EPILEPSY
ONE day after he stops drinking, a 50-year-old alcoholic experiences a generalized tonic-clonic convulsion; a 30-year-old man with AIDS watches his arm jerk uncontrollably for two minutes; a 70-year-old woman suddenly develops bizarre behavior that lasts two days; a 4-year-old child stares blankly for 30 seconds and then continues to play. Despite grossly disparate etiologies and varying prognoses, all four experienced a seizure.
Epidemiology

Seizures account for at least 1% of ED visits. The prevalence of active epilepsy is approximately 6 per 1000; one-quarter to one-half of patients with epilepsy continue to have recurrent seizures despite therapy. Under the best of circumstances, excluding noncompliance and other variables, 5%-10% of patients have intractable epilepsy despite optimal medical management.
The incidence of seizures is high in the first year of life, decreases throughout childhood, and remains relatively stable and low throughout mid-life. At age 55, the incidence begins to increase, peaking in persons 75 years and older. The increase in the partial epilepsies coincides with the age related rise in degenerative, neoplastic, and vascular pathologies.
Using a 30-minute criterion for status epilepticus, at least 50 per 100,000 population will suffer this condition. In one study, over half of patients presenting to the ED in status had no prior seizure history.

Mortality in patients with status epilepticus is linked to the duration of the seizures and the underlying etiology. The mortality is high—22%-23% for children and 26% for adults.
Secondary seizures are associated with acute or progressive neurological insult, or systemic stressors.
Reversible causes must remain high in the differential diagnosis.
Hypoglycemia is the most common metabolic cause of seizures.
Hyponatremia, hypocalcaemia, and hypomagnesemia are rare etiologies.
Metabolic encephalopathies such as nonketotic hyperglycemia and uremia can cause both focal and generalized seizures.
Alcohol is the most common toxin associated with seizures, followed by tricyclics, cocaine, amphetamines, antihistamines, theophylline, and isoniazid. Drug withdrawal and noncompliance with anticonvulsant medications are leading causes of recurrent seizures. Infections can lower the seizure threshold.
Classification Of Seizures

Partial Seizures
- Simple Partial
  - motor
  - somatosensory
  - autonomic
  - psychic
- Complex Partial
  - with focal onset prior to alteration in consciousness
  - without focal onset prior to alteration in consciousness

Generalized Seizures
- Primary Generalized
  - Nonconvulsive
    - absence
  - Convulsive

- tonic-clonic
- clonic
- tonic
- myoclonic
- atonic

Secondary Generalized
- convulsive
- nonconvulsive

Status Epilepticus
- Convulsive Generalized
  - primary generalized
  - secondary generalized

Convulsive Focal
- Nonconvulsive
  - primary generalized
    - absence
  - partial with or without secondary generalization
    - (complex partial)
**Pathophysiology**

Seizures result from either recurrent excitatory connections

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**Table 2. Etiologies Of Secondary Seizures.**

<table>
<thead>
<tr>
<th>Tumors</th>
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<tbody>
<tr>
<td>Vascular event</td>
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<tr>
<td>• Subarachnoid hemorrhage</td>
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<tr>
<td>• Subdural hemorrhage</td>
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<td>• Epidural hemorrhage</td>
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<tr>
<td>• Stroke</td>
<td></td>
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<tr>
<td>• Vasculitis</td>
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| Infection               |   |
| • Meningitis            |   |
| • Encephalitis          |   |
| • Abscess               |   |

| Metabolic               |   |
| • Hypoglycemia (the most common metabolic cause of seizures) |   |
| • Hyponatremia (a rare cause of seizures except in infants younger than 6 months) |   |

| Toxic                   |   |
| • Cocaine and sympathomimetics |   |
| • Tricyclic antidepressants |   |
| • Anticholinergics       |   |
| • Theophylline           |   |
| • Isoniazid              |   |

| Eclampsia               |   |
During a convulsion, there is often a period of transient apnea and hypoxia. Body temperature is frequently elevated; up to 43% of patients with a generalized convulsion have a transient rise in temperature above 100°F. Early in a motor seizure, blood pressure increases, followed by a later fall. Serum lactate and glucose levels increase. Acidosis due to elevated lactate occurs within 60 seconds of a convulsive event and normalizes within one hour after ictus. A rise in the peripheral white blood cell count is routine (without an increase in bands).
If the seizure lasts more than 30 minutes, homeostatic mechanisms deteriorate.

Though the current evidence is weak, it appears that status epilepticus alone may result in cognitive impairment regardless of the inciting cause.
Differential Diagnosis

A number of conditions mimic seizures. These include convulsive syncope, with or without cardiac dysrhythmias; decerebrate posturing; psychogenic events; dystonia; and migraine headaches. Patients with strychnine poisoning may develop seizure-like activity yet demonstrate normal mental status. When faced with a new-onset seizure, consider these “mimics” since misdiagnosis may have profound consequences.
Pre-hospital Management

Pre-hospital management of the convulsing patient centers on securing the airway, maintaining oxygenation, obtaining intravenous access, and protecting the patient from injury. Fortunately, the majority of seizures are of a short duration, and in most cases, little else is required. The use of a Padded tongue blade is contraindicated since it may induce emesis or break a tooth; a nasal airway can help maintain The airway when needed.
Ascertain the use of anticonvulsants and other medications. Noncompliance with anticonvulsants is the Most common cause of recurrent seizures in this group of Patients. The use of anticoagulants such as warfarin Should increase suspicion for intracranial bleeding. Determine whether the patient is a diabetic, as glucose Abnormalities are a frequent cause of seizures. Suicidal patients on INH may overdose on this medication.
A social history is also important. A recent decrease in alcohol is a common cause of seizures. The emergency physician should also ask regarding illicit drug use, especially targeting seizure-prone drugs such as cocaine, phencyclidine (PCP), and sympathomimetics such as ecstasy.
Differential Diagnosis Of Altered Mental Status In The Patient Who Has Seized

- Hypoglycemia
- CNS infection
- Mass lesion (sub-dural, epidural)
- CNS vascular event
- Non-convulsive status or Subtle convulsive status
- Drug toxicity
- Psychiatric disorder
- Postictal state
3-Monitoring

Most patients who suffer an isolated seizure need no special monitoring. However, patients who continue to seize or those suspected of overdose may benefit from cardiac monitoring. An ECG may reveal evidence of drug toxicity. Tricyclic cardiotoxicity may manifest as a QRS complex greater than 0.10 seconds or a rightward shift of the terminal 40 ms of the frontal plane QRS complex (a prominent terminal R wave in lead AVR). Patients in status should be monitored by continuous pulse oximetry to detect seizure-related hypoxia. Of course, most, if not all, patients with unrelenting convulsive status will require intubation.
There is no “standard” diagnostic screening that applies to all patients with seizures; one individual may require no tests, while another may need” work-up. The direction and scope of laboratory testing depends upon the findings present on history and physical examination.
New-Onset Seizure; Normal Examination

The ACEP clinical policy recommends a serum glucose level and electrolytes (as well as a pregnancy test for women of childbearing age). If a patient with a new-onset seizure has no significant co-morbid disease, and a normal examination including a normal mental status), the likelihood of an electrolyte disorder is very low. In one prospective study of 136 patients with new-onset seizures, only two had electrolyte abnormalities not suspected on the basis of history and physical examination (both had hypoglycemia). Other studies confirm that routine measurements of electrolytes is not helpful in adults Consider ordering a screen for drugs of abuse in selected patients. No studies support routine ED testing of phosphate, calcium, or magnesium in either children or adults who suffer seizures.
However, laboratory tests may be indicated in patients who are on dialysis, malnourished, taking diuretics or hypoglycemic agents, or in those who have significant medical disorders. Under the appropriate clinical circumstances, such tests might include blood urea nitrogen (BUN), creatinine, calcium, phosphate, magnesium, and an urinalysis.
Known Seizure Disorder; Normal Examination

Patients with a known seizure disorder who have a “typical” event while on medications but who are asymptomatic, alert, and oriented in the ED need only a serum anticonvulsant level. One exception includes those with an underlying disease such as diabetes that could result in a metabolic derangement. In such patients, it is important to investigate for precipitants such as infections or new medications.
Seizure; Abnormal Findings On Examination

Patients in convulsive status epilepticus, and patients who are not actively convulsing but who are persistently postictal, require additional observation and diagnostic Testing. Tests may include a determination of serum glucose, electrolytes, urea nitrogen, creatinine, magnesium, phosphate, calcium, complete blood count, pregnancy test In women of childbearing age, anti-epileptic drug levels, Liver function tests, and screen for drugs of abuse.
an anion gap metabolic acidosis, usually secondary to lactic acidosis. The anion gap acidosis should resolve in less than one hour after the seizure ends; persistence beyond this time suggests an underlying abnormality. In such cases check for ketosis (alcoholic or diabetic) and consider poisoning (methanol, iron, isoniazid, ethylene glycol, salicylates, carbon monoxide or cyanide). In cases of Prolonged seizures, an ABG can provide information Regarding hypercarbia and oxygenation.
Rhabdomyolysis, is a rare consequence of a seizure, and should be suspected if the urine dips positive for blood in the absence of red blood cells on the microscopic exam. A serum creatine phosphokinase (CPK) level is indicated in these cases.
Tests To Determine Whether A Seizure Occurred

Prolactin is released during periods of significant stress. Serum levels are elevated following generalized motor seizures in approximately 90% of cases, and following complex partial seizures in about 70% of cases. Non Motor seizures and psychogenic seizures do not normally Elevate prolactin levels. Prolactin peaks at 20 minutes after The seizure ends and returns to baseline within 60 minutes. Some drugs including opiates phenothiazines and most anti-epileptic drugs, can also elevate serum levels.
In one retrospective study, total CPK (not cardiac isoenzymes) measured at least three hours after the event correlated with generalized seizures. However, the gold standard for whether or not the patient actually had a seizure was really a “best guess” by a blinded reviewer. In another smaller but more rigorous trial (using video EEG recordings), the authors did not find serum CPK levels to be useful in differentiating seizures from other causes of loss of consciousness. In one ED study on syncope, the serum bicarbonate was decreased in 70% of the patients who were presumed to have had seizures. If ordered, it must be drawn within 30-40 minutes of the event because of the rapid clearance of lactate.
Electroencephalography (EEG)

An urgent EEG in the ED may be valuable for those Patients with persistent altered mental status in whom Subtle convulsive or non-convulsive status epilepticus is Suspected. An EEG is also required when a seizing patient’s motor activity has been suppressed by either paralysis or barbiturate coma and there is the need to assess ongoing seizure activity.
Management Of Convulsive Status Epilepticus

- **Stabilization**
  - Protect the patient; do not place anything in the mouth
  - Secure the airway; intubate if evidence of ineffective respirations/oxygenation
  - Establish intravenous access with non-dextrose solution
  - Activated charcoal if drug overdose is considered after intubation to protect the airway
• **Initial Interventions**
  - • Dextrose, if hypoglycemic, 50 cc of 50% glucose for adults; in children 2 cc/kg of 25% glucose; Thiamine 100 mg IV or IM before glucose (if malnourished)
  - • Ceftriaxone 100 mg/kg up to 2 gm IV, if meningitis is suspected
  - • Lorazepam 0.1 mg/kg at 2 mg/min to a maximum of 10 mg; or diazepam 0.2 mg/kg at 5 mg/min to a maximum of 20 mg
  - • Phenytoin 18 mg/kg IV at 25 mg/kg in patients with cardiac disease (otherwise 50 mg/min); in children 1 mg/kg/min OR fosphenytoin 18 PE/kg of phenytoin equivalent units IV at 150 PE/min
• **Persisting Seizures**
  - Give additional IV phenytoin, or fosphenytoin, up to 30mg/kg **OR** Phenobarbital 20 mg/kg at 100 mg/min IV

• **Refractory Seizures**
  - Pentobarbital 5 mg/kg IV at 25 mg/min followed by 0.5-3.0 mg/kg/hr **OR**
  - Benzodiazepine infusion:
    - Midazolam IV bolus of 200 mcg/kg followed by 1-10 mcg/kg/min;
    - Lorazepam 0.3-9.0 mg/hr.
Other Therapies

- Valproic acid has recently been made available in an intravenous preparation. The average dose is 10-15 mg/kg/m, but a 20 mg/kg load has been safely used. Although not yet approved for this use in the United States, intravenous valproic acid can successfully treat convulsive status epilepticus. It has also been used (at a dose of 500 mg over 20 minutes) to manage non-convulsive status epilepticus.

- The drug is contraindicated in patients with hepatic dysfunction, as it may cause hepatic failure, usually in the first six months of therapy. Because the medication cannot be infused faster than 20 mg per minute, a loading dose may require an hour’s infusion.
Pentobarbital (3-5 mg/kg followed by an infusion of 0.5-3.0 mg/kg/hr) is effective in suppressing electrical discharges. Pentobarbital can compromise cardiovascular status, and its use necessitates EEG monitoring, since it can curb motor activity. Use fluid boluses to treat pentobarbital induced hypotension, and consider dopamine in case of persistent hypotension.
A continuous benzodiazepine infusion is also useful to treat refractory status epilepticus. Options include lorazepam at a dose of 0.3-9.0 mg/hr; midazolam 0.5 mg/hr; and diazepam 8 mg/hr. Interestingly, some evidence questions the utility of these infusions, since there may be a loss of GABA-mediated inhibition after prolonged seizure activity.

The third option in refractory status epilepticus is propofol (1-2 mg/kg intravenously followed by 2-10 mg/kg/hr).
Non-Convulsive Status Epilepticus

like convulsive status epilepticus, is a state of continuous or intermittent seizure activity lasting more than 30 minutes without a return to baseline function. The hallmark of NCS is altered mental status, and unless it is suspected, the diagnosis is easily missed. Though the distinction is not clear in the literature, NCS in general should be distinguished from subtle generalized convulsive status epilepticus. In subtle generalized convulsive status epilepticus, the patient is in continuous coma but has subtle motor convulsions
Unlike NCS, this entity has a very poor prognosis. The literature is rife with patients who present with altered mental status and were initially labeled as having psychiatric problems. Only later was the NCS recognized, either by EEG or a subsequent convulsion. Nonconvulsive status can be either a primary generalized process (absence status) or secondarily generalized (complex partial status).
Diagnosis Of NCS

A history of a seizure disorder, especially when the patient’s symptoms are temporally related to a convulsive event, is a red flag that needs to be pursued. Prolonged “postictal periods,” persisting aphasic, somatosensory, or psychic findings after ictus all suggest possible ongoing epileptogenic activity. Automatisms, abnormal eye movements, persistent twitches, or blinking provide clues to nonconvulsive status. When NCS is suspected, obtain an EEG. Ictal EEG findings are varied, and can show spike and slow wave complexes, polyspike discharges, irregular sharp and slow waves, or rhythmical slowing.
Treatment

For short-term control, benzodiazepines are useful; either diazepam or lorazepam. Benzodiazepines are not effective for long lasting seizure control, and when indicated, administer a second long-acting anticonvulsant. The literature is unclear as to the urgency of controlling NCS, though there is evidence that ongoing neuronal firing does result in neuronal injury.
Special Situations

- Alcohol Withdrawal Seizures
  Seizures occur in approximately 10% of patients who withdraw from alcohol. Alcohol abuse also increases the risk of having a seizure or developing a seizure disorder independent of withdrawal. Alcohol withdrawal seizures usually occur between six and 48 hours after cessation of drinking. Withdrawal seizures are usually generalized events that can be multiple but rarely persist past 12 hours from onset. The patient may or may not have other signs of alcohol withdrawal, such as tachycardia, confusion, or tremors.
The diagnosis is based on history of recurrent events temporally related to stopping (or significantly decreasing) alcohol intake. Consequently, a first-time withdrawal seizure must be worked up as any first-time seizure, including the need for CT. Once a patient with an Alcohol withdrawal seizure is brought to the ED, clinical Findings cannot predict which of those patients are likely To have recurrent seizures in the department.
There is good evidence to recommend benzodiazepines, even in a patient who is not actively seizing. A recent double-blind, placebo-controlled study showed that 2 mg IV lorazepam decreases recurrent seizures related to alcohol use and reduces the need for hospitalization.
Phenytoin does not have a role in managing either withdrawal seizures or controlling recurrent alcohol-related seizures in the ED. However, many alcoholics may have an underlying seizure disorder from prior head trauma or other causes. For this reason, phenytoin may play a role in management of alcoholic with seizure in ED.
• Drug-Induced Seizures

– Most drug-induced seizures, especially those due to cocaine and other stimulants, best respond to benzodiazepines.

– Some patients may require astounding doses. Phenytoin is less effective for most drug-induced seizures than phenobarbital or benzodiazepines.

– One unusual cause of status epilepticus is isoniazid (INH) overdose. With the rise in tuberculosis, it is a growing problem; over 500 cases were reported in 1996.
It is resistant to all pharmacologic interventions save heroic doses of pyridoxine—5 grams or more. One-third or more of hospitals do not have adequate stores to treat a single INH overdose. Emergency physicians should realize that they are unlikely to find 50 ampules of B6 during a frantic 3 a.m. scavenger hunt.
Seizure In Pregnancy
Management of seizures in pregnancy depends on whether the seizure is of new onset or chronic. In patients more than 20 weeks’ gestation, eclampsia is an important consideration. Assess such patients for hypertension, proteinuria, and edema. In large women who are postictal, the pregnancy status may not be immediately obvious. A pregnancy test, checking for fetal heart, or an ED ultrasound may be helpful.
Pregnant patients with new-onset seizures (not eclamptic) should be worked up as any new-onset seizure patient with a metabolic profile and head CT. (The need for abdominal shielding in pregnant women undergoing head CT is unclear; some argue that the radiation of CT is so planar that abdominal shielding is unnecessary.) Precipitating etiologies such as infections and drug toxicities should also be investigated. If no source is identified, anticonvulsants should be withheld and the patient referred for close follow-up. In pregnant patients with epilepsy, noncompliance and sleep deprivation are common causes for seizures.
Patients who are actively seizing should be managed just as the non-pregnant patient. The risks to the fetus from hypoxia and acidosis are greater than the potential teratogenicity of anticonvulsant medications. Arrange for fetal monitoring during and after a seizure in patients of more than 24 weeks’ gestation. Phenytoin and phenobarbital have similar teratogenic profiles; carbamazepine is probably safest in pregnancy. In regards to eclampsia, two prospective trials have clearly demonstrated that magnesium sulfate is superior to phenytoin in the prevention of eclampsia. and superior to diazepam or phenytoin in the treatment of eclamptic Seizures. In the eclamptic patient, give 4 grams IV of Mg-sulphate followed by 2g/hr IV drip.
• **Seizure After Trauma**

The risk of developing a seizure disorder after a traumatic brain injury (TBI) is related to the severity of the injury. The incidence after minor TBI (GCS score > 12) is 1.5%, the incidence increases to 17% after a severe TBI (GCS score < 9). Although the incidence of post-traumatic seizures in the first week is decreased to less than 4% by the early use of phenytoin, after the first week, there is no statistical difference in seizure incidence whether or not patients are treated. In addition, though the incidence of an early post-traumatic seizure is decreased with AED use, there is no change in outcome.
For these reasons, prophylactic antiepileptic drugs are not indicated to prevent late post-traumatic seizures. The American Academy of Neurologic Surgeons state that the use of an AED in the first week after severe head injury is only an “option”; not a rule or guideline.
• **Initiating Anticonvulsant Therapy In The ED For First-Time Seizures**

There is no set standard for this intervention. The decision to initiate anticonvulsants in the ED for a first-time seizure varies depending upon the patient, physician, and local practices. This decision is best made in conjunction with the patient’s primary care provider or neurologist and should consider the predicted risk for seizure recurrence. The chance of a recurrent event after one unprovoked seizure varies depending on the patient’s age and the underlying etiology. Seizure etiology combined with EEG findings are the best predictors of recurrence; when no etiology is identified and the EEG is normal, the recurrence rate is 24% at two years. Patients who have structural
• Seizures In The Elderly

The elderly represent a unique subset in the treatment of seizures. Age-related physiologic changes affect pharmacokinetics, dosage, and titration regimens. In the Treatment of elderly patients, phenytoin and carbamazepine are considered first-line agents in the treatment of partial seizures, while phenytoin, carbamazepine, and valproic acid are primary therapies for generalized seizures. The role of the newer anti-epileptics in the elderly remains unclear.
Disposition

- Disposition from the ED must take into consideration the patient’s social situation, resources, and compliance.
- Patients who have had a first-time seizure but have a completely normal neurologic exam and no underlying medical problems do not usually require admission, especially if good follow-up can be provided.
All patients who have had a seizure must be advised not to drive and to avoid placing themselves or others in potentially dangerous situations until assessed by their physician.
Sample Discharge Instructions For Patients With Seizures.

- A seizure (convulsion or “fit”) is caused when the electrical messages in the brain rapidly repeat themselves. It can happen for lots of reasons; some serious, most not.
- A person having a seizure may lose consciousness, have stiffness or jerking motions, and may lose control of their bladder (urinate).
- Seizures usually last only a few minutes. Most people are sleepy or confused for a little while after having a seizure.
- Most seizures are not dangerous unless they last for more than 10 to 15 minutes.
• Most injuries occur because a person falls, has a car accident, or drowns when having a seizure.
• If you are with a person having a seizure, you can help by keeping them from falling or hitting anything.
• *Never* put anything in their mouth — no one ever “swallows their tongue.” Roll them on their side if they start to vomit.
• If the seizure does not stop after several minutes or the person does not wake up quickly, call for help.
• **What to do if you or your loved one has seizures:**
  - Do *not* drive, operate machinery, work at heights, swim, or bathe in a tub without someone nearby, or do any other hazardous activity until you are “okayed” by your doctor.
  - Do *not* stay alone for the next 24 hours. Have an adult stay with you.
  - Do *not* drink alcohol, use street drugs, or drink caffeine. These make seizures worse.
  - *Always* take your seizure medicine as instructed by your doctor.
  - Follow up with your doctor for further evaluation and treatment.
Call your doctor or return to the emergency department if you experience any of the following:

- Frequent seizures
- Seizures that last longer than 5 to 10 minutes
- Staying confused for a longer time than usual after a seizure
- A bad headache or a stiff neck
- A new rash
- Fever greater than 101°F
- Seizures caused by running out of medicine or not taking your medicine
- Injuries caused by a seizure
- Any new or worsening symptom(s) that concerns you
• Remember that the emergency department is open 24 hours a day, every day, and we are always glad to see you.
Clinical Pathway: Management Of Status Seizures

If patient still seizing, proceed; if seizures stop, see "Clinical Pathway: Evaluation Of Seizures"

- Assess and secure the ABCs
- Protect the patient from harm
- Check glucose and give dextrose if <80
- Perform a physical assessment
- Monitor vital signs, ECG, pulse oximetry

Assess need for:
- Antibiotics or antiviral agents
- Charcoal
- Toxin-specific therapy (e.g., B6 for INH OD, HCO3 for tricyclic OD)

Lorazepam 2 mg / min to a max of 10 mg (Class I)
- may need to use higher doses in cocaine- or amphetamine-induced seizures (Class IIb)
- 0.1 mg/kg in children (Class IIa)

- Phenytoin 18 mg / kg at 25-50 mg / min## (Class IIa)
- Phenytoin 18 PE / kg at 150 PE / min (Class IIa)

- Repeat phenytoin or fosphenytoin at 1/2 the initial dose (Class IIb)
- Phenobarbital 20 mg / kg at 100 mg / min (Class IIb)

- Midazolam 200 mcg/kg bolus then 1-10 mcg/kg/min (Class IIb)
- Pentobarbital* 3-5 mg/kg at 25 mg/min then drip at 0.5-3.0 mg/min (Class IIb)
- Propofol 1-2 mg/kg bolus then 2-10 mg/kg/hr (Class IIb)

Consider bedside EEG (Class IIb)
- Paralytics may be given if patient is developing hyperthermia, rhabdomyolysis, or severe acidosis.
- Bedside EEG mandatory in such cases.

- Reassess patient
- Intubate at any time airway or breathing is compromised
- Consider CT / LP

## Slower rates for patients with cardiovascular disease.
Infusion should be through a large-bore IV
- PE = phenytoin equivalent
- **Watch for hypotension and treat initially with fluids; dopamine if needed
AED = antiepileptic drug

The evidence for recommendations is graded using the following scale. For complete definitions, see back page. Class I: Definitely recommended. Definitive, excellent evidence provides support. Class IIa: Acceptable and useful. Very good evidence provides support. Class IIb: Acceptable and useful. Fair-to-good evidence provides support. Class III: Not acceptable, not useful, may be harmful. Indeterminate: Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute, professional judgment and may be changed depending upon a patient’s individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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Emergency Medicine Practice
Thank you