The First Seizure

Seizures need to be distinguished from other common differential diagnoses, and seizure type must be determined because it dictates management and counseling.

By Christine Hung, MD

A first seizure is potentially the most terrifying life event a person can experience. Questions about the ability to work, maintaining financial stability, driving, caregiving, or childbearing suddenly cloud future plans. Empathic attentiveness to an individual’s questions is an important aspect of seizure management. Exploration of personal and cultural understanding of seizures is also important in order to provide responsive counseling that mitigates potential discrimination and stigma from family, educators, and employers.

In the US, approximately 150,000 adults per year will present with a first unprovoked seizure.1 Up to 2% of all emergency room visits or 1 in every 100 emergency room visits in the US are for seizures.2 The lifetime incidence of seizures is approximately 10%, and 1 in 26 people in the US develop epilepsy.3 Approximately 3.4 million people in the US (1.2% of the population) and 70 million people, globally, have epilepsy.4 Epilepsy is the fourth most common neurologic condition.

The established definitions of seizures and epilepsy are listed in Box 1.6 Determining the underlying cause of a seizure and distinguishing a seizure from epilepsy determines treatment decisions, prognosis, and counseling. Correct identification of epilepsy is a clinical care gap; there is up to a 3-year delay in antiseizure medication (ASM) initiation in 36.7% of people with newly diagnosed epilepsy, which may be larger when the 2014 definition of epilepsy is used in future studies.7

**Differential Diagnosis**

Transient loss of consciousness is one of the most common presenting complaints in people who may have had a seizure. The estimated lifetime incidence of transient loss of consciousness is as high as 50%.8 Over 90% of those presenting with transient loss of consciousness are found to have syncope, psychogenic nonepileptic seizures, and epileptic seizures.

**Nonepileptic Diagnoses**

Syncope. Caused by cerebral hypoperfusion, syncope presents as an abrupt and complete loss of consciousness and postural tone followed by a rapid spontaneous recovery (Table 1). A nonepileptic convolution may occur during syncope. Different types of syncope include orthostatic related, reflex (vasovagal being a common type), cardiac, and volume deple-

### Box 1. International League Against Epilepsy Definitions

Seizure: A transient occurrence of signs and/or symptoms owing to abnormal excessive or synchronous neuronal activity in the brain.

Epilepsy: For diagnosis, the person must have 1 of the following:

1. An identifiable epilepsy syndrome (typically the genetic or idiopathic epilepsies).
2. At least 2 unprovoked (or reflex) seizures or clusters of seizures occurring at least 24 hours apart
3. A single unprovoked (or reflex) seizure that has at least a 60% chance of recurrence in the next 10 years.

Epilepsy resolution: For epilepsy to be considered resolved, there must be a 10-year period of seizure freedom, the last 5 of which have included no treatment with antiseizure medications (ASMs). For age-dependent epilepsy syndromes, the individual must be seizure free and more than the applicable age for that syndrome.

a Added to the definition of epilepsy in 2014. Studies to determine what constitutes at least a 60% chance of recurrence are ongoing.
Epileptic Seizures

Epileptic seizures often have certain historical elements and stereotyped presenting semiologies. If the above diagnoses are lower on the differential diagnosis list, specific screening questions regarding the event (Box 2) may help determine whether an epileptic seizure occurred. Because it is rare for a person who had a seizure to be able to describe it accurately, it is important to ask any witnesses to the event the same questions. Clinical correlates are diverse, ranging from a barely perceptible microsecond loss of attention to oral or picking automatisms, focal twitch or dystonia, to a full body convulsion and transient loss of consciousness. After a seizure, there can be a postictal period that physiologically correlates with loss of neural function and often clinically correlates with absent or altered consciousness.

The 2017 International League Against Epilepsy (ILAE) guidelines for describing seizures are also a helpful diagnostic tool. A shared descriptive terminology for seizures and epilepsy types allows for more accurate diagnosis and treatment (Table 2).13,14

Distinguishing whether a seizure is an acute symptomatic seizure, unprovoked seizure, or an epilepsy syndrome helps determine treatment decisions, prognosis, and counseling.

Symptomatic vs Unprovoked Seizures

Acute Symptomatic Seizures. Acute symptomatic seizures occur at the time or within 7 days of an identifiable acute event. Incidence is 29 to 39 per 100,000 people annually and acute symptomatic seizures comprise 34% to 50% of reported afebrile seizures. The most common causes are cerebrovascular disease, central nervous system infections, traumatic brain injuries (TBIs), acute drug exposures or withdrawals, and metabolic insults (Table 3).1,15-24 Other acute causes include intracranial surgery, anoxic brain insult, and active multiple sclerosis (MS) or other autoimmune diseases of the central nervous system (CNS). A careful history and appropriate imaging, laboratory tests, and drug screens are helpful in diagnosis.

<table>
<thead>
<tr>
<th>TABLE 1. NONEPILEPTIC SEIZURES</th>
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<tbody>
<tr>
<td>Syncope</td>
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<tr>
<td>• Occurs immediately upon rising from seated position, or after prolonged standing, micturition, defecation, or venipuncture</td>
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<tr>
<td>• Brief or no prodrome</td>
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<td>• Lightheadedness</td>
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<td>• Tunnel vision, greying out of vision, or blurred vision</td>
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<td>• Hearing fading out</td>
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<td>• Diaphoresis, pallor, nausea, warmth</td>
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<tr>
<td>• Palpitations/tachycardia or bradycardia</td>
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<tr>
<td>• No postictal period</td>
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<tr>
<td>• History of cardiac disease</td>
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<tr>
<td>• Orthostatic tachycardia or hypotension</td>
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<tr>
<td>• Abnormal cardiac auscultation</td>
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Box 2. Risk Factors for Seizures

In childhood, were there birth complications?
Did you have seizures with fever in childhood?
Were you uncoordinated or clumsy as a child? (screens for juvenile myoclonic epilepsy)
Was your school performance poor? (screens for juvenile myoclonic epilepsy)
Have you had any head trauma with or without loss of consciousness?
Have you ever had a stroke?
Have you ever had a brain infection?
Have you ever had a brain tumor?
Did you serve in the military? If so, did you have a blast injury of any kind?
Have you traveled or changed workplaces recently? (screens for toxin/infection exposure)
Have you been sleeping the same as usual? (screen for sleep deprivation)
Have you been under increased stress?
What medications were you taking when you had a seizure?
Do you use any nutritional supplements?
Do you use any recreational drugs?
Has anyone in your family ever had seizures?
If reversible causes are avoided and there is no permanent brain damage, recurrence is unlikely. Individuals with acute symptomatic seizures from CNS infection, TBI, or stroke, however, were 8.9 times more likely to die in the first 30 days compared with patients who had a first unprovoked seizure. Beyond 30 days, the 10 year mortality rate for acute symptomatic seizure was equivalent to a first unprovoked seizure. Furthermore, the acute symptomatic seizure patients were 80% less likely to have subsequent seizures.\(^{25}\)

**Unprovoked Seizures.** A single seizure or a cluster of seizures in a 24-hour period with no identifiable trigger is termed unprovoked. Incidence of unprovoked seizures is approximately 42 to 61 per 100,000 annually, and a standardized mortality ratio (SMR) of 2.3 has been reported.\(^{1}\)

Some unprovoked seizures will have history, physical, labs, imaging, and EEG that are unrevealing. Typically, starting an ASM is not warranted in this situation.

Alternatively, unprovoked seizures can be remote symptomatic seizures with an underlying anatomic insult from more than 7 days earlier. Prior ischemic strokes, intracranial hemorrhage, CNS infection, TBI, PML, brain neoplasms, neurodegenerative diseases, paraneoplastic processes, and autoimmune disease can be associated with remote symptomatic seizure. Approximately 43-45\% of unprovoked remote symptomatic seizures will have a recurrent seizure within 2 years.\(^{26}\) The underlying pathology influences recurrence rates. Ischemic strokes may lead to 25 times increased risk of recurrence whereas intracranial hemorrhage increases risk of recurrence in the next year tenfold.\(^{19,21}\) Recurrence risk is 7 times higher over a 10-year period with CNS infection.\(^{27}\) The 5-year cumulative seizure probability is 0.7% for mild TBI, 1.2% for moderate TBI, and 10% for severe TBI.\(^{28}\) Studies suggest people who serve in the military have increased likelihood of post-traumatic epilepsy (PTE) and that 86% of veterans who have a single posttraumatic seizure will have another within 2 years.\(^{24}\) This suggests posttraumatic seizures may meet the new criteria for epilepsy (a single unprovoked or reflex seizure with a 60\% or greater chance of recurrence in the next 10 years) and warrant ASM initiation after the first posttraumatic unprovoked seizure.

Individuals who had a first unprovoked seizure should be informed they have a 21\% to 45\% chance of recurrent seizure within the next 2 years with higher likelihood in the first year.\(^{28}\) If they have a history of stroke, head trauma, epileptiform EEG, significant abnormal results on head imaging, and/or nocturnal seizures, their risk is increased further. The recent update to the definition of epilepsy (a single unprovoked or reflex seizure with a 60\% or greater chance of recurrence in the next 10 years) raises questions of whether ASM treatment should be initiated. Understanding what supports a 60\% chance of recurrence, however, is undetermined and an area requiring further research. After a second seizure, recurrence risk increases to 57\% at 1 year, 61\% at 2 years, and 73\% at 5 years.\(^{31}\)

**Epilepsy Syndromes.** Diagnosis of epilepsy, including generalized genetic epilepsies and idiopathic generalized epilepsies (eg, childhood absence, juvenile absence, juvenile myoclonic) is reliant on a history of previously unrecognized stereotypic seizures, family history, EEG findings, imaging, laboratory test findings, and, if available, genetic testing. For all new diagnoses of epilepsy, the risk of sudden unexpected death in epilepsy (SUDEP) should be discussed. Rates of SUDEP increase proportionally to severity of epilepsy: 0.9 to 2.3 per 1000 patient-years in the community vs 3.2 to 5.9 in medically refractory epilepsy, and 6.3 to 9.3 in people who are candidates for epilepsy surgery.\(^{22,32}\)

**Management and Counseling**

**Initiating Antiseizure Medications**

Initiating ASM treatment after a first seizure is likely to reduce relative risk for seizure recurrence in the next 2 years by 35\% but does not necessarily improve quality of life. Treatment
with ASMs does not affect risk of SUDEP, does not affect timing of ASMs and does not affect chance of seizure freedom 3 years after an initial seizure. Typically, starting an ASM is not warranted in this situation. If a second unprovoked seizure occurs, the diagnosis of epilepsy is made, and ASMs should be initiated.

The decision to start ASMs should be an integrative individualized discussion that considers personal preferences and lifestyle. Maintaining employment, caring for family members, and driving may play a large role in the decision. Driving, in particular, is critical because seizure freedom for a certain period of time may need to be established to maintain licensure, even after a first seizure, depending on variable state regulations. The Epilepsy Foundation maintains a searchable State Driving Laws Database that includes professional reporting mandates and minimum seizure freedom requirements.

Risks of Antiseizure Medications

Adverse side effects of ASMs occur in 7% to 31% of people treated, depending on which drug is used. Most are mild and reversible. Women of childbearing age taking ASMs need counseling on risk of birth defects and access to birth control if desired. They should also be informed that good seizure control and coordination with their health care team, they can still make a plan for conception if that is a goal.

Comorbid Conditions, Lifestyle, and Psychosocial Factors

Major depression and suicidality are frequent comorbidities of epilepsy. Screening for and documenting any depression and thoughts of suicide or homicide should be done reflexively and reassessed frequently for everyone who has had a seizure. If ASMs are initiated, this assessment is critical because some ASMs may worsen depression and suicidal ideation. A low threshold for supportive services referral should be maintained.

Seizure threshold can be lowered by stress, including sleep deprivation, nutrition deprivation, extreme heat, and extreme emotional distress. People should be counseled to avoid these situations, if possible. Counseling for safety precautions includes avoiding bathtubs, swimming alone, going to heights, and operating heavy machinery.

The psychosocial impact of seizures and epilepsy should be explored, including how seizures and/or epilepsy may affect their interpersonal relationships, education or employment, and lifestyle. Some cultures or belief systems ostracize seizures and this possibility should be explored with each individual. Again, a low threshold to refer to supportive services should be observed. There are many resources and communities online via social media as well as professional societies with resources, including the ILAE, the American Epilepsy Society, and the Epilepsy Foundation. The Epilepsy Foundation also has local chapters with information on local support group meetings.


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