CHAPTER 15 Seizures

Ana M. Davitt and Charles V. Pollack, Jr.

PERSPECTIVE

Seizure is defined as abnormal neurologic functioning caused by abnormally excessive activation of neurons, either in the cerebral cortex or in the deep limbic system. *Epilepsy* is defined as recurrent unprovoked seizures due to a genetically determined or acquired brain disorder[1]; it is not an appropriate term for seizures that occur intermittently and predictably after a known insult, such as alcohol intoxication and withdrawal.

Presentation to the emergency department (ED) with a generalized convulsive seizure prompts immediate concern for airway protection and stabilization, followed by a focused search for the cause. Nonconvulsive seizures, which are much less common, may be relatively obscure in their presentation, more diverse in their etiology, and are sometimes more difficult to recognize and control acutely.

Epidemiology and Classification

It is estimated that 6% of the U.S. population experience at least one nonfebrile seizure during their lifetime; the annual incidence among adults is 84 per 100,000 population, and more than half of these individuals develop epilepsy.[2] In one study, approximately 1% of ED visits were for seizure-related complaints.[3] Nearly half of these patients had alcohol or low antiepileptic drug levels implicated as contributing factors.

Seizures can be classified as primary or secondary (the latter also termed *reactive*), as generalized or focal (partial), or as convulsive or nonconvulsive. Table 15-1 shows the distribution of seizures in a typical population of patients. A generalized seizure is defined as abnormal neuronal activity in both cerebral hemispheres. Seizues may be divided into tonic-clonic, absence, and myoclonic. Partial seizures or focal seizures usually involve one hemisphere. They are divided into simple partial (in which consciousness is maintained), complex partial (in which consciousness is lost), and those that become secondarily generalized. Some seizures are impossible to classify because of inadequate or inaccurate description of the ictal activity.[2,3]

Status epilepticus is defined as at least 30 minutes of persistent seizures or a series of recurrent seizures without intervening return to full consciousness,[4] although several authors have proposed shortening the time criterion from 30 minutes to 5 minutes.[5]

Secondary seizures may occur as a result of a vast array of injuries and of illnesses such as intoxication or poisoning, encephalitis, encephalopathy, organ failure, other metabolic disturbances, infections of the central nervous system, cerebral tumors, pregnancy, and, paradoxically, supratherapeutic levels of anticonvulsants.

Seizures in children follow a different distribution, primarily because of the relatively high incidence of febrile seizures and the frequently uncertain observational history of possible ictal activity. Febrile seizure is the most common pediatric seizure, occurring in 2 to 5% of children between 6 months and 5 years of age; 20 to 30% of those children have at least one recurrence. It is important to differentiate between febrile seizure and seizure with fever.[6] First-time seizures in infants younger than 6 months may indicate significant underlying pathology and warrant a full assessment.[7]

Pathophysiology

Seizures occur when the abnormal increased electrical activity of the initiating neurons activates adjacent neurons and propagates until the thalamus and other subcortical structures are similarly stimulated. At a cellular level, the pathophysiology is not well understood, although recent research in specific epilepsy syndromes is elucidating possible mechanisms. Investigation of rare inherited epilepsy syndromes has identified mutations in neuronal ion channel proteins, limiting intracellular passage of potassium. Given that the potassium current is the primary force behind repolarization of membranes, depolarization is prolonged in these patients, leading to an increase in neuronal hyperexcitability.[1] Other studies have found that malformations of cortical development and glial cells may play a role in epileptogenesis.[1]

Clinical seizure activity typically, but not always, reflects the initiating focus. When the ictal discharge extends below the cortex to deeper structures, the reticular activating system in the brainstem may be affected, altering consciousness. In generalized seizures, the focus is often deep and midline, which explains the prompt loss of consciousness and bilateral involvement. Seizures are typically self-limited; at some point the hyperpolarization subsides and the bursts of electrical discharges from the focus terminate. This cessation may be related to reflex inhibition, neuronal exhaustion, or alteration of the local balance of neurotransmitters.

Partial seizures may represent a similar pathophysiologic process in which less recruitment occurs and the ictal activity does not cross the midline. Because of the more limited focus of abnormal activity, convulsive motor activity may not be the predominant clinical manifestation.[3]

■ DIAGNOSTIC APPROACH

Differential Considerations

Because an incorrect diagnosis is expensive and involves loss of driving privileges and exposure to potentially toxic medicines, the first diagnostic task is to determine whether the patient is having a "true" seizure.[8] Ictal activity can be irrefutably verified only by electroencephalography (EEG). Other abnormal movements and states of consciousness, including pseudoseizures, can be confused with ictal activity. Other disorders mimicking seizures are listed in Table 15-2.[7]

Syncope, whether vasodepressive (vagal syncope), orthostatic, or dysrhythmia related, can be confused with seizures by observers. A sudden loss of consciousness followed by abnormal movements can be ictal or syncopal in origin, hence the consideration "fit versus faint." One video analysis of 56 brief syncopal episodes showed myoclonic activity in 90% of patients, together with frequent head turns, upward gaze, oral automatisms, and righting movements. These are likely a transient response by the brain to sudden deprivation of blood flow. Generally, ictal tonic-clonic movements are more forceful and prolonged than the "twitches" sometimes associated with fainting. In addition, most generalized seizures are characterized by a postictal state (an important exception being atonic drop attack ictus), which syncope patients do not manifest.[9]

The cause of an unwitnessed, unprovoked loss of consciousness with a fall, after which the patient presents to the ED, may be difficult to determine. Suggestions of an ictal diagnosis include retrograde amnesia, loss of continence, and evidence of tongue biting.[10] If blood was drawn by emergency medical service personnel soon after a true seizure, it often demonstrates a metabolic acidosis that has resolved by the time a repeat analysis is performed in the ED.

Table 15-1 Classification of Seizures in a General Adult Population

SEIZURE TYPE	PERCENTAGE
Generalized	
Tonic-clonic	35
Absence	1
Myoclonic	<1
Others	2–3
Partial	
Simple partial	3
Complex partial	11
Secondarily generalized	27
Mixed partial	12
Unclassified	9

Rapid Assessment and Stabilization

The patient who arrives with a history of possible seizure activity should be placed in a monitored area of the ED and prepared for prompt physician examination.[4] An IV line or saline lock catheter should be placed in case anticonvulsants are emergently indicated. Blood glucose is checked at the bedside, and a thorough list of all medications currently being used by the patient is obtained.

If the patient is seizing in the ED, the first step is to confirm that a pulse is present and that the "seizure" activity is not the result of cerebral hypoxia from lack of blood flow. After this, attention is paid to protecting and maintaining the airway, including use of a nasopharyngeal airway and ready availability of oxygen and suction. The patient should be protected from self-injury during this time.[11]

Table 15-2 Differential Considerations for the Diagnosis of Seizure*

DISORDER	CLASSIFICATION	ICTAL-LIKE MANIFESTATIONS
Syncope	Vasodepressive vs dysrhythmogenic (including long QT syndrome) vs orthostatic Preictal or postictal twitching	"Fit vs. faint"
Hyperventilation syndrome		Mood disturbances Posturing of extremities
Prolonged breath-holding	More typical in children	Tonic-clonic movements Loss of urinary continence
Toxic and metabolic disorders	Alcohol abuse/withdrawal Hypoglycemia Phencyclidine Tetanus Strychnine and camphor Extrapyramidal reactions	Delirium tremens, blackout Abnormal behavior Buccolingual spasms Myotonic spasms Myotonic spasms Posturing, deviation of eyes
Nonictal CNS events	Transient ischemic attacks Transient global amnesia Hemiparetic migraine Carotid sinus hypersensitivity Narcolepsy	Drop attacks, "fit vs. faint" Similar to postictal state, absence status Todd's paralysis Drop attacks, "fit vs. faint" Drop attacks, "fit vs. faint"
Movement disorders	Hemiballismus, tics	Convulsions
Psychiatric disorders	Fugue state Panic attacks	Similar to postictal state, absence status Twitching, altered mental state
Functional disorders	Pseudoseizure	May closely resemble ictal activity; patients may have both true seizures and pseudoseizures

*Electroencephalography provides the definitive diagnosis in unclear cases.
CNS, central nervous system.

A pulse oximeter should be applied and oxygen administered as necessary. Optimally, the patient is turned on his or her side to protect the airway from aspiration. If the patient is immobilized on a spine board after trauma, the entire board is tipped up to one side. Preparation should be made for endotracheal intubation in case anticonvulsant drugs fail to terminate the seizure. While these procedures are accomplished, an assistant should be establishing IV access.[11]

Hypoglycemia is the most common metabolic cause of seizure activity. The only treatment required for the patient may be administration of IV glucose. *Prolonged* seizure activity may also *cause* hypoglycemia, so that the cause-and-effect relationship may sometimes be reversed and further therapy is required. Benzodiazepines are the optimal first-line agents for stopping seizure activity in patients of all ages. Available agents include lorazepam (Ativan), diazepam (Valium), and midazolam (Versed). All three are efficacious in terminating seizure activity (see Table 15-3 for doses), but if IV access cannot be achieved, diazepam may be given rectally, endotracheally, or intraosseously; rectal diazepam stops seizures in 70% of patients, compared with 60 to 80% for IV dosing.[12] Midazolam can be given intramuscularly, and recent research shows that buccal midazolam works in children.[13] If IV access is obtained, however, lorazepam is the agent of choice for initial management of status epilepticus, particularly because its longer half-life leads to less recurrence of seizures.[14] Lorazepam is also specifically recommended for alcohol withdrawal seizures, again due to its longer duration of action.[15]

If benzodiazepines do not abort seizure activity, the airway should be reevaluated. If the patient's ability to protect the airway is compromised or oxygen saturation remains persistently below 90%, emergent intubation should be performed. If the seizure has not terminated 5 to 7 minutes after benzodiazepine administration, or if the maximum dose of lorazepam (0.1 mg/kg) or diazepam (0.15 mg/kg)[16] has been reached, a second drug should be given.[16] Use of maximal doses of benzodiazepines may require intubation and ventilatory support. Phenytoin is recommended as second-line therapy for adults with persistent seizure activity.[16] The prodrug, fosphenytoin, can be administered more quickly, can be given intramuscularly, and has less tendency to cause hypotension, but is significantly more expensive.[17] (See Table 15-3).[18,19] Second-line therapy for children is phenobarbital. Third-line therapy is phenytoin for children and phenobarbital for adults.[20-23] IV valproic acid is safe[24] and should be considered for patients who are on chronic valproic therapy and whose levels are subtherapeutic.[25] If a patient's seizures are refractory to benzodiazepines, consider isoniazid overdose as the cause. Pyridoxine

Table 15-3 Drugs and Dosages for Abortive Treatment of Seizures in the Emergency Department*

DRUG	ADULT DOSE	PEDIATRIC DOSE	COMMENTS
Glucose	50 mL of 50% glucose	0–1 month: 2 mL/kg IV of D10W 1 month–2 years: 2 mL/kg IV of D25W >2 years: 2 mL/kg IV of D50W	1 month–2 years: 2 mL/kg IV of D25W
Magnesium sulfate		6 g over 15–20 min followed by 2 g/hr	First-line therapy for eclamptic seizures
Diazepam	0.2 mg/kg IV at 2 mg/min up to 20 mg	0.2–0.5 mg/kg IV/IO/ET *or* 0.5–1.0 mg/kg PR up to 20 mg	Monitor airway protection and respiratory drive
Lorazepam	0.1 mg/kg IV at 1–2 mg/min to up to 10 mg	0.05–0.1 mg/kg IV	Monitor airway protection and respiratory drive
Midazolam	0.1 mg/kg given at 1 mg/min up to 10 mg IV 0.2 mg/kg IM 0.5 mg/kg buccal	0.15 mg/kg IV, then 2–10 mcg/kg/min	Monitor airway protection and respiratory drive
Phenytoin	20 mg/kg IV at ≤40 mg/min	20 mg/kg IV at 1 mg/kg/min	During infusion patient should have continuous cardiac and blood pressure monitoring
Fosphenytoin	15–20 mg/kg IV at 100–150 mg/min *or* 20 mg/kg IM	20–25 mg/kg IV, then up to 3 mg/kg/min IV up to 159 mg/min IV	Level of monitoring directed by patient's status, not drug use
Propofol	3–5 mg/kg initial dose, then 1–15 mg/kg/hr infusion		Used for status epilepticus; intubation required
Phenobarbital	20–30 mg/kg IV at 60–100 mg/min or as single IM dose		Intubation may be required
Valproate	20 mg/kg PR or 10–15 mg/kg IV (initial dose)		Maximum dosage 60 mg/kg/day Dilute 1:1 with water; onset is slow
Pentobarbital	5 mg/kg IV at 25 mg/min, then titrate to EEG		Intubation, ventilation, and pressor support are required
Isoflurane	Via general endotracheal anesthesia		Monitor with EEG

*Although alternative routes of administration (e.g., IO, PR) have not all been studied in adults, appropriate weight or length based on dosing by pediatric guidelines can be used when the clinical situation dictates.

EEG, electroencephalogram; ET, endotracheal; IM, intramuscular; IO, intraosseous; IV, intravenous; PR, rectal administration.

is the only fully effective pharmacologic treatment for toxic isoniazid seizures, although benzodiazepines have been shown to suppress seizure activity in some cases.[26] In seizing females of childbearing age, eclampsia should be considered; in this case, intravenous magnesium (6 g) is the drug of choice. (See Chapter 177.) Approximately 10% of patients will have a second seizure despite magnesium; these patients should get a second 2-g bolus of magnesium.[27] If the eclamptic patient continues seizing, magnesium dosing should be repeated; refractory eclamptic seizures can also respond to benzodiazepines or barbiturates with or without phenytoin. Children and psychiatric patients at risk for water intoxication should be considered potential candidates for hypertonic saline therapy, after laboratory confirmation of hyponatremia.

Patients who remain unresponsive to the third-level choice of pharmacologic intervention are by definition in *refractory* status epilepticus. Further choices for therapy at that juncture are general anesthetic doses of midazolam or propofol, barbiturate coma and isoflurane anesthesia; all of which mandate endotracheal intubation.[22,23,29] A neuromuscular blocking agent is administered concomitantly to reduce the metabolic burden and potential hyperthermia that can ensue from prolonged status seizures. Anesthetic dosing of midazolam is 0.2 to 0.3 mg/kg bolus, then 0.05 to 2.0 mg/kg/hr, and for propofol it is 2 to 4 mg/kg, then 1 to 15 mg/kg/hr. Both drugs are usually well-tolerated and can be titrated to effect, although propofol is preferable because of its rapid onset and offset of action, which allows the patient to be "awakened" intermittently for examination in the event that continuous EEG monitoring is not available.[16]

Pivotal Findings

When the patient is stabilized with a secure airway and ictal activity is controlled, attention is turned to gathering more complete data.

History

History taking in the patient with seizure is directed by two main questions. First, "Was the incident truly a seizure?" This is important because of the broad differential diagnosis for seizures (see Table 15-2) and the notoriously inaccurate descriptions of seizure-like activity from laypersons.[10] In general, however, ictal events have six properties:

1. *Abrupt onset*: Generalized seizures typically occur without an aura.
2. *Brief duration*: Seizures rarely last longer than 90 to 120 seconds, although bystanders typically overestimate the duration.
3. *Altered mental status*: Present by definition, except for simple partial seizures.
4. *Purposeless activity*: For example, automatisms and undirected tonic-clonic movements.
5. *Unprovoked*: Especially with regard to emotional stimuli; fever in children and substance withdrawal in adults are notable exceptions.
6. *Postictal state*: An acute confusional state that typically occurs with all seizures except simple partial and absence.

Information regarding focality of onset, loss of bowel or bladder control, or tongue biting should also be elicited.

The second question to direct the history is, "Does this patient have a history of seizures?" If he or she does have a documented history of seizures, ED evaluation may be limited to a thorough history and consideration of measurement of anticonvulsant drug levels. History should focus on intercurrent illness or trauma, drug or alcohol use, potential adverse drug-drug interactions with anticonvulsants, medication compliance, a recent change in anticonvulsant dosing regimens, or a change in ictal pattern or characteristics.[2,11]

Supratherapeutic and toxic levels of some anticonvulsants such as phenytoin and carbamazepine, whether attained chronically or after acute overdose, may *cause* seizures. If empiric anticonvulsant therapy is indicated before the serum level is available, only 50% of a full loading dose should be given unless the patient is known reliably not to be taking anticonvulsant medication.

If the patient does not have a history of seizures and the description of the event is truly consistent with a seizure, the history should focus on potential underlying medical, toxicologic, or neurologic causes.

A personal history from the patient, close friend, relative, or medical record may reveal potential ictogenic factors such as recent or remote head trauma, developmental abnormalities, metabolic diseases, drug or alcohol abuse, sleep deprivation, pregnancy, recent travel, previous seizures, or use of herbal supplements. When no witness or family member is available, extensive questioning must await clearance of the postictal confusional state.

Physical Examination

The physical manifestations of convulsive ictal activity include hypertension, tachycardia, and tachypnea from sympathetic stimulation. These signs typically resolve quickly after the seizure activity ceases. With more prolonged convulsions, skeletal muscle damage, lactic acidosis, and, rarely, frank rhabdomyolysis may ensue. Autonomic discharges and bulbar muscle involvement may result in urinary or fecal incontinence, vomiting (with significant aspiration risk), tongue biting, and airway impairment. All of these signs are helpful discriminators in the differential evaluation of seizure-like spells.

After the seizure activity has ceased, resting vital signs should be evaluated. Fever and underlying infection can cause seizures, although there may be a low-grade temperature elevation immediately after a convulsive generalized seizure. Tachypnea, tachycardia, or an abnormal blood pressure that persists beyond the immediate postictal period may indicate toxic exposure, hypoxia, or a central nervous system lesion. Pertinent physical findings may include nuchal rigidity, stigmata of substance abuse, lymphadenopathy suggestive of HIV disease or malignancy, dysmorphic features, or skin lesions. The examination should also focus on potential adverse sequelae of convulsive seizures, such as head trauma, tongue injury, posterior shoulder dislocation, or back pain.

Finally, a complete neurologic examination must be performed. A persistent focal deficit after a seizure (e.g., Todd's paralysis) often indicates the focal origin of the event but also can be evidence of an underlying stroke. The patient should be carefully examined for papilledema; elevated intracranial pressure can both cause and result from ictal activity. Failure to note steady improvement of postictal depression of consciousness suggests the possibility of an underlying encephalopathy or nonconvulsive status epilepticus.

Ancillary Testing

Laboratory. Routine screening studies such as a complete blood count and chemistry profile have little use in the neurologically normal, otherwise healthy, postictal patient with a known seizure disorder for whom a reliable history can be obtained.

Table 15-4 Indications for Emergent Head CT for New-Onset Seizure Patients

Acute intracranial process is suspected
History of acute head trauma
History of malignancy
Immunocompromise
Fever
Persistent headache
History of anticoagulation
New focal neurologic examination
Age older than 40 years
Focal onset before generalization
Persistently altered mental status

CT, computed tomography.

Bedside blood glucose is measured early. Anticonvulsant levels are appropriate in patients known or thought to be taking anticonvulsant medication. Febrile patients are evaluated for the source of the fever. For medically ill adults (e.g., diabetic patients, cancer patients, patients with liver disease, patients taking medications that can affect serum electrolyte levels) and in those presenting with a first-time seizure, appropriate chemistry studies are ordered, including electrolytes and liver function tests.[8] Directed toxicologic screens should be obtained if substance abuse is possible. Serum sodium should be evaluated, particularly if mental status remains altered after apparent recovery from the postictal state. Pregnancy testing is useful if eclampsia is possible. If there is *any* suggestion of meningitis or subarachnoid hemorrhage, lumbar puncture should be performed, with a preceding cranial computed tomography (CT) scan.[30]

Imaging. In the fully recovered patient without headache and with fully normal mental status and neurologic examination who has had a single, brief seizure, a cranial CT scan can be obtained in the ED or at a follow-up visit at the discretion of the treating physician.[4,29] Table 15-4 lists the circumstances under which a head CT is recommended in the ED due to a higher likelihood of discovering an acute abnormality.[4]

The literature on this issue for first-time nonfebrile seizures in children is also inconclusive.[31] Cranial CT is indicated in any age group when there is a possibility of head trauma, elevated intracranial pressure, intracranial mass, persistently abnormal mental status or focal neurologic abnormality, or HIV disease.

Electroencephalography. EEG is not consistently available in the ED. It may be particularly useful in specific cases, such as the diagnosis of nonconvulsive status epilepticus, to monitor seizure activity after intubation and neuromuscular blockade, and to help differentiate seizures from other similar presentations. In general, EEGs are most appropriate for the follow-up evaluation of first-time seizures without clear cause after a complete ED evaluation.[19]

MANAGEMENT

Usually, an acute seizure self-terminates or can be pharmacologically terminated before a need arises for active airway management. Rapidly reversible ictal insults (e.g., hypoglycemia, hypoxemia, isoniazid ingestion) should be considered and, if found, treated. Primary abortive therapy in the ED is accomplished as described earlier. Although a number of newer antiepileptic medications have become available, their therapeutic purpose is directed toward chronic rather than acute seizures.[32]

Identifying a new-onset seizure in the ED generates consideration for further management. The choice to initiate anticonvulsant therapy depends on the risk of seizure recurrence and any underlying predisposing disease, and the risk of initiating anticonvulsant therapy is typically not made by the emergency physician. The initiation of anticonvulsant therapy after a single seizure is an issue of considerable controversy and should be undertaken in consultation with the neurologist who will be following the patient after discharge from the ED.[33,34] Prompt treatment of any apparent ictal source discovered in the ED, however, is always appropriate.

DISPOSITION

Disposition plans must be individualized according to the findings of the ED evaluation and the presence or absence of underlying disease. One quarter of adult patients presenting with seizure-related complaints have new-onset seizures.[3] Almost half of them require admission, most because of abnormal CT scans or persistent focal abnormalities; 95% of those who retrospectively required admission were correctly identified by using an ED evaluation consistent with that recommended previously. Patients may be discharged home with early referral to a neurologist if they have a normal neurologic exam, no comorbidities, no known structural brain disease, do not require the use of an antiepileptic drug in the ED, and are felt to be sufficiently resourceful and reliable to comply with follow-up instructions.[4] Patients discharged home from the ED should receive appropriate state-specific guidance regarding driver's license privileges and information for prompt follow-up with a neurologist.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.