A seizure is a transient paroxysmal episode of excessive and/or synchronous neuronal activity within the cerebral cortex resulting in a varied clinical manifestation. The initial seizure discharge can start in a single focal area or can involve both cerebral hemispheres synchronously from the start. Seizure terminology and classification are currently very controversial topics. Attempts are being made in veterinary medicine to conform to the nomenclature of the International League against Epilepsy (ILAE).

**SEIZURE TERMINOLOGY:** Epilepsy refers to recurrent seizures of primary brain origin. **Idiopathic Epilepsy** (IE) is a functional disorder of the cerebral cortex (i.e., no underlying structural brain lesion) that is typically age-related and is usually suspected to have a genetic origin. IE is usually associated with generalized motor seizures. **Symptomatic Epilepsy** results from a structural brain disorder such as neoplasia, malformation and inflammation. **Probably Symptomatic Epilepsy** refers to epilepsy that likely has a structural cause (i.e., symptomatic) but with the current technology, no specific etiology can be determined (e.g. cortical dysplasia). Probably symptomatic and idiopathic are often grouped together since clinical distinction can be difficult and treatment options are often similar. Reactive epilepsy refers to seizures caused by metabolic disorders such as hypoglycemia.

A seizure may be preceded by the prodrome, which is not part of the seizure based on EEG recordings. This period may last several hours to several days during which the patient’s behaviour is abnormal (e.g. withdrawn, seeks owner). The aura, when present, is currently considered to be the true onset of the seizure and is thought to reflect focal seizure activity that usually rapidly generalizes. This is a very important concept since lateralization during the aura can localize the seizure focus to the contralateral cerebral cortex and influences diagnostic approach and choice of antiepileptic drug (AED). The ictus typically lasts 1-2 minutes and is varied in appearance, often including abnormal mentation, motor movement, and autonomic signs such as urination, defecation and/or salivation. The post-ictal period which follows the ictus lasts several minutes to hours and occasionally several days. Restlessness, increased appetite and thirst, disorientation, blindness and aggression can occur during this period.

**SEIZURE CLASSIFICATION:** Seizure classification is currently also under review. **Generalized seizures** involve both sides of the body, usually (some say always) have loss of consciousness and can be either convulsive (tonic-clonic often with autonomic release) or non-convulsive (“absence”, brief loss of contact with environment without motor component). Non-convulsive seizures are thought to be uncommon or at least poorly recognized in veterinary medicine. **Focal** (formerly partial) seizures are likely more common than originally suspected especially since it is currently suspected that the aura is a focal seizure. A focal seizure may or may not progress into a generalized seizure. Focal seizures without generalization are more common in the cat than the dog. It has been suggested that the terms simple partial and complex partial seizures no longer be used.
**DIAGNOSTIC APPROACH TO SEIZURES:** Determining the cause of seizures should start with evaluation of the patient’s signalment, history including seizure type and pattern, physical examination, and neurological examination. When considering intracranial causes, using age grouping of 0 to 6 months, 6 months to 5 years and greater than 5 years of age, allows for a logical approach to the seizure patient.

**SEIZURE THERAPY/MANAGEMENT:** The decision to start AED therapy should be based on each individual case. General recommendations for initiating therapy include a single seizure occurring more than once every 4-6 weeks, cluster seizure activity (i.e., greater than one seizure within 24 h) or status epilepticus regardless of frequency. The primary goal of therapy is to balance adequate seizure control with acceptable drug adverse effects. The owner should understand that complete elimination of seizure activity is our aim but might be an unrealistic goal. We hope that AED therapy will decrease the severity, duration, and frequency of the seizure activity.

**ANTIEPILEPTIC DRUGS:** In general AEDs, act through enhancement of inhibitory processes via GABA (gamma aminobutyric acid), reduction of excitatory transmission and/or control of membrane cation conductance such as sodium and calcium. Factors influencing the choice of AED include general patient health, cost, owner lifestyle, dosing frequency, drug toxicity and seizure type and pattern. While monotherapy is preferred, 20-50% of patients will require multiple AED therapy. In general, the following formula can be used to calculate desired changes in AED dosages: New dose = (Actual drug dose divided by Actual serum [drug]) X Desired serum [drug].

**Bromide (Br) usually as Potassium Bromide (KBr):** Bromide (Br) is a safe and effective AED that can be used as a sole drug or as part of a multiple drug regimen. Although Br has traditionally been the second line AED, Br has emerged for some neurologists as a first line drug in the dog. This is especially the case in young dogs or dogs with liver disease. Br is not protein bound so drug interactions are minimal and Br does not undergo hepatic metabolism. It is renally excreted so should be used with caution in patients with renal disease. As the % chloride in the diet increases, the absorption of Br decreases and the renal excretion of Br increases, resulting in a decrease of the serum Br level. This important fact needs to be considered with any changes in diet and water. As a result of this link with chloride, intravenous NaCl and loop diuretics can be used to treat Br toxicosis.

Since Br has a long half-life (t ½) of usually 21-38 days, it can take several months to reach steady state serum levels. The recommended dose of KBr in the dog is 20-40 mg/kg q 24 h or 10-20 mg/kg q 12 h. Dogs will often tolerate higher doses such as 40-60 mg/kg/day if KBr is used as a single AED. Therapeutic Br serum levels are reported as 10-20 mmol/L but dogs will often tolerate serum Br levels up to 20-30 mmol/L especially if KBr is used as a single AED. Although usually well tolerated, adverse effects of Br include sedation, weakness and ataxia especially pelvic limbs and PU/PD. Less frequent adverse effects include GIT irritation, pruritus and pancreatitis (especially when used in combination with phenobarbital). In cats, the use of KBr has been associated with a potentially life-threatening asthma-like syndrome with eosinophilic pulmonary infiltrates so this drug is currently not recommended for use in this species.
To achieve serum Br levels more rapidly, some authors recommend an oral loading KBr dose of 400-600 mg/kg divided q 3-4 h over 24 h or alternatively 75 mg/kg PO q 12 h for 10 treatments followed by maintenance Br dosing. This loading protocol is usually not necessary. If seizure control is required rapidly, I prefer an initial Br dose of 30 mg/kg PO q 12 h for 10 treatments either alone or combined with short-term phenobarbital therapy. Based on the long t½ of Br, serum Br levels should be measured 6-8 weeks after onset of therapy with a follow-up level at approximately 3-4 months. If a loading dose of KBr is used, initially measure serum Br levels at approximately two weeks after onset of therapy. Routine serum Br levels, CBC and serum chemistries should be evaluated every 6-12 months pending progress.

**Phenobarbital:** Although phenobarbital (PB) is still considered by many as the first line AED in the dog, it is now often used as a second line drug, as an alternative to Br or add-on with Br. This shift from phenobarbital to Br is based on the potential for PB to have drug interactions, interfere with serum chemistries and laboratory testing (e.g. serum SAP level, ACTH stimulation and dexamethasone suppression), induction of cytochrome p450 microsomal enzyme function and potential hepatotoxicity. Phenobarbital currently remains the AED of choice in the cat.

The recommended starting dose of PB in the dog is 2-2.5 mg/kg q 12 h and in the cat is 1-2 mg/kg (usually 3.25 to 7.5 mg/cat) PO q 12 h. In puppies, the starting dose of PB is higher at 5 mg/kg q 12 h. Based on a t½ of approximately 45 h, steady state serum levels are achieved by 10-12 days. Trough serum PB levels should be measured 2-4 weeks after initiating therapy and after each dose change. Although the laboratory reference range is approximately 85-185 umol/L, trough levels in the dog should not exceed 140 umol/L to avoid hepatotoxicity. In the cat, therapeutic levels are likely lower than the dog at 50-100 umol/L. If serum PB levels are subtherapeutic but seizure control is good, then the PB dose does not need to be increased. Routine serum PB levels, CBC and serum chemistries should be measured every 6 months.

Potential adverse effects of PB in the dog include PU/PD/PP, sedation (usually transient), hepatotoxicity, pancreatitis and rarely, a life-threatening bone marrow suppression including severe neutropenia, thrombocytopenia and/or anemia. CBC should be assessed at one and three months after initiation of treatment to evaluate for these rare blood dyscrasias which are usually reversible.

In the event that PB therapy needs to be discontinued, the weaning process should be performed slowly, usually in 7.5-15 mg decrements alternating between morning and evening treatments every 2-3 weeks, usually taking approximately 16 weeks. Only in cases of bone marrow suppression or severe hepatic disease should PB withdrawal be performed rapidly.

**Benzodiazepines:** Benzodiazepines are not very useful as maintenance AEDs in the dog. **Diazepam** (DZ) in the dog has a short t½ and rapid development of tolerance which limits its use to the management of status epilepticus and cluster seizure activity. In the cat, the longer t½ and lower development of tolerance allows for the use of DZ as a maintenance AED at 0.5-1.0 mg/kg q 12 h. However, a potentially life threatening hepatic necrosis along with other more common side effects including ataxia, sedation, increased appetite and behaviour changes need to be considered when using DZ in this species. Hepatic enzymes should be closely monitored in the cat starting 4 to 5 days after the onset of therapy monitoring for hepatic necrosis. **Clonazepam** (0.1-0.5 mg/kg...
PO q 8 h) and clorazepate (1-3 mg/kg PO q 12 h) are occasionally used as add-on AEDs in the dog but their use is limited by rapid drug tolerance. Clonazepam can be used in the cat as a maintenance or add-on AED at a dose of 1/8 of 0.5 mg tablet PO q 8-12 h. Withdrawal seizures can occur with benzodiazepines so drug withdrawal should occur slowly.

**REFRACTORY SEIZURE PATIENT:** When the seizure patient is refractory to phenobarbital and/or Br, therapy becomes more complicated with increased cost, sometimes greater potential for adverse effects and drug interactions and often increased dosing frequencies.

**Levetiracetam:** Levetiracetam is a piracetam analog that is approved for partial onset seizures with and without generalization in man. It is primarily renally excreted with minimal hepatic metabolism in the dog and has a low potential for drug interactions. Based on the t ½ of 3-8 h, dosing every 8 h is usually is required. It appears to be relatively safe in the dog and cat with initial reports suggesting a significant improvement in seizure control. Transient sedation may be noted. It can be added to the phenobarbital and/or Br therapy (hopefully to allow decrease of the PB dose) or as a sole agent. The suggested dose of levetiracetam is 20 mg/kg q 8h often starting at q 12 h. Based on cost, it is beneficial to use lowest dose required for seizure control. Generic form now available in Canada.

**Zonisamide:** Zonisamide is a sulfonamide derivative that is used for partial onset seizures in man. Zonisamide is suitable for q 12 h dosing in the dog based on the t ½ of 15-20 h. It is 80% excreted in the urine with minimal hepatic metabolism and low potential for drug interactions based on low protein binding. Side effects appear to be mild in the dog, including sedation and ataxia. Suggested dosage is 4-10 mg/kg q 12 h. Cost may be a factor especially in large dogs. Generic form now available in USA.

**Gabapentin:** Gabapentin is used for partial and generalized seizures in man. In the dog q 6-8 h dosing is required because of short t ½ of 2-4 h. Gabapentin is both renally excreted and undergoes hepatic metabolism (30-40 %). Gabapentin has a low potential for drug interactions based on its lack of protein binding. Gabapentin is well tolerated with sedation reported as an uncommon adverse effect. Suggested dose is 8-20 mg/kg q 6-8h. Gabapentin may prove more useful in the management of neuropathic pain and Chiari-like malformation of cavalier spaniels. Gabapentin has been suggested for treatment of feline hyperesthesia syndrome with suggested doses including 50 mg/cat q 24 h with gradual increase to q 12h then q 8h if required, or 5-10 mg/kg q 12h.

**Felbamate:** Felbamate is a dicarbamate compound used in man for partial onset seizures. It has occasionally been associated with severe hepatotoxicity and aplastic anemia in man. It is primarily renally excreted in dogs with some hepatic metabolism. Suggested starting dose of felbamate is 15-20 mg/kg q 8 h. The adverse effects of felbamate include occasional blood dyscrasias such as thrombocytopenia and leucopenia and hepatic disease so routine CBC and serum chemistries should be evaluated q 2-6 months.

**Alternative Options:** Acupuncture, diet management, vagal nerve stimulation, homeopathy References available upon request.