Epileptic Emergencies

**STATUS EPILEPTICUS IN CANINE PATIENTS**

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Status epilepticus (SE) is characterized by epileptic seizures that continue for more than 5 minutes, or the occurrence of more than 1 seizure within a 5-minute period in which the human or animal does not return to “normal” in between seizures. Some seizures may last 20 to 30 minutes or longer.

The official definition—as defined by the International League Against Epilepsy—is a seizure that shows no clinical signs of arresting after a duration encompassing the great majority of seizures of that type in most patients, or recurrent seizures without resumption of baseline central nervous system function interictally.

Nearly 60% of epileptic dogs will—at some point in their lifetime—experience one or more SE events.¹ The prognosis for dogs with SE is quite poor—up to 25% of affected dogs will not survive to hospital discharge.¹ Moreover, the life span of epileptic patients with SE is drastically shortened compared with the life span of epileptic patients experiencing other types of epilepsy (ie, 3-year difference).² Therefore, SE creates much concern among clinicians and pet owners alike.

**SEIZURE TYPES**

**Cluster seizures** may be a precursor of SE, and are defined as 2 or more seizures within 24 hours. However, they differ from SE because, during cluster seizures, patients regain consciousness, or return to baseline central nervous system function, between seizures.²

SE may be classified as either convulsive or nonconvulsive. **Convulsive** SE is the classic tonic-clonic seizure presentation, where first muscles stiffen, then the body begins to rhythmically jerk. SE is defined as **nonconvulsive** if patients do not regain consciousness within 30 minutes to an hour after a seizure, but are still experiencing subclinical cerebral seizure activity. Nonconvulsive SE is characterized by the presence of a stuporous, unresponsive state rather than active convulsions. Electroencephalography (EEG) may show epileptiform activity, even if the patient does not appear to be in a classic seizure-like state (Figures 1 and 2).


**FIGURE 2.** Seizures originate in the forebrain (cerebrum and diencephalon); the dots highlight these areas of the brain and suggest possible locations for lesions that might cause SE. Reproduced with permission from Chrisman CL. Neurology for the Small Animal Practitioner. Jackson, WY: Teton NewMedia, 2003.
PATHOPHYSIOLOGY
When seizures occur, functional abnormalities of neuronal cell membrane ion pumps (such as sodium-potassium ATPase and Ca\(^{2+}\) ATPase) cause an imbalance of the intracellular and extracellular concentrations of potassium and calcium, which leads to depolarization. Neurons become more excitable, which allows the seizure to spread more easily. When SE develops, excessive excitation occurs and inhibition, which would stop an isolated seizure event, fails.2

SE has 2 separate phases: early and late; then, the patient enters the maintenance or self-sustaining phase of seizure activity.

Typically, the **early phase** occurs in the first 30 minutes:
- Stress-induced release of catecholamines causes cardiovascular effects—increased heart rate and systemic blood pressure, along with elevated left atrial and central venous pressure; arrhythmias are also common.
- An increase in bronchial secretions and salivation, and a decrease in ventilation, can result in hypoxemia.
- Increased muscle activity causes overheating and the patient becomes hyperthermic.

The **late phase** occurs during the latter portion of an SE event, after the 30-minute mark:
- Respiratory compromise may occur due to neurogenic pulmonary edema, which is characterized by accumulation of pulmonary interstitial and alveolar fluid, most severe in the dorsocaudal lung fields, that is triggered by brain stem hypoxia. Aspiration of saliva and regurgitated gastric contents can also occur and contribute to respiratory complications. Consequently, hypoxia and hypercarbia may result.
- Prolonged sympathetic nervous system stimulation and excessive release of catecholamines may damage cardiac myocytes, leading to impaired cardiac contractility. Decreased cardiac output is exacerbated by hypovolemia, resulting in hypotension, which decreases perfusion to the brain, myocardium, and viscera. Cardiac arrhythmias may result from acidemia, hypoxemia, electrolyte abnormalities, and sympathetic stimulation, further decreasing cardiac output.2
- Poor kidney perfusion and rhabdomyolysis may result in acute kidney injury or acute renal failure.

Once the patient reaches the **maintenance** or **self-sustaining phase**, a certain amount of neurologic damage has occurred and spontaneous resolution of the seizure becomes less likely. As SE progresses, hyperexcitable networks are enhanced and the seizure becomes more difficult to treat, garnering a poorer prognosis.

**CLINICAL APPROACH**
In patients with SE, the essential goals for the veterinary team are to:
1. **Stabilize** the patient
2. **End** seizure activity
3. **Correct** adverse consequences of SE.

**STABILIZATION: MEDICATIONS**
Currently, there are no FDA-approved drugs specifically for SE in either human or veterinary patients. Instead, standard anticonvulsant and anesthetic drugs are used IV to end seizure activity.

**Immediate Medical Therapy**
As in most emergency situations, when a patient experiencing an SE episode is presented, the veterinary team should:
- Place an IV catheter and begin administration of antiepileptic drugs (AEDs) (*Table 1*).
- Provide oxygen by mask or flow-by administration. It is critical to act quickly because neurologic damage continues to occur until seizure activity is ended.

At the time of IV catheter placement, it is beneficial to obtain a blood sample to perform an initial evaluation of blood glucose and electrolytes, which assists in ruling out a metabolic cause of seizures. Obtaining a packed cell volume/total solids is also ideal to help guide fluid therapy. A brief physical examination should evaluate airway patency, pulse quality, and rectal temperature. **Diazepam** is typically administered via the IV route. If IV access is not possible, diazepam can be delivered rectally or intranasally, but it may have variable efficacy via these alternate routes. With regard to rectal administration, the presence of feces, extensive first-pass hepatic metabolism, ejection of the drug, and unpredictable absorption may contribute to lower efficacy.3

Effective vascular access must be established, if necessary, by surgical cut-down or by placement of an intraosseous catheter. If there is no response to IV diazepam after 1 to 2 doses, another AED may be chosen.

**Levetiracetam** is usually the next AED of choice and can be administered via IV, SC, or IM routes.
This drug has less profound sedative effects than diazepam, and may be a better option for patients already in a dull state.2 Because levetiracetam is not metabolized by the liver, it is a safer drug for patients with hepatic compromise. However, it is excreted through the renal system, and patients with kidney disease may not be prime candidates for its use. Lorazepam and midazolam are other options for AED therapy. Although more expensive, lorazepam tends to provide longer lasting seizure control compared with diazepam.

- One or 2 initial IV dose(s) of lorazepam or midazolam is given and, if effective, can be followed by a constant rate infusion (CRI) in order to prevent recurrence of the seizure.1
- Animals must be monitored for excessive cerebral depression while receiving CRIs of benzodiazepines, and the dose reduced over time to the minimum required to control seizures while maintaining a gag reflex.
- Typically, patients are maintained on the CRI for 12 to 24 hours; then weaned off the CRI while being monitored carefully.

Ongoing Antiepileptic Drug Therapy
Once the patient is stabilized, long-term anticonvulsants can be initiated to prevent recurrence of seizure activity in the coming hours. Phenobarbital is commonly used for long-term antiepileptic therapy, and it can be used IV for acute therapy of SE. However, it tends to cause significant cerebral depression and may cause hypotension and respiratory depression, necessitating monitoring of blood pressure and respiratory function. A loading dose of phenobarbital is calculated using this equation:

\[
\text{Body weight (kg)} \times 0.8 \ L/kg \times \text{desired phenobarbital serum concentration}^1 = \text{Dose (mg) of phenobarbital to administer}
\]

The total calculated dose is divided into 4 to 6 aliquots, which are given no more than every 30 minutes. If the patient becomes excessively sedated, the subsequent aliquot can be skipped or delayed.

If the patient continues to seizure despite administration of benzodiazepines, levetiracetam, and phenobarbital, the following drugs can be added to therapy:

### TABLE 1.

**Recommended Dosages of Antiepileptic Drugs for Use in Dogs with SE**

<table>
<thead>
<tr>
<th>ANTIPILEPTIC DRUG</th>
<th>RECOMMENDED DOSAGES</th>
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<tbody>
<tr>
<td>Diazepam</td>
<td>0.5–2 mg/kg IV (up to 20 mg)</td>
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<tr>
<td></td>
<td>• If patient is receiving phenobarbital, higher dose of 2 mg/kg may be needed</td>
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<tr>
<td></td>
<td>• Monitor for cardiac/respiratory depression, nausea, agitation²</td>
</tr>
<tr>
<td>Fosphenytoin</td>
<td>15 mg/kg phenytoin equivalents IV or IM (starting dose for dogs)¹</td>
</tr>
<tr>
<td>Ketamine</td>
<td>3–5 mg/kg IV bolus; then 0.2–0.6 mg/kg/H IV CRI³</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>20–60 mg/kg IV bolus injection over 5 minutes Q 8 H in-hospital; 20 mg/kg PO Q 8 H⁴</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.05–0.2 mg/kg IV bolus; then 0.2–0.4 mg/kg/H IV CRI¹</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.5–2 mg/kg IV or IM; then 0.2–1 mg/kg/H IV CRI¹</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>12–24 mg/kg IV loading dose, which is administered in aliquots of 2–4 mg/kg IV Q 20–30 min (max, 24 mg/kg over 24 H)²</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>15–20 mg/kg IV³ slow bolus</td>
</tr>
<tr>
<td>Propofol</td>
<td>1–2 mg/kg IV bolus; then 0.05–0.6 mg/kg/min IV CRI (titrate to effect)²</td>
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**MEDICAL THERAPY AT HOME**
In some cases of SE, the client cannot bring the patient to the hospital quickly enough for management and must administer antiepileptic therapy at home prior to transport to the clinic. **Note.** For safety, clients should never give oral medications to an animal having seizure activity.

- Recommended therapy for patients at home is a 1 mg/kg bolus of diazepam rectally Q 20 minutes, for a total of 4 or 5 doses after the second or third seizure.⁵
- Many clients can be trained to administer rescue medications, such as midazolam, by IM injection prior to transport, with a more predictable response than that to rectally administered drugs. **Note:** Diazepam is not well absorbed when administered IM.
- The attending neurologist may recommend that other maintenance AEDs, such as levetiracetam, phenobarbital, or zonisamide, be incorporated into the long-term seizure management protocol.
- Ultimately, after 3 seizures within a 24-hour period, the client should bring the patient to the veterinary hospital for IV treatment and monitoring.
• Fosphenytoin: Important to monitor for hypotension, arrhythmias, ataxia, and vomiting; a multicenter study is assessing the use and efficacy of this drug
• Phenytoin: Administration should be slow to prevent cardiotoxicity and hypotension
• Propofol: Often considered a last line of defense in patients with SE; those receiving this agent should be monitored closely for adverse blood pressure and respiratory effects
• Ketamine: May have neuroprotective benefits and help end the maintenance, or self-sustaining, phase.2

STABILIZATION: FURTHER CARE
The stabilization process involves many other elements in addition to control of seizure activity (Table 2).

Physiologic Concerns

Blood Pressure. Because hypertension, and then hypotension, is common in these patients and can worsen with addition of AEDs, monitor blood pressure at least every 1 to 2 hours while the patient is sedated, more frequently if it becomes abnormal, and maintain systolic blood pressure between 100 and 150 mm Hg.

Technicians should be aware of the Cushing’s reflex in these patients: if hypertension is noted alongside bradycardia, it raises concern for presence of high intracranial pressure. In hypotensive patients, hypertonic saline may be considered at 4 mL/kg over 10 minutes. Administer a balanced electrolyte replacement solution at a maintenance rate or, if needed to treat hypotension, at a higher rate.

Temperature. Patients often are hyperthermic, and body temperature should be regulated, if possible. If the patient has a temperature higher than 104°F, begin passive cooling, and monitor rectal temperature every 15 minutes; end cooling efforts once the patient’s temperature reaches 102°F. Hypothermia may occur in heavily sedated animals once seizure activity stops, and warming may be needed at that time.

Respiration. Patients with SE may be heavily sedated while receiving AED therapy and, therefore, have difficulty protecting their upper airways. Assess gag reflex every 15 to 20 minutes if the patient is unresponsive. If the gag reflex is insufficient or absent, it may be necessary to intubate these patients to help prevent and treat hypoxemia and protect the airway from aspiration. In intubated patients, carbon dioxide (CO₂) should be monitored using end-tidal capnography or blood gases.

• If CO₂ levels exceed 45 mm Hg, discuss with the clinician placing the patient on a ventilator.
• If CO₂ levels exceed 60 mm Hg, immediately begin mechanical ventilation using an Ambubag.

Note: Nasal oxygen should not be administered because it may increase intracranial pressure.6 For conscious patients, a face mask, oxygen cage, or flow-by method can be used to administer oxygen. If patients are unconscious and have lost their gag reflex, oxygen is most safely and effectively provided via an endotracheal tube.

Oxygenation should be monitored by the arterial blood gas PaO₂ or SaO₂, which indicates the level of oxygen saturation of hemoglobin. Pulse oximetry can be monitored cageside as an additional continuous indicator of oxygenation levels.

Metabolic Abnormalities
Sodium abnormalities, along with hypocalcemia and hypoglycemia, can occur. During treatment of

### TABLE 2. Additional Medications for Care During Stabilization

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PURPOSE</th>
<th>RECOMMENDED DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% calcium gluconate</td>
<td>Correct hypocalcemia</td>
<td>0.5–1.5 mL/kg IV administered over 10 min</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Relieve agitation/anxiety</td>
<td>0.5 mcg/kg/H as CRI with initial loading dose of 0.5 mcg/kg IV</td>
</tr>
<tr>
<td>50% dextrose</td>
<td>Correct hypoglycemia</td>
<td>1 mL/kg diluted to 25%, administered over 15 min*</td>
</tr>
<tr>
<td>Furosemide</td>
<td>Decrease intracranial pressure by establishing diuresis</td>
<td>0.7 mg/kg IVb</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Decrease intracranial pressure by direct osmotic effect on neurons</td>
<td>0.25–1 g/kg IV, administered over 20 minb</td>
</tr>
</tbody>
</table>

* To avoid adverse effects of hyperglycemia, administer thiamine, 20 to 59 mg/animal IM, prior to administering glucose
b. Administer furosemide 15 minutes after mannitol administration
electrolyte imbalances, monitor heart rate and rhythm via electrocardiography, paying close attention to whether bradycardia is present. Cease treatment and contact a clinician if bradycardia occurs.

**Sodium.** Sodium should be corrected slowly to avoid contributing to neurologic deficits. In patients with hypernatremia, serum sodium levels should be lowered at a rate of 0.5 to 1 mEq/L/H, as cerebral edema may occur if plasma sodium levels change too quickly.

Administer hypotonic IV fluids to provide free water, diluting the high plasma sodium. If hypernatremia has existed more than 24 hours, perform correction at a slower rate. In rare cases of hyponaotremia, 3% saline may be utilized, and the rate of correction should not exceed 0.5 mEq/L/H.

Plasma sodium should be monitored initially every 2 to 4 hours, to ensure that the correction rate is appropriate and allow adjustment of fluid dose and rate, if necessary.

**Calcium.** Hypocalcemia can be treated by slow administration of 10% calcium gluconate, 0.5 to 1.5 mL/kg IV over 10 minutes.

**Glucose.** Hypoglycemia is often treated with slow administration of a bolus of 50% dextrose, 1 mL/kg diluted to 25%, over 15 minutes. To avoid adverse effects of hyperglycemia, such as contributing to neuronal injury, administer thiamine, 20 to 59 mg/animal IM, prior to administration of dextrose.²

**Neurologic Protection**
Protecting the brain during stabilization is vital, as SE can lead to such sequelae as cerebral edema, neuronal necrosis, and increased intracranial pressure.

- Mannitol, 0.25 to 1 g/kg IV, can be administered over 20 minutes; then 15 minutes later, furosemide, 0.7 mg/kg IV, can be administered to help with diuresis. Furosemide may be avoided in hypotensive patients.
- While the patient is resting, elevate the top half of the body (not just the head) 30° to help reduce intracranial pressure.
- Avoid jugular blood collection and catheters, nasogastric tubes, and nasal oxygen catheters to decrease the risk for elevating intracranial pressure.
- If intubation is necessary, administer IV lidocaine ahead of time to reduce the associated cough reflex.⁷

**Additional Nursing Care**
Other nursing care advised for patients with SE includes:
- Recumbent patient care, padded cages, and rotation every 4 hours
- Close monitoring of vitals, especially blood pressure, and weight
- Lubrication of eyes and removal of secretions from the mouth, pharynx, and airway, if necessary
- Placement of a urinary catheter, with urine output monitored every 4 hours
- If needed, dexmedetomidine as a low-dose CRI to help relieve agitation and anxiety during the recovery period.

**DIAGNOSTIC APPROACH**
Once the patient is stabilized, further diagnostics, such as EEG and magnetic resonance imaging (MRI), may be pursued.

EEG should be considered the gold standard for diagnosis of patients with SE. In particular, it is useful for:
- Determining whether emergency drug therapy is managing the seizure
- Ascertaining whether the brain is continuing to actively seize even though the physical signs have resolved.

Patients in nonconvulsive SE—rather than presenting with a classic grand mal seizure—may instead present in a stuporous and/or unresponsive state or have subtle twitching. Additionally, when patients have received multiple drugs to control SE, as they awake, it may be difficult to distinguish recurrence of seizure activity from normal sedative recovery. Investigation with EEG can help better diagnose these patients and lead to correct treatment.

**Diagnostic Imaging**
MRI and computed tomography can help determine structural damage as a cause or consequence of seizure activity. On MRI, lesions can appear within the piriform/temporal lobes as a result of SE, but once a patient is seizure-free, they resolve within 10 days to 18 weeks.²

**Laboratory Analysis**
Blood analysis is also an important diagnostic tool in patients with SE.

- In particular, blood analysis is key in evaluating glucose, sodium, and calcium levels.
- SE, in general, may cause hypoxia and hypotension, resulting in elevated liver enzymes.
- Patients experiencing convulsive SE may have increases in muscle enzymes.
- Hypovolemia can lead to elevation of kidney values.
Onset of pneumonia can lead to changes in \textit{white blood cell count}. Blood analysis can also reveal \textit{metabolic disturbances} that may have triggered SE activity.\textsuperscript{2}

\textbf{IN SUMMARY}

Although SE cases can be intensive and difficult to manage, it is important for technicians and supportive veterinary team members to implement the necessary nursing care.

- The excessive seizure activity itself can cause metabolic imbalances and harmful effects on intracranial pressure that must be closely managed.
- Technical staff should understand the adverse effects and risks of certain AEDs, such as hypotension, excessive sedation, hypoxemia, and bradycardia.
- Appropriate recumbent care, along with close monitoring of awareness level, gag reflex, blood pressure, oxygenation, and pupillary light reflexes, is necessary. Successful outcomes for these patients often rely on top-notch, observant nursing care.

\textit{AED} = antiepileptic drug; \textit{CO}_2 = carbon dioxide; \textit{CRI} = constant rate infusion; \textit{EEG} = electroencephalography; \textit{MRI} = magnetic resonance imaging; \textit{PaO}_2 = partial pressure of oxygen; \textit{SaO}_2 = hemoglobin saturation with oxygen; \textit{SE} = status epilepticus

\textbf{References}