is similar to phenobarbitone (and due to the anticonvulsant effects primarily of phenobarbitone) however it may be more effective than phenobarb in the occasional dog. Sedation and hepatotoxicity is more frequently seen with Primidone than phenobarbitone alone. Monitoring is as for phenobarbitone.

**Potassium bromide** (20-30mg /kg q24 hours as single or divided doses) may be used if seizures are not well controlled with phenobarbitone alone or if the side effects of phenobarbitone are not tolerated. KBr can be used as a single drug and is useful also in animals where 2x daily dosing is difficult. **KBr must be given with food** (a reasonable amount and with a consistent salt content). KBr may take 16 weeks to reach a steady serum level. KBr may cause pulmonary disease (which can be fatal) in cats and should not be used unless as a last resort and owners are informed of risks. Bromide levels >20mmol/L in animals on combination therapy may cause clinical signs of toxicity (sedation, ataxia -often cerebellar in character, behavioural changes and occasionally odd motor movements eg yawning, head flicking). Megaesophagus has also been reported associated with Bromide administration. The clinical signs of Bromide toxicity are often misinterpreted as indicative of progressive intracranial disease. Bromide levels continue to increase in animals for the first 4 months of therapy and can change even in animals that have been relatively stable for long periods. Many of the anticonvulsant drugs used to treat epilepsy in humans are not effective in dogs. Anticonvulsant medication will reduce the incidence of seizures in most animals (70%) with epilepsy although treatment is unlikely to eliminate seizures completely.

The aim of treatment is to reduce the frequency and severity of seizures. Epilepsy is not a "curable" disease and this should be stressed to owners. Animals on long term anticonvulsant medication require veterinary reassessment regularly and monitoring of liver function (yearly or more frequently if higher drug levels are required to control seizures). Most animals receiving phenobarbitone will show an elevation in Alkaline Phosphatase and to a much lesser extent ALT. This is due to enzyme induction rather than hepatic injury. However in animals with significant increases in ALT or other biochemical parameters of liver disease potential hepatotoxicity should be investigated (liver function test and liver ultrasound), Rarely blood dyscrasias (neutropenia, thrombocytopenia) may be seen with phenobarb administration.

If serum levels of drugs are monitored blood should be collected when the animal has been on the usual maintenance regimen with no additional drugs for the previous 2 weeks. "Peak" and "trough" levels are probably not significantly different in most animals but I usually recommend collecting blood within 3-4 hours of the next scheduled dose.

Side effects associated with anticonvulsant drugs may be seen with higher doses and in some cases the medication induced complications have to be weighed against the benefits of treatment. **Treatment may fail** for several reasons including improper administration (forgetting doses, dog spitting tablets out), gastrointestinal upset preventing drug absorption and interactions with other drugs. Sodium chloride content of diet will affect the absorption of KBr- have seen problems in dogs whose diet has been changed and dogs that swim in salt water also presumably due to swallowing water (treatment with KBr will also result in artefactual elevation of chloride on some biochemical assays). Oestrus may cause an increase in seizure frequency.

Newer anticonvulsants- gabapentin (Neurontin and generic) levetiracetam (Keppra) Zonisamide (Zonegran) and Pregabalin (Lyrica) may reduce frequency of seizures in some dogs with refractory seizures. These drugs are used as add on drugs (to phenobarbitone and KBr) in most cases. The doses given are often empiric and based on trial and error- with the upper limit determined by side effects (predominantly sedation and /or ataxia). All can be used as single agent anti epileptic drugs.

**Gabapentin** The initial starting dose is generally recommended as 10-15mg/kg q8 hours but this can be increased (doubled or tripled). It is apparently safe (no metabolic side effects) however sedation is commonly seen especially at higher doses (additive with phenobarbitone and KBr) and has not been useful in my hands in reducing seizure frequency in animals with refractory epilepsy over and above control achieved with phenobarbitone and KBr. Gabapentin is primarily used in humans to treat partial and complex partial seizures. Gabapentin is apparently safe to use in cats but there is little information on its usefulness as an anticonvulsant. Liquid forms of gabapentin contain xylitol which can be toxic and should not be used in dogs or cats. 100mg capsules can be reformulated into smaller doses for small animals.

**Levetiracetam (Keppra)** is a newer human anticonvulsant used to treat generalised and partial seizures. Its mechanism of action is unknown and is not metabolised by the liver and excreted essentially unchanged in the urine. The initial recommended dose is 20mg/kg q8 hours however this can be increased (doubled). Sedation and ataxia are common side effects and increase with increased dose. It is not associated with other known side effects. My experience in using levetiracetam in dogs with refractory cluster seizures that have not been adequately controlled with phenobarbitone and KBr is that a reduction in frequency is often seen for about 4 months then seizure frequency increases again (honeymoon effect). It may be very useful as a treatment during cluster seizures (as "pulse" therapy rather than a maintenance therapy) and can be used to treat status epilepticus. Generic forms of this drug are available and has become more affordable. An injectable form is also available and can be used to treat status epilepticus. Its onset of action is more rapid than phenobarbitone and may be less sedating (sedation varies from dog to dog). It can be given IV or subcutaneously but must be diluted. Its onset if given orally is within 1 hour.

Levetiracetam can also be safely given in cats at the same dose and in my experience seizure frequency is often reduced however increased seizure frequency is often seen again after approx 6 months. Three times a day dosing is difficult for many owners and owner compliance is often poor as a maintenance drug.

**Zonisamide (Zonegran)** is now available in Australia. It is an effective anticonvulsant in dogs and is usually used as an add on drug (at least initially) in the treatment of refractory seizures. It can be used a single agent (first choice) anticonvulsant but is currently expensive. Dose is up to 10mg/kg every 12 hours. Liver enzymes should be monitored and has been reported (rarely) to cause both acute hepatotoxicity and blood dyscrasias.

Pregabalin (similar class of drug to gabapentin) is also available in Australia but is expensive. Felbamate is not currently available in Australia. Topiramine (Topamax) which is used in humans with partial and generalised seizures has also been used as an add on anticonvulsant in dogs with refractory epilepsy and may be helpful in some dogs but overall. Chorazepate is not currently available in Australia.

Diazepam can be used as an alternative to phenobarbitone in cats at a dose of 0.5-2mg/kg/day divided q8 hourly. Functional tolerance does not seem to develop to the anticonvulsant effects of diazepam in cats. Diazepam can cause idiosyncratic hepatotoxicity in cats. Diazepam should be discontinued if a cat becomes unduly sedated, lethargic or anorectic or vomits in the first week of treatment. A biochemical liver profile should be done prior to therapy and 3-5 days after treatment is started.

In dogs the short half life and rapid development of functional tolerance to the anticonvulsant effects of diazepam make it a poor maintenance anticonvulsant.

**Some animals with epilepsy will continue to have severe seizures and require intensive medical management despite daily medication. Increased frequency and severity of seizures is not necessarily an indication of underlying progressive disease. Approximately 20-30 % of epileptics will become refractory to treatment. This is seen more commonly in some breeds but is seen across breed boundaries.** Euthanasia as a result of refractory seizure activity is a significant cause of death in epileptic dogs and cats. An increase the severity of seizures does not indicate an underlying progressive disease in most cases but brain damage can occur in refractory epileptics due to repeated seizures. Repetitive neuronal firing can result in cell death, brain hypoxia and /or hyperthermia due to inadequate ventilation and excessive muscle activity during prolonged seizures can all result in the development of cerebral oedema and cerebral ischaemia.

Desexing should be considered in all epileptic dogs. Females have a higher incidence of seizures during oestrus. Idiopathic epilepsy is likely to be genetic and therefore potentially heritable.

### **Emergency treatment of animals presented with refractory seizures (status epilepticus or repeated seizures-generalised or partial- without recovery between seizures)**

- Provide O2 if necessary and intubate if required
- Control seizures- place IV catheter and if animal is seizing administer diazepam 0.5mg/kg slowly IV to a maximum of 20mg/dog. If seizures do not stop administer propofol bolus to effect (1-5mg/kg) or thiopentone bolus to effect (sedation with seizure control not surgical plane of anaesthesia). IV diazepam may cause hyperexcitability in post ictal animals. Care in cats-diazepam can induce vasculitis in small vessels and should only be given IV via patent catheter.
- If unable to gain IV access can administer diazepam ( 0.5mg/kg up to 2mg/kg max 20mg/dog) per rectum (preferred) or IM (up to 1mg/kg max 20mg/dog). Cats can be anaesthetised with isoflurane or sevoflurane in a cat box. Self trauma associated with claws is a significant concern with seizing cats.

Midazolam can be used instead of diazepam IV or IM.

- In an animal not known to be an epileptic- check blood glucose, calcium, urine ketones, electrolytes if possible and provide appropriate treatment if necessary. Blood can be drawn for a full CBC and biochemistry profile however values may be altered by prolonged seizures and not necessarily reflect the underlying cause.
- Check body temp and cool if necessary-wet towels, fan, cold water bath, cold water enema if necessary
- In animals without a previous seizure history (ie not a known epileptic) consider all possible causes of seizures (extracranial and intracranial) and formulate a diagnostic plan.
- For known epileptics record all medication given in the preceding 24 hours

### **Specific treatment for metabolic abnormalities**

#### **Hypoglycaemia**

If able to eat-feed small amount of dog food often

If unable to eat or glucose remains below 2.5mmol/L start IV fluids with 2.5-5% glucose

If unconscious or seizing give up to 1ml/kg 50% glucose IV diluted 1:1 in saline very slowly IV and maintain with 2.5 -5% glucose solution.

#### **Hyponatremia/hyponatremia**

Correct Na<sup>+</sup> very slowly as rapid changes may cause myelinolysis (predominantly brainstem)

#### **Hypocalcemia**

Calcium gluconate 10% 0.5-1ml/kg slowly IV. Monitor heart rate

#### **Thiamine (Vit B1) deficiency**

Uncommon cause of seizures. May be associated with prolonged anorexia or feeding of sulphite treated pet meat.

Thiamine 100-250mg SC q12-24 hours or 2mg (dogs)-4mg(cats) /kg PO q24 hours.

**If poisoning is suspected or possible (sudden onset severe seizures in a previously healthy dog) anaesthetise animal** with propofol or thiopentone, intubate and maintain with isoflurane and O2 to enable gastric lavage and/or enema and maintain anaesthesia until seizing stops (keep anaesthetised for 1-2 hours then try to recover-if seizing continues deepen plane of anaesthesia and repeat again in an hour).Take care to prevent aspiration. Alternatively, pentobarbitone IV can be given to effect (**do not give** calculated anaesthetic dose as bolus). Pentobarbitone currently difficult to access and does not prevent seizing on EEG. It

does reduce muscle activity and apnea however that results in hypoxia and hyperthermia causing significant morbidity and mortality in status epilepticus. For animals with Brunfelsia poisoning the rectum often contains large amounts of vegetable material and seeds at the time of presentation.

**If poisoning is unlikely and animal presented seizing** -give Diazepam 0.5-1mg/kg IV (max 20mg per dog). This can be given per rectum if necessary. This dose can be repeated IV in 5 mins and per rectum in 20 minutes. No more than three doses of **Diazepam should be given by any route in 24 hours**. The depressive cardiac and respiratory effects increase with repeated doses and are much longer lasting than anticonvulsant effects.

**IN ALL (known epileptics, suspect poisonings and seizures with as yet unknown aetiology) start Phenobarbitone at 2-10mg/kg (initially 2-4mg/kg) IV,IM or PO q6-12hours.** The dose given depends on what other drugs have been given and whether or not the dog is already receiving maintenance anticonvulsant medication. In dogs on Phenobarbitone already a maximum cumulative dose (add amount given by all routes) is 20mg/kg q12 hours. Phenobarbitone is drug with a wide margin of safety.

Loading with phenobarbitone (especially in dogs that are phenobarbitone naïve) has been recommended by giving 2-4mg/kg IV at 30min intervals to a total cumulative dose of 20mg/kg. This dose will cause marked sedation in dogs that have not been exposed to phenobarbitone before. There is probably no advantage over giving a larger dose less frequently.

**In cats all doses (diazepam /phenobarb etc) should be halved.**

**Phenobarbitone will take 30 mins to be effective even if given IV and take >1 hour for peak effect) but has a longer duration of action than benzodiazepines.** Phenobarbitone and Diazepam act synergistically and can cause significant cardiovascular and respiratory depression. Animals need 24 hour care and monitoring as cerebral hypoxia and poor cerebral perfusion can result in further brain injury. **Diazepam (and other benzodiazepines) may also be associated with increased risk of aspiration.** Animals that have received a large amount of diazepam or midazolam will have markedly increased serum phenobarbitone levels.

**If seizures are not controlled with Diazepam/Midazolam (max 2 doses) and phenobarbitone either**

- Bolus of propofol (0.5-5mg/kg) slowly to effect then constant rate infusion (0.02-0.5mg/kg/min. This is now standard treatment in humans with refractory seizures. Preferred option. Note recovery from propofol CRI is prolonged in cats (due to deficiency in glucuronide synthetase). If prolonged anaesthesia required in cats consider 2<sup>nd</sup> option. **Recovery from propofol anaesthesia can mimic seizure activity** with muscle rigidity, opisthotonos and paddling. This activity usually stops if the animal is patted, moved or rolled (doesn't stop if seizure activity) and is not associated with autonomic signs (salivation etc)

OR

- Anaesthetise with propofol or thiopentone (minimum dose required), intubate and maintain with isofurane (preferable) and O<sub>2</sub>. Anaesthetise for at least 1 hour then lighten plane of anaesthesia. If still seizing reanaesthetise and repeat again in an hour. May be cheaper option than propofol infusion in larger dogs and 2<sup>nd</sup> preferred option. Alfaxan may also be used as an induction agent.

OR

- Start constant rate infusion Diazepam 0.1-1mg/kg/hour added to 0.9% NaCl maintenance fluid requirement. Make up only 2 hours at a time as diazepam adheres to plastic of infusion line. Start at lower end of dose recommendation and protect tubing from light. CRI of midazolam (0.1-0.5mg/kg/hr) may be used instead of diazepam. However continuous benzodiazepine administration in prolonged status epilepticus should be avoided as

tolerance develops to Diazepam and may develop to midazolam. Diazepam is probably a better anticonvulsant than midazolam, If seizures continue beyond several hours switch to something else.

OR

- Anaesthetise with pentobarbitone to effect (not to surgical plane anaesthesia) and monitor carefully. Remember recovery from pentobarb anaesthesia often difficult to distinguish from seizures. Care needs to be taken not to overdose unnecessarily.

**Levetiracetam IV** ( 30-60mg/kg over 2 minutes) may be useful in controlling seizures acutely – dilute as per instructions for human administration. IV use with diazepam potentiates the anticonvulsant effects of both. **Levetiracetam may also be diluted and given subcutaneously.** It can be given concurrently with phenobarbitone (or other agents eg anaesthetic agents). Continue treatment at 20mg/kg every 8 hours (IV, subcutaneously or orally) for at least 24 hours after seizures have stopped.

**In all of the above continue to give Phenobarbitone 2- 10mg/kg/q 6-12 hourly IV, IM or SC .** Monitor respiration, blood pressure, temperature, hydration, and urine output. All of the above drugs will result in some degree of cardiovascular and respiratory depression, hypotension and reduced swallowing and lower oesophageal sphincter tone increasing the risk of aspiration pneumonia. IV fluids (monitor electrolytes after 48 hours), good nursing care, soft bedding and turning recumbent animals are imperative. Nutritional support may be necessary in animals that require treatment for longer than 72 hours.

Treatment with thiamine (thiamine dependent coenzymes necessary for glucose metabolism), a broad spectrum antibiotic and possibly a corticosteroid (single dose dexamethasone no more than 0.5mg/kg- controversial ) should be given in animals with prolonged seizure activity requiring parenteral treatment for >24 hours). **Corticosteroids should not be given to dogs where brain trauma is a cause of seizure activity.**

Monitor neurologic status –level of consciousness; responsiveness to stimuli; respiratory pattern; pupil size, symmetry and light reflexes and vestibulo-ocular reflexes. **Post ictal state and all drugs will significantly alter neurologic examination.** Deteriorating neurologic status (especially decreasing level of consciousness or lack of vestibulo-ocular reflexes in the absence of additional drug administration or alterations in respiratory pattern or elevation in systemic blood pressure with decreasing heart rate) may be associated with increased intracranial pressure and treatment for increased ICP should be instigated. Adequate ventilation and oxygenation and maintenance of normotension imperative. Mannitol 0.5-1g/kg slowly IV (15-20mins) can be given (no more than 3x in 24 hours)

**If the cause of seizures is not apparent** and metabolic disease is ruled out consider empiric treatment for possible causes of encephalitis +/- intracranial tumour based on index of suspicion until further diagnostics can be undertaken.

Phenobarbitone should be continued at a minimum of 2-4mg /kg q12 hours PO (or parenterally if oral route not possible) until cause of seizures either resolved (eg poisoning) or established. Dexamethasone should be given to dogs where intracranial tumour or non infectious inflammatory CNS disease (and possibly as a single dose to those with an infectious cause) are a possible cause of seizures.

**Neurologic abnormalities may be seen for days to weeks** in animals after an episode of cluster seizures or status epilepticus regardless of the cause (including primary epilepsy) but neurologic status should improve. If neurologic abnormalities are persistent or neurologic deterioration is seen in the absence of further seizures investigation for causes of progressive intracranial disease should be pursued.

**For animals presented after a single seizure or having had a cluster of short seizures from which they recover quickly** treat with Phenobarbitone 2-10mg /kg PO or IM and repeat q12 hours (dose depends on previous exposure to phenobarbitone). Phenobarbitone will take 30

mins to be effective even if given IV. If Diazepam is given -give per rectum if possible as effect is more prolonged and less hyperexcitability is associated with this route. **There is no point in giving an animal diazepam after a seizure unless dog has a history of cluster seizures with an interval between seizures of <1 hour. Diazepam should be given IV only if a seizure continues for more than 2 minutes.**

**In animals that are conscious and able to stand- treatment with levetiracetam orally (initially 40-60mg/kg)** followed by 20mg/kg q8 hours for 24-48 hours is a better option. Levetiracetam will be effective if given orally within 1 hour.

**In animals that have a history of cluster seizures home management can be attempted.** Diazepam 0.5-2mg/kg can be given per rectum (max 20mg per dog). This dose can be repeated in 20 mins and again in a further 20 mins. A maximum of 3 doses can be given in a 24 hour period. If seizures are still occurring with decreasing interval veterinary attention should be sought.

**Levetiracetam may also be useful used as “pulse” therapy** during cluster seizure activity and can be given at home- same dose as above. Pharmacoresistance to this drug may not develop as quickly if used as a pulse drug. It may be less sedating than phenobarbitone in higher doses. Some animals may also be managed with extra Phenobarbitone given orally. For a known epileptic up to 4 regular doses can be given in a 24 hour period (no more than 2x regular dose in 12 hours) for up to 48 hours in effort to reduce the number of seizures in a cluster.