



Seizure Therapy

What is a Seizure?

A seizure represents the clinical, or outward appearance of abnormal, excessive brain (**cerebral cortex**) discharge. The nerve cells (neurons) of the cerebral cortex of the brain operate under the strict control and regulation of the surrounding population of neurons. When the intrinsic control measures of the cerebral cortex fail, uncontrolled and excessive discharge of one, or a group of neurons (**seizure focus**), may occur. This excessive and continuous discharge of a group of nerve cells or neurons can pull other neurons into the electrical discharge resulting in excessive and inappropriate stimulation to and regions of the brain (**generalized seizure**) resulting in the stimulation of the muscles of the body and internal organs. If the seizure focus remains localized to one area of the brain, a portion of the body will be involved in the abnormal cortical discharge (**partial seizure**).

How do we control seizures?

Not all seizures need to be treated. As a general rule, anticonvulsants should be instituted whenever a single seizure occurs more frequently than once every 4 weeks or if more than one seizure occurs within a 24-hour period. *Exceptions to this rule occur of course, with earlier intervention often instituted after the first noted seizure in breeds with a high likelihood of epilepsy.*

Anticonvulsants are natural or synthetic pharmaceutical or salt agents that when administered act to prevent or abolish seizures by suppressing the origin and/or spread of abnormal electrical discharge from one neuron to another. Few anticonvulsants are approved for use in companion animals. To date, Phenobarbital and Diazepam remain FDA approved for use in the dog. This necessitates the need for off label use of most anticonvulsants in the treatment of companion animal seizures. In addition, *most anticonvulsants are controlled substances requiring strict monitoring and annual physical examination for renewed prescriptions.* Significant advances in the understanding of the pharmacodynamic properties of these agents in companion animals has resulted in improved use and greater control of seizures in the dog and cat.

The use of anticonvulsants should be based upon the type and frequency of seizures, as well as cause of seizures in your pet. Side effects, potential toxicity, and frequency of administration and cost are all factors, which are considered when choosing an anticonvulsant agent. Strict adherence to dosage, dosing frequency, and serum testing is vital for the long-term success and management of your pet's seizures. Despite current treatment options, adequate control is accomplished in 66-75 % of the cases. *This leaves 25-33% of all cases of recurrent seizures without adequate control.*

Chronic Anticonvulsant Choices

Phenobarbital is one of the most common anticonvulsants employed in the treatment of seizures in dogs and cats. Phenobarbital is a controlled drug, which is inexpensive with a twice-a-day administration frequency. Phenobarbital induces behavioral side effects of increased appetite, increased thirst, and increased urinary habits. Long-term use has been associated with bone marrow suppression of white blood cells, red blood cells, and platelets and liver disease (chronic active hepatitis and cirrhosis). *The frequency of idiosyncratic and/or toxic reactions due to Phenobarbital is felt to be infrequent and is more common when used at high dosages over long period of time and in combination with multiple anticonvulsants.*

Potassium and Sodium Bromide are natural, salts with anticonvulsant properties when taken in a chronic fashion. Bromide is the active component of these salts. Hyperpolarization of neuronal membranes and inhibition of generation and spread of the seizure is felt to be the mechanism of action of the Bromide ion. The efficacy of either form of the salt is the same, with the bioavailability of the sodium form greater than the potassium form. The reduced amount required to produce similar serum bromide concentrations is offset by the higher cost of the sodium form of the bromide salt. Bromide therapy is felt to be to the safest anticonvulsant management therapy in the dog at this time. The long **half-life** (duration of action of the drug) allows for once or twice a day therapy. Steady-state (*where serum concentrations are the same throughout the day and night*) serum concentrations are not attained until 4 months in the dog. Potassium and/or sodium Bromide is often used in combination at this time in canine and recurrent seizures. *Potassium and sodium Bromide is also used with success in feline seizures, although the long-term use of Bromide in cats has been associated with "asthma-like" respiratory disease. Because of this, utilization of either form of the Bromide salt on a long-term basis is discouraged in the feline species.*

What do we do when Primary Anticonvulsants are not working?

Tertiary Anticonvulsants: Newer anticonvulsants are being utilized with greater knowledge of their efficacy and side effects. These ***tertiary*** anticonvulsants include ***Zonisamide, Felbamate, and Chlorazepate dipotassium, Clonazepam, Gabapentin and Levetiracetam.*** Greater expense and more frequent administration is a reality with the use of these newer agents. The need for the use of a tertiary agent will be left up to the managing doctor and owner's wishes.

Single versus Combination Anticonvulsant Therapy. Who? When? Why?

Combination therapy is the use of two or more anticonvulsants at one time to treat seizures. Combination therapy is utilized for animals that experience more than two "***pair***" three seizures, "***cluster***" in a 24 hours period, or for animals experiencing seizures of increasing frequency, severity, or prolonged recovery. Combination therapy can be on a constant basis (***chronic***) or only when seizures occur (***pulsatile***). Implementation of ***combination*** anticonvulsant therapy allows for greater seizure control due to ***synergism*** (one agent increasing the effectiveness of another, only when both agents are used together) of anticonvulsants with lessened toxicity and potential for idiosyncratic reactions that may harm the patient. Adequate serum anticonvulsant level testing coupled with laboratory testing to ensure safety of the bone marrow and internal organs is vital when utilizing combination anticonvulsant therapy.

When are Seizures an Emergency?

It is important to remember that anticonvulsant therapy will not stop all seizures. The goal of anticonvulsant therapy is to reduce the frequency and severity of seizures while improving the post-ictal recovery. It is important to know when a seizure needs to be treated by professionals.

A Seizure is an Emergency when:

- ∞ There is the onset of cluster seizures.
- ∞ A seizure lasts longer than 5 minutes or seizures occur in succession without a break that allows your pet to recover, drink water and have a return to normal of respirations.
- ∞ When your pet does not regain consciousness and become responsive to verbal stimulation-look at you when you say their name.
- ∞ More than 3 seizures without a sufficient inter-ictal period to recover.

For patients known to have Cluster Seizures:

- ∞ More than 5 general motor seizures in 1 hour.
- ∞ Seizure occurs and pet does not regain consciousness within 5 min.
- ∞ If a seizure lasts more than 5 minutes.

"The more seizures, the greater the stress that is placed on the body. When in doubt head out to your veterinarian or the nearest emergency hospital!"

How are cluster seizures treated at home?

Management of recurrent seizures may entail the use of pulsatile anticonvulsants at home. Their use are dependent upon the severity and duration of your pets seizures. This will often prevent, or limit further seizures and negate the need to take your pet to the emergency room for treatment.

Per Rectal Diazepam(Valium)

Given after the first noted seizure. May or may not be followed with oral Clonazepam or Diazepam. Duration of activity is 6 hours. Sedation is a side effect of Valium derivative administration, and may last for up to 6 hours following the administration of per rectal Diazepam alone.

Oral Clonazepam/Diazepam:

Should be started after the administration of per rectal Diazepam. Commonly used q 8 hours (Clonazepam) and q 3 hours (Diazepam) until patient has been seizure free for 24 hours. Sedation characterized by a drunken state is not uncommon.

Oral Leviteracitam:

A newer generation pulsatile anticonvulsant that can be used on the day of seizure. After the first noted seizure, Leviteracitam is immediately given and followed by administration every 8 hours for a 24-hour period.

Blood Levels... Why do I need them checked? When do they need to be Checked? How often?

The use of anticonvulsants to control your pet's seizures is not without risk for organ injury and potentially life threatening consequences. This often requires blood testing and examinations. While this is an inconvenience and can lead to added costs, it will allow for the safest and greatest control of your pets seizures. ***As a general rule, anticonvulsant levels need to be assessed after attaining steady state (point when the blood level does not change during the day) concentrations, the dosage has been changed, or there has been a recent break through of seizures after adequate control had been attained. Your veterinarian and neurologist will help direct you in when appropriate testing is necessary.***

When do I call you?

It is important to keep us apprised of all seizures. This will allow us to intervene when necessary and help prevent further seizures or detrimental side effects. If we do not know, we cannot help.