Seizure Diagnosis and Management in Pets

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Seizures are one of the most common disorders we face in neurology. The variety of presentations, age, causes, and severity all play a role in considerations for management. An important point to keep in mind is that one medication or treatment does not fix all. Following is a brief overview of typical causes and types of seizures in pets, diagnostics and treatment protocols to aid in management.

Seizures in pets can occur due to a wide variety of causes including:

Systemic causes
External: Environmental Toxins (e.g. antifreeze, chocolate)
Internal: Liver, kidney, pancreatic, thyroid, renal electrolyte, glucose disorders

Structural Causes
Strokes
Tumors
Head/Brain Trauma
Infection (e.g. distemper, encephalitis)
Immune

Primary/ idiopathic epilepsy (of unknown cause -- possibly due to a genetic component when all other causes have been ruled out by process of elimination).

Types of Seizures in pets:

Generalized (also called Grand Mal or Tonic Clonic) Seizure
A generalized seizure, in effect, is a widespread electrical storm occurring in the brain that disrupts normal brain neuron function. Although there are variations and they may differ in severity, generalized seizures are usually characterized by the pet losing consciousness and exhibiting muscle rigidity (tonic) and/or paddling/jerking (clonic) behavior.

Focal (Partial) Seizure (simple or complex)
A focal seizure affects one isolated portion of the brain. (Focalized seizures can remain focalized/isolated, but sometimes can progress, becoming more widespread and manifesting into a generalized seizure.) Focal seizures do not result in loss of consciousness. Depending upon which section of the brain is affected, a pet experiencing a typical simple focal seizure may experience motor function activity such as staring, blinking or twitching in the face or a limb. Complex focal seizures, however, affect those parts of the brain that control emotions and behavior. A pet suffering a complex focal seizure may engage in episodic fly-biting or tail-chasing behavior, run wildly or even exhibit irrational fear or aggression, among other things. (It's important to rule out compulsive disorder as a possible cause, particularly with repetitive behaviors.)

Depending upon initial assessment, diagnostics on a pet with seizures would/may include:

- Medical history and physical exam
- Neurological exam
- Bloodwork including CBC, serum chemistry, urine analysis, bile acids assay, antibody titers, thyroid function
- MRI
- EEG
- Spinal fluid analysis

INITIATING A TREATMENT PROTOCOL

There are compelling reasons to establish a treatment protocol to gain early control of seizures, particularly frequent or severe ones, in order to avoid the possibility of death or further systemic brain damage that may occur:

Status Epilepticus

In the past status epilepticus (SE) has been defined as a continuous seizure of more than 30 minutes in duration or two or more sequential seizures without full recovery between seizures. While treatment for SE is typically started at 5 to 10 minutes, the official definition of SE had stated a time of 30 minutes before injury occurs. However, in 2015 SE has been given a proposed new definition and treatment protocol which applies to treatment of both epileptic and non-epileptic seizures. The proposed new definition, published in *Epilepsia*, gives two time points. The first time point indicates the earliest time when treatment should be started. The second indicates when long-term consequences, such as neuronal injury, neuronal death, alteration of neuronal networks, and functional deficits, are increasingly likely. [1]

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Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected

Type of SE	Operational dimension 1 Time (t_1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t_2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic–clonic SE	5 min	30 min
Focal SE with impaired consciousness	10 min	>60 min
Absence status epilepticus	10–15 min[a]	Unknown

[a]Evidence for the time frame is currently limited and future data may lead to modifications.

Cluster Seizures

More than one seizure occurring in a 24 hour period. As stated above, if more than three seizures occur in a 24 hour period, it may be indicative that the pet's condition is progressing toward status epilepticus.

Kindling Effect

Evidence suggests a process where having repetitive seizures lowers the seizure threshold for having more seizures. The more frequent the seizures, the more likely to get progressively more frequent because the brain sets up a neural circuit that makes it not only easier to seizure, but more difficult to treat -- it becomes more engrained.

Mirroring
A process whereby seizures which start on only one side of the brain in time can "mirror" themselves on the other side of the brain thus increasing the frequency of the seizures.

In summary, I cannot stress enough the importance of establishing control over seizures in pets as quickly as possible. After diagnostics are completed, treatment should begin immediately especially when there has been any episode of status epilepticus or cluster seizures, regardless of frequency, and in instances where there is more than one seizure per month.

RECOMMENDED TREATMENT PROTOCOLS

Consideration of age, systemic disease and underling neurological disease all factor into developing an appropriate treatment protocol for pets with seizures. The following are some examples of therapies I have utilized and have found them to be effective:

Young idiopathic epileptic

If seizures are **isolated** consider starting with Keppra Extended Release (40mg/kg starting dose) (Note: Keppra Extended Release only comes in 500mg and 750mg tablet size so for small dogs it is not an option for BID dosing thus standard Keppra needs to be given at TID instead of BID for the Extended Release; also the Extended Release CANNOT be split – the medication loses the Extended Release component which is the micropores in the capsule which let the drug leach out slowly). A second choice would be Zonisamide 5mg/kg BID.

If seizures are **severe, no matter what the cause is** (e.g. cluster seizures/status epilepticus) then start with Phenobarbital 3mg/kg BID.

Liver disease
Start with Keppra, Lyrica (2mg/kg starting BID. Due to expense, consider compounding from 300mg capsules to the appropriate dose), or KBr 30mg/kg with a loading of 100mg/kg BID for 2 days.

Renal disease
Start Zonisamide 5mg/kg BID. Also consider Phenobarbital, Rufinamide (5mg/kg BID – it's expensive, but can be imported from Canada at a reduced price).

Structural disease (hydrocephalus, tumors, stroke, encephalitis, etc.)
Start with Keppra or Zonisamide (unless seizures are severe then consider Phenobarbital).

EMERGENCY TREATMENT AT HOME FOR STATUS EPILEPTICUS

First and foremost, it's very important to stress to the client that **frequently** the home therapies **DO NOT** stop or control the seizures, and that they should still take their pet to the ER if the seizure lasts more than 5 minutes or there are more than 3 seizures in a 12 hour period. Clients should never get a false sense of security administering at home therapies, and they should be fully prepared to act quickly to get professional medical attention for their pet if needed.

Rectal valium: I typically **DO NOT** recommend this. Why? The absorption times vary from 10 to 30 minutes – hardly an effective treatment for status epilepticus. Also absorption is erratic and there is also a first pass effect through the liver.

Nasal valium/midazolam (0.5mg/kg starting dose): Absorption is quicker and there is no first pass effect. I do NOT recommend this for brachycephalic dogs.

Midazolam (0.5mg/kg IM) combined with Keppra (20mg/kg SQ): This is the most rapid onset and best guarantee that the full dose is administered. Obviously the owners need to feel comfortable with this method of administration (although we have had considerable success teaching owners how to administer SQ fluids or SQ insulin at home).

After the first seizure stops I also recommend starting C**lorazepate** at 0.5mg/kg PO TID until the dog is seizure free for 24 hours. I stress to the client that the dog may be much more sedate than normal, but this is typically safer than severe clusters.

OTHER THERAPIES

There are multiple other medications available including Felbamate, Gabapentin, Lacosamide, Topiramate, Clobazam, and many more that can be used in refractory patients.

There are numerous other adjunct therapies to manage seizures which have no large studies to support them. Most are benign and are worth trying. These include:

Diet changes: It's very rare to have dietary-induced seizures. Consider grain free or homemade diets.

Acupuncture: There are many different protocols available.

Cannabidiol (CBD oils) is presently receiving lots of attention. However, there are no studies supporting or refuting this currently.

Vagal Nerve Stimulation: An implantable device that sends intermittent low voltage stimulation to the vagal nerve. (Please see below.)

NEW THERAPY – EXTERNAL VAGAL NERVE STIMULATION

Hard to Manage Epileptics? Guardian Veterinary Specialists New Horizons Research Team is currently conducting a prospective study on an external hand held vagal nerve stimulation device for treatment of cluster seizures, status epilepticus and frequent hard to control seizures. If you have a patient who is difficult to control, please have the client make an appointment, and I can discuss this therapy and other options for the pet. ■

REFERENCES

1. Trinka, E., Cock, H., Hesdorffer, D., Rossetti, A. O., Scheffer, I. E., Shinnar, S., Shorvon, S. and Lowenstein, D. H. (2015), A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia, 56: 1515–1523. doi:10.1111/epi.13121
Link to full article: http://onlinelibrary.wiley.com/doi/10.1111/epi.13121/full

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Dr. Jason Berg is a highly respected veterinary specialist who has devoted his life to practicing veterinary medicine with a difference. Incorporating compassion and sensitivity to pet parents and their pets with professionalism, integrity, and values, he strives to make a meaningful difference in the lives of pets and toward advancing veterinary medicine.

Receiving his doctor of veterinary medicine degree from Texas A&M University in 1996, Dr. Berg went on to complete his internship followed by residency training in veterinary neurology and internal medicine in 2000 at The Animal Medical Center in New York City. He received board certification in neurology in 2000 and in internal medicine in 2002. An experienced business founder and owner, he launched Animal MR, Animal Specialty Center, and Bloodhound Laboratories. In spring 2017 Dr. Berg will launch Guardian Veterinary Specialists, a new 29,000 square foot advanced, state-of-the-art emergency, critical care and specialty hospital in Brewster, NY. He has held multiple positions with the American College of Veterinary Internal Medicine, and he is president of the Westchester Rockland Veterinary Medical Association. A much sought-after lecturer and instructor, both nationally and internationally, Dr. Berg is also a published author with articles in peer-reviewed journals, such as the American Veterinary Medical Association, Veterinary Internal Medicine, and American Animal Hospital Association, among others. In addition, Dr. Berg has received numerous accolades and awards for his compassionate work with the shelter and rescue communities, and he is currently on the advisory board for the Westchester SPCA.

FOR ASSISTANCE WITH PATIENT CASES

Until Guardian Veterinary Specialists opens this spring, Dr. Berg is seeing patients at South Putnam Animal Hospital, 230b Baldwin Place Road, Mahopac, NY 10541. Dr. Berg welcomes calls from community veterinarians to discuss patient cases, and he is on call 24/7 for all neurological emergencies. To contact Dr. Berg about a patient case or to schedule a client/patient appointment, please call 914-564-9810. Dr. Berg provides comprehensive neurology and internal medicine services for referring veterinarians, their clients and patients. Services include: consultations, neurosurgery, MRI, CT, EMG, endoscopy, ultrasound, outpatient ultrasound, among other services.

Please don’t hesitate to reach out to Dr. Berg for questions or any type of assistance. He’s here to help and happy to speak with you!