Epilepsy is a common canine disease—thought to affect up to 1 in 20 dogs—and potentially life threatening. A useful working understanding is essential for the small animal practitioner.

When a patient presents for an episode of odd behavior or movement, the clinician must immediately consider 4 questions:
1. Are the events described by the owner (or recorded on video) truly a seizure?
2. Can an underlying cause be identified and treated versus treating only the seizure?
3. Should an anti-epileptic drug (AED) be administered?
4. If medical therapy is pursued, which AED should be chosen?

Is the event a seizure?
There are many behaviors, events, and diseases that mimic a true seizure (Table 1).

**Electroencephalography**
Electroencephalography (EEG) records the brain’s electrical activity and is considered by many human physicians to be an essential tool for characterizing seizure events.

**Profile of Epilepsy**
**Definition**
Epilepsy is defined as 2 or more seizures, at least 24 hours apart, resulting from a nontoxic, nonmetabolic cause.

An epileptic seizure is defined as a transient occurrence of signs, symptoms, or both due to abnormal, excessive, or synchronous neuronal activity in the brain. Seizure events can result from:
- Disease localized to the brain (symptomatic/structural)
- A reaction of the healthy brain to a metabolic or toxic insult (reactive)
- An unknown or genetic cause (idiopathic).

In human medicine, the term idiopathic has been replaced by the terms genetic or seizure of unknown cause.

**Classification by Frequency**
Seizures can be classified into 3 categories based on frequency:
- **Cluster**: 2 or more seizures within 24 hours
- **Acute repetitive**: 2 or more seizures within 5 to 12 hours, separate from normal seizure pattern
- **Status epilepticus**: Continuous seizure for 5 minutes or 2 or more seizures with no recovery between seizures

**Classification by Breed**
In veterinary medicine, epilepsy is considered genetic when the frequency in a breed exceeds that of the general population (eg, Petit Basset Griffon Vendeen). Classifying seizures by breed is important—certain types of genetic epilepsy have different prognoses, and much interest exists with regard to using dogs as models for human epilepsy.

Border collies have a 2-year median survival from time of seizure onset, with 94% affected by cluster seizures, 53% status epilepticus, and 71% rate of drug resistance. Conversely, the Lagotto Romagnolo has seizure onset at 5 weeks, which spontaneously resolves by 13 weeks, similar to benign familial neonatal seizure in humans.

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**Table 1. Behaviors, Events, & Diseases with Seizure-Like Appearance**

- Atlantoaxial subluxation
- Breed and drug induced dyskinesia/movement disorders
- Cataplexy, narcolepsy, rapid eye movement (REM) sleep disorder
- Cervical muscle spasm
- Chiari malformation/syringomyelia associated episodes
- Encephalitis
- Episodic neuromuscular disease
- Exercise-induced collapse
- Extreme agitation
- Head bobbing/tremor syndromes
- Intermittent decerebrate/decerebellate rigidity
- Jaw chomping/fly biting
- Metabolic/toxic event
- Myoclonus
- Syncope
- Vestibular episode
events (Figures 1–3). However, EEG is not a readily available clinical tool in veterinary medicine, and a first-time EEG recorded between seizures in an epileptic human or dog has about a 25% chance of identifying the event as a seizure.7

**Observation**
Identification of a seizure is most often achieved by comparing the observed event to what is considered a typical seizure.

- **Generalized tonic clonic seizures** typically last 1 to 2 minutes, and characteristically feature loss of consciousness, muscle tone and movement (tonic/clonic), jaw chomping, and profuse salivation, followed by gradual return to consciousness and normal ambulation.

- **Partial or nonconvulsive seizures** are more difficult to recognize, with the latter requiring an EEG recording during the event.8

In human medicine, classifying events by description alone (without EEG) is accurate, but also allows overdiagnosis of nonepileptic events as seizures. Therefore, observation has high sensitivity, low specificity, and low positive predictive value.9 Accordingly, clinicians should be aware that they may be treating nonepileptic events with an AED.10

**2 DOES THE SEIZURE HAVE AN UNDERLYING CAUSE?**
Identifying an underlying cause for the seizure yields better seizure control, quality of life, and accurate prognosis. The most recent seizure classification system—by cause—groups seizures into 3 causes: genetic, structural/metabolic, and unknown.

**Genetic & Unknown Causes**
Diagnosis of idiopathic epilepsy (IE) is made when:

- Genetic basis is suspected
- Testing has failed to reveal a cause for the seizure.

**Structural/Metabolic Causes**
- Diagnosis of structural epilepsy is often made by magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis, with common causes, including brain tumor, infarct or hemorrhage, or encephalitis.

- Technically, most metabolic causes of seizure are not a form of epilepsy because the brain itself is normal and reacting to an extracranial insult, which once eliminated, results in cessation of seizure.

Because MRI and CSF analysis are expensive and not readily available, the primary care clinician is often faced with making a difficult decision about whether to refer a patient or simply prescribe an AED. Key factors in assessing a seizure patient include:

**Age**
As a guideline, dogs with IE typically have their first seizure between 6 months and 6 years of age. However, at seizure onset, about 20% of dogs older than 6 years, and 2% of dogs younger than 6 months, do not have an identifiable cause for seizure.11

**Breed**
There are, however, some exceptions to the age rule noted above. Seizure is a very common presenting complaint in...
dogs with brain tumors such that, in certain breeds (eg, golden retriever, boxer, Boston terrier, French bulldog), even 1 seizure at 4 years or older should be cause for concern.24 In young (1–5 years of age), small breed dogs (eg, pug, Chihuahua, Maltese, poodle) that have 3 or more seizures within a few months, meningoencephalitis of unknown etiology (MUE) should be considered a likely cause for the seizures.

**Behavior**

Even subtle behavior changes around the time of the first seizure indicate that a patient is likely to have symptomatic epilepsy (Table 2).

<table>
<thead>
<tr>
<th>TABLE 2. Common Behavior Changes in Dogs with Structural Brain Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Aggression</td>
</tr>
<tr>
<td>• Inappropriate elimination</td>
</tr>
<tr>
<td>• Irritability</td>
</tr>
<tr>
<td>• Lethargy/head pressing</td>
</tr>
<tr>
<td>• Not greeting owners</td>
</tr>
<tr>
<td>• Restless at night</td>
</tr>
<tr>
<td>• Sleeping more during the day</td>
</tr>
</tbody>
</table>

**Examination Findings**

If a neurologic examination performed between seizures has abnormal results, there is a high probability that a structural brain lesion is the cause of the seizure. However, 30% of brain tumor patients will have a normal examination, and 18% of idiopathic epileptics can have a transiently abnormal examination.10

It is useful to observe a seizure patient in the examination room to evaluate gait and behavior, coupled with an examination of the postural reactions and menace response. As a guideline, the following findings suggest structural disease, although other causes are possible:

• Confusion
• Circling to one side
• Postural reaction
• Menace deficits on one side.

**SHOULD AN AED BE ADMINISTERED?**

AED drug therapy is recommended if any of the following are present/occur:

• Structural cause for the seizure
• Severe first seizure or post-ictal period
• Owner preference to reduce chances of another seizure.

For IE, I recommend AED therapy after 1 or 2 seizures in a 6- to 12-month period for several reasons:

1. Although rarely life-threatening, seizures are very upsetting to owners, and a recent owner survey showed that most owners felt the only acceptable seizure control is no seizure.13
2. AED therapy likely reduces the chance of a life-threatening seizure/status epilepticus.
3. Although controversial, there is both bench-top and clinical data that demonstrates every seizure a patient experiences increases the chance for another seizure, independent of the seizure cause. In other words, seizure begets seizure.14,15
4. Newer generation AEDs do not have as many side effects or organ toxicities compared to older AEDs, and are now available in generic or cost-effective formulations (Table 3, page 34).16-18

**WHICH AED SHOULD BE CHOSEN FOR THERAPY?**

**Maintenance Therapy**

When and which AED to apply in the clinical setting remains uncertain and controversial (see Studies Evaluating AED Efficacy & Safety). Some reasonable guidelines for seizure management are to:

• Use one medication at a time
• Choose medications with best efficacy, lowest cost/dosing interval, fewest side effects, and lowest risk of toxicity

**When to Change.** Side effects or lack of efficacy can prompt the need to change AEDs. Studies show that only about 70% of dogs are well controlled on an AED,17 and fewer than half the dogs on phenobarbital and/or bromide are seizure-free without adverse medication-related side effects.20

Treating with multiple AEDs may be beneficial because...
they act on a broader range of mechanisms or synergistically; however, side effects can be additive, and determining which AED is effective is difficult when more than one medication is administered. Generally, I recommend using one AED at a time; therefore, AEDs often need to be switched rather than added.

Transition Period. Abrupt cessation or missed doses of AEDs is a common cause of seizure and status epilepticus in humans. This may be of less concern in dogs—only 6% of status epilepticus cases in one study resulted from low AED concentration. Nevertheless, tapering the dose prior to stopping an AED is recommended. Risk of seizure can be further reduced if at least one AED is maintained in the therapeutic range during the transition. See Step-by-Step: Transitioning to Newer Generation AEDs.

Rescue Therapy
AED therapy—additional or different, oral or parenteral—to control cluster seizures or status epilepticus is called rescue therapy. Rescue plans for epilepsy patients are recommended because, among dogs being treated for IE, a 59% incidence of status epilepticus and higher rates of cluster seizures have been described. Furthermore, a 25% mortality rate among all dogs that present for status epilepticus has been reported.

Predicting Seizures. Recent EEG evidence suggests seizures in dogs are not random events, and that forecasting seizures is possible. Therefore, while therapy can be initiated after a seizure, it can potentially be administered before a seizure, as many owners feel they can predict when seizures will occur.

Oral Therapy. Oral rescue therapy is appropriate if time to next seizure is an hour or greater, allowing for gastrointestinal absorption and development of useful serum concentration. For example, levetiracetam takes about 81 minutes to reach maximal serum concentration following oral administration.

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**TABLE 3. AED Maintenance Therapy in Dogs**
(Side Effect Scale: 1 = Relatively Mild; 5 = Relatively Severe)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE</th>
<th>SIDE EFFECT SCALE</th>
<th>PRIMARY SIDE EFFECTS</th>
<th>REPORTED TOXICITY/DYSFUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetiracetam*</td>
<td>20–50 mg/kg PO Q 8 H</td>
<td>1</td>
<td>Ataxia, sedation</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>(or Q 12 H for extended release)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zonisamide*</td>
<td>5–10 mg/kg PO Q 12 H</td>
<td>2</td>
<td>Ataxia, decreased eating, sedation</td>
<td>Affects liver and kidneys</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Causes urinary calculi</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>10–30 mg/kg PO Q 8 H</td>
<td>2</td>
<td>Sedation</td>
<td>None</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>2–4 mg/kg PO Q 12 H</td>
<td>2</td>
<td>Sedation</td>
<td>None</td>
</tr>
<tr>
<td>Phenobarbital*</td>
<td>2–6 mg/kg PO Q 12 H</td>
<td>4</td>
<td>Ataxia, polydipsia, polyphagia, polyuria, sedation, weakness</td>
<td>Affects liver, bone marrow, skin, and endocrine system</td>
</tr>
<tr>
<td>Bromide*</td>
<td>25–50 mg/kg PO Q 8 H</td>
<td>5</td>
<td>Ataxia, diarrhea, polydipsia, polyphagia, polyuria, sedation, vomiting, weakness</td>
<td>Affects esophagus and pancreas Causes gastritis and panniculitis</td>
</tr>
<tr>
<td>Felbamate</td>
<td>10–40 mg/kg PO Q 8 H</td>
<td>1</td>
<td>Tremors (rare)</td>
<td>Affects liver and bone marrow Causes keratoconjunctivitis sicca</td>
</tr>
<tr>
<td>Topiramate</td>
<td>5–10 mg/kg PO Q 8–12 H</td>
<td>1</td>
<td>Sedation</td>
<td>May cause urinary calculi</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>0.05–2 mg/kg PO Q 12 H</td>
<td>3</td>
<td>Ataxia, polyphagia, sedation, weakness</td>
<td>None</td>
</tr>
</tbody>
</table>

* Serum drug monitoring recommended

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**STEP-BY-STEP: TRANSITIONING TO NEWER GENERATION AEDS**
1. For 1 week, add a new AED to the patient’s current regimen.
2. For the next 5 days, reduce the dose of the former AED by 50%.
3. For the next 5 days, reduce the frequency of the former AED to once a day.
4. Discontinue administration of the former AED.
   - If marked sedation, ataxia, or weakness are noted with the new AED, more rapid tapering or discontinuation of the former AED is advised.
   - If marked increase in seizure frequency is noted in the following weeks to months, a return to the former AED or addition/substitution of a new, different AED is recommended.
Although studies are lacking, administration of an extra dose of maintenance AED and initiation of a novel AED for a short period of time (pulse therapy) is advised to control cluster seizures and status epilepticus (Table 4).

I advise owners to give a dose of AED used for pulse therapy between seizures to assess side effects, and determine best tolerated dose, prior to using the medication in the post-ictal period.

Other Types of Therapy. Intranasal (IN), subcutaneous (SC), intramuscular (IM), and rectal AED administration have been advocated when (Table 5):

- Patient is unable to swallow
- Rapid cessation of seizure activity is required
- Intravenous (IV) route is unavailable.

I advise owners to give levetiracetam (60 mg/kg SC) plus midazolam (0.2 mg/kg IM) or diazepam injectable solution (2 mg/kg by rectum).

AED = anti-epileptic drug; CSF = cerebrospinal fluid; EEG = electroencephalography; IE = idiopathic epilepsy; IM = intramuscular; IN = Intranasal; IV = intravenous; MRI = magnetic resonance imaging; MUE = meningoencephalitis of unknown etiology; SC = subcutaneous

View a video showing a seizure in a dog at todaysveterinarypractice.com/resources.asp.

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