Evaluation and management of the first seizure in adults

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Literature review current through: **Jan 2024.**
This topic last updated: **Oct 26, 2022.**

INTRODUCTION

Seizures are a common occurrence, affecting an estimated 8 to 10 percent of the population over a lifetime [1,2]. Seizures account for 1 to 2 percent of all emergency department visits, and approximately one-quarter of these will be a first seizure [3].

The primary goal in evaluating a patient's first seizure is to identify whether the seizure resulted from a treatable systemic process or intrinsic dysfunction of the central nervous system and, if the latter, the nature of the underlying brain pathology. This evaluation will determine the likelihood that a patient will have additional seizures, assist in the decision whether to begin antiseizure medication therapy, and direct appropriate treatment to the underlying cause, if known.

The differential diagnosis and clinical features of seizures and the diagnostic evaluation of the first seizure in adults are reviewed here. Other paroxysmal events that can mimic seizure in adults, including syncope, migraine, transient ischemic attack, and psychogenic nonepileptic seizures, are reviewed separately. (See "Nonepileptic paroxysmal disorders in adolescents and adults" and "Syncope in adults: Clinical manifestations and initial diagnostic evaluation" and "Pathophysiology, clinical manifestations, and diagnosis of migraine in adults" and "Definition, etiology, and clinical manifestations of transient ischemic attack" and "Psychogenic nonepileptic seizures: Etiology, clinical features, and diagnosis".)

The evaluation and management of convulsive and nonconvulsive status epilepticus, which are occasionally the first presentations of seizure, as well as the management of chronic epilepsy are reviewed separately. (See "Convulsive status epilepticus in adults: Classification, clinical features, and diagnosis" and "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis" and "Overview of the management of epilepsy in adults" and "Initial treatment of epilepsy in adults".)

DEFINITIONS

A seizure is a sudden change in behavior caused by electrical hypersynchronization of neuronal networks in the cerebral cortex.

Acute symptomatic seizure — Acute symptomatic seizure refers to a seizure that occurs at the time of a systemic insult or in close temporal association with a documented brain insult [4]. Such insults include metabolic derangements, drug or alcohol withdrawal, and acute neurologic disorders such as stroke, encephalitis, or acute head injury. (See 'Causes of seizures' below.)

The time window within which a seizure may be considered acute symptomatic has not been clearly defined and may vary based on the type of insult. One consensus panel recommendation suggests the following ranges [4]:

- Within one week of stroke, traumatic brain injury, anoxic encephalopathy, or intracranial surgery
- At first identification of subdural hematoma
- During the active phase of a central nervous system infection
- Within 24 hours of a severe metabolic derangement

In population-based studies, acute symptomatic seizures make up 25 to 30 percent of first seizures [1,5].

Acute symptomatic seizures may recur during the index illness but generally carry a low risk for future epilepsy compared with unprovoked seizures. That said, some patients will go on to develop remote symptomatic seizures or epilepsy related to a prior stroke, hemorrhage, or head injury. (See "Overview of the management of epilepsy in adults", section on 'Poststroke seizures' and "Posttraumatic seizures and epilepsy", section on 'Early posttraumatic seizures'.)

Unprovoked seizure — Unprovoked seizure refers to a seizure of unknown etiology as well as one that occurs in relation to a preexisting brain lesion or progressive nervous system disorder. Unprovoked seizures that are determined to be due to an underlying brain lesion or disorder

are also referred to as remote symptomatic seizures. They carry a higher risk of future epilepsy compared with acute symptomatic seizures. (See "Initial treatment of epilepsy in adults", section on 'Risk of seizure recurrence'.)

Epilepsy — Epilepsy is defined as when any of the following exist [6]:

- At least two unprovoked seizures occurring more than 24 hours apart.
- One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures (eg, ≥60 percent) occurring over the next 10 years. This may be the case with remote structural lesions such as stroke, central nervous system infection, or certain types of traumatic brain injury.
- Diagnosis of an epilepsy syndrome.

The second criterion was added by the International League Against Epilepsy (ILAE) working group in 2014 and emphasizes the importance of neuroimaging and electroencephalography (EEG) in the evaluation of patients with a first-time seizure, as some of these patients will meet criteria for epilepsy at the time of a first seizure. (See "Initial treatment of epilepsy in adults", section on 'First-time unprovoked seizure'.)

Note that there is no distinction in meaning between the terms "seizure disorder" and "epilepsy"; the two are synonymous. However, epilepsy is defined by the ILAE and is therefore the more precise term [6,7].

TYPES OF SEIZURES

Most seizures can be categorized as either focal or generalized according to whether the onset of electrical activity involves a focal region of the brain or both sides of the brain simultaneously. The clinical manifestations of seizures vary based on the location of the seizure in the brain and the amount of cortex that is involved. Focal seizures are further classified according to whether consciousness is altered or not during the event (table 1).

Focal seizures with retained awareness — The symptoms of focal seizures with retained awareness (previously called simple partial seizures) vary from one patient to another and depend entirely on the part of the cortex that is disrupted at the onset of the seizure.

A seizure that begins in the occipital cortex may result in flashing lights, while a seizure that affects the motor cortex will result in rhythmic jerking movements of the face, arm, or leg on the side of the body opposite to the involved cortex (Jacksonian seizure). A seizure that begins

in the parietal cortex may cause distortion of spatial perception; a seizure that begins in the dominant frontal lobe may cause sudden speech difficulties.

The symptoms that a patient experiences at the beginning of a seizure are sometimes referred to as the warning or aura. Auras are focal seizures that affect enough of the brain to cause symptoms, but not enough to interfere with consciousness. Auras that commonly occur in patients with epilepsy are shown in the table (table 2).

Some patients may have brief, subtle auras that go unrecognized or unreported for many months before they present with a more prolonged seizure or one that evolves into a bilateral tonic-clonic seizure. A history of such events increases diagnostic confidence in seizure versus other paroxysmal events and has implications for treatment. (See 'Prior events' below.)

Postictally, patients may return immediately to their pre-event baseline or may experience a period of worsened neurologic function related to the location of the seizure in the brain. For example, patients with a simple motor seizure involving the left arm may have postictal weakness lasting for minutes to hours, referred to as a postictal Todd paralysis. In some cases, postictal weakness or aphasia is more prominent than the ictal phase of the seizure, leading clinicians to consider transient ischemic attack or stroke as a possible diagnosis at the time of initial presentation. (See 'Postictal period' below.)

Focal seizures with impaired awareness — Some focal seizures are associated with altered awareness at the onset of the seizure or as it progresses. These seizures, previously called complex partial seizures, are the most common type of seizure in adults with epilepsy. (See "Focal epilepsy: Causes and clinical features", section on 'Clinical features'.)

During a typical focal seizure with impaired awareness, patients appear to be awake but are not in contact with others in their environment and do not respond normally to instructions or questions. They may stare into space and either remain motionless or engage in repetitive behaviors, called automatisms, such as facial grimacing, gesturing, chewing, lip smacking, or repeating words or phrases. Some patients may become hostile or aggressive if physically restrained.

Focal seizures with impaired awareness typically last less than three minutes and may begin with a phase of preserved awareness, which the patient sometimes can later describe. Afterward, the patient enters the postictal phase, often characterized by somnolence, confusion, and headache for up to several hours (table 3). Patients often have no memory of what took place during the seizure other than, perhaps, the aura.

Focal seizures of both types may propagate diffusely to cause bilateral tonic-clonic seizures (previously referred to as secondarily generalized seizures). If propagation is slow, initial focal symptoms may be readily evident to the patient and observers prior to onset of the convulsive movements. If propagation is rapid, the seizures may closely resemble generalized-onset tonic-clonic seizures. In either case, patients may be amnestic to the initial focal phase of the seizure due to the effects of the generalized seizure. (See 'Generalized seizures' below.)

Generalized seizures — Generalized tonic-clonic seizures (also called grand mal seizures, major motor seizures, or convulsions) are the most common type of generalized seizures.

Generalized tonic-clonic seizures begin with an abrupt loss of consciousness, sometimes in association with a scream or choking sound (table 4). All of the muscles of the arms and legs as well as the chest and back then become stiff. The patient may begin to appear cyanotic during this tonic phase. After approximately one minute, the muscles begin to jerk and twitch for an additional one to two minutes. During this clonic phase the tongue can be bitten, and frothy and bloody sputum may be seen coming out of the mouth. The postictal phase begins once the twitching movements end. The patient is initially in a deep sleep, breathing deeply, and then gradually wakes up. Postictal confusion or agitation is common. (See 'Postictal period' below.)

In adults with a first-time seizure, most unprovoked generalized seizures represent secondarily generalized seizures that have evolved from a focal-onset seizure. As discussed above, symptoms of the focal phase of the seizure may be subtle or so brief that the patient has no recollection or warning prior to losing consciousness.

Other subtypes of generalized seizures are absence seizures, more often seen in childhood in association with generalized epilepsy syndromes, and clonic, myoclonic, tonic, and atonic seizures.

- Absence seizures (previously called petit mal) usually occur during childhood and typically last between 5 and 10 seconds. They frequently occur in clusters and may take place dozens or even hundreds of times a day. The onset is marked by behavioral arrest (the affected individual suddenly stops all activity) accompanied by staring with a blank facial expression and impaired consciousness. If an absence seizure lasts for 10 seconds or more, there may also be eye blinking and lip smacking. Absence seizures are discussed in greater detail separately. (See "Epilepsy syndromes in children", section on 'Absence epilepsies'.)

- Atypical absence seizures may be longer, have a slower onset and offset, and involve different symptoms, including staring with a blank facial expression and impaired

consciousness, a change in muscle tone and movement, and repetitive blinking, sometimes accompanied by behaviors such as lip smacking, chewing movements, and finger or hand movements. The occurrence of these behaviors and the longer length of atypical absence seizures, up to 20 seconds or longer, may make it difficult to distinguish atypical absence seizures at the bedside from focal seizures with impaired awareness.

- Clonic seizures cause rhythmic jerking muscle contractions that usually involve the arms, neck, and face.
- Myoclonic seizures consist of sudden, brief muscle contractions that may occur singly or in clusters and that can affect any group of muscles, although typically the arms are affected. Consciousness is usually not impaired.
- Tonic seizures cause sudden muscle stiffening, often associated with impaired consciousness and falling to the ground.
- Atonic seizures (also known as drop seizures) produce the opposite effect of tonic seizures: a sudden loss of control of the muscles, particularly of the legs, that results in collapsing to the ground and possible injuries.

CAUSES OF SEIZURES

The causes of seizures and epilepsy are numerous and vary according to both the setting of the seizure (ie, acute symptomatic versus unprovoked) and the type of seizure (ie, focal versus generalized onset). Compared with children and young adults, older adults with a first seizure are more likely to have a cause of seizure identified by an initial evaluation and neuroimaging.

Acute symptomatic seizures — Virtually any acute insult to the brain can cause a seizure. In adults, common causes include:

- Acute ischemic or hemorrhagic stroke, particularly lobar hemorrhage (see "Spontaneous intracerebral hemorrhage: Pathogenesis, clinical features, and diagnosis", section on 'Clinical presentation')
- Subdural hematoma (see "Subdural hematoma in adults: Etiology, clinical features, and diagnosis", section on 'Clinical manifestations')
- Subarachnoid hemorrhage (see "Aneurysmal subarachnoid hemorrhage: Treatment and prognosis", section on 'Seizures')

- Cerebral venous thrombosis (see "Cerebral venous thrombosis: Etiology, clinical features, and diagnosis", section on 'Seizures')
- Traumatic brain injury (see "Acute mild traumatic brain injury (concussion) in adults", section on 'Seizures' and "Management of acute moderate and severe traumatic brain injury")
- Eclampsia (see "Eclampsia", section on 'Characteristics of eclamptic seizures')
- Posterior reversible encephalopathy syndrome (PRES) (see "Reversible posterior leukoencephalopathy syndrome", section on 'Clinical manifestations')
- Hypoxic-ischemic injury (see "Acute toxic-metabolic encephalopathy in adults", section on 'Hypoxic-ischemic encephalopathy')
- Brain abscess (see "Pathogenesis, clinical manifestations, and diagnosis of brain abscess", section on 'Clinical manifestations')
- Meningitis or encephalitis (see "Clinical features and diagnosis of acute bacterial meningitis in adults", section on 'Presenting manifestations' and "Aseptic meningitis in adults" and "Viral encephalitis in adults")

Acute symptomatic seizures may also be caused by an acute medical illness, metabolic disturbance, substance ingestion or withdrawal, and medication exposure (table 5). The risk of seizures in this setting is felt to occur in proportion to the rapidity of the onset, rather than to the severity of the underlying metabolic disturbance [4,8]. These conditions include:

- Hypoglycemia – Hypoglycemic seizures are most common in diabetic patients who take excessive amounts of insulin or oral hypoglycemics; islet cell tumors are much less common, but seizures may be the initial presentation. Prodromal symptoms of hypoglycemic seizures include diaphoresis, tachycardia, anxiety, and confusion.
- Hyperglycemia – Nonketotic hyperglycemia most commonly occurs in diabetic older adults and can cause focal motor seizures.
- Hyponatremia – Precipitous falls in serum sodium concentrations can trigger generalized tonic-clonic seizures (see 'Generalized seizures' above), usually in association with a prodrome of confusion and depressed level of consciousness. These convulsions are associated with a high risk of mortality and must be treated urgently. Care should be taken to avoid overly rapid correction of severe hyponatremia. (See "Manifestations of hyponatremia and hypernatremia in adults".)

- Hypocalcemia – Hypocalcemia is a rare cause of seizures and most often occurs in neonates. In adults, hypocalcemia may occur after thyroid or parathyroid surgery or in association with renal failure, hypoparathyroidism, or pancreatitis. Typical prodromic symptoms and signs are mental status changes and tetany. (See "Clinical manifestations of hypocalcemia".)

- Hypomagnesemia – Magnesium levels below 0.8 mEq/L may result in irritability, agitation, confusion, myoclonus, tetany, and convulsions, and may be accompanied by hypocalcemia. (See "Hypomagnesemia: Clinical manifestations of magnesium depletion".)

- Uremia – Renal failure and uremia are often associated with seizures, particularly myoclonic seizures (see 'Generalized seizures' above). Generalized tonic-clonic seizures occur in approximately 10 percent of patients with chronic renal failure, usually late in the course. Seizures may also occur in patients undergoing dialysis as part of the dialysis disequilibrium syndrome; associated symptoms are headache, nausea, muscle cramps, irritability, confusion, and depressed level of consciousness. (See "Seizures in patients undergoing hemodialysis".)

- Hyperthyroidism – Hyperthyroidism can cause seizures and can exacerbate seizures in patients with epilepsy. (See "Neurologic manifestations of hyperthyroidism and Graves' disease".)

- Disorders of porphyrin metabolism – Acute intermittent porphyria (AIP) is due to a partial deficiency of porphobilinogen deaminase, which results in excess delta-aminolevulinic acid and porphobilinogen in the urine. Seizures occur in approximately 15 percent of AIP attacks and are usually generalized tonic-clonic seizures, although focal seizures may occur (see 'Focal seizures with retained awareness' above and 'Focal seizures with impaired awareness' above). Other symptoms of AIP include abdominal pain and behavioral changes. (See "Acute intermittent porphyria: Pathogenesis, clinical features, and diagnosis".)

- Withdrawal states – Substance or medication withdrawal, particularly alcohol and benzodiazepine withdrawal, is associated with seizures. Alcohol withdrawal seizures typically occur within 7 to 48 hours of the last drink. (See "Management of moderate and severe alcohol withdrawal syndromes".)

- Drug intoxication, poisoning, and overdose – Cocaine, amphetamines, and other illicit substances may cause seizures after acute intoxication. Prescribed medications that may lower the seizure threshold or cause seizures in overdose are listed in the table (table 6). (See "Cocaine: Acute intoxication", section on 'Central nervous system' and

"Methamphetamine: Acute intoxication" and "Phencyclidine (PCP) intoxication in adults" and "General approach to drug poisoning in adults".)

Underlying epilepsy — A first unprovoked seizure may be the initial presentation of epilepsy. The causes of epilepsy can be broadly categorized as genetic, structural, metabolic, immune, infectious, and unknown (figure 1). (See "ILAE classification of seizures and epilepsy".)

The relative frequency of each of these as a cause of new-onset epilepsy varies across the lifespan. While a significant proportion of epilepsy in childhood has a genetic, metabolic, or congenital structural basis, epilepsy diagnosed in adults is more likely to be due to an acquired vascular, degenerative, or neoplastic etiology [9-11]. Up to 60 percent of patients have an unknown cause of epilepsy, even with complete evaluation.

Some of the more commonly identified etiologies of focal epilepsy in adults include the following:

- Mesial temporal lobe epilepsy (>80 percent of patients have seizure onset in adolescence, but presentation may be delayed into young adulthood) (see "Focal epilepsy: Causes and clinical features", section on 'Mesial temporal lobe epilepsy')
- Cerebrovascular disease (see "Seizures and epilepsy in older adults: Etiology, clinical presentation, and diagnosis" and "Overview of the management of epilepsy in adults", section on 'Poststroke seizures')
- Primary or metastatic brain tumors (see "Seizures in patients with primary and metastatic brain tumors")
- Vascular malformations (see "Vascular malformations of the central nervous system")
- Prior central nervous system infection, such as neurocysticercosis (see "Cysticercosis: Clinical manifestations and diagnosis" and "Cysticercosis: Treatment")
- Head injury (see "Posttraumatic seizures and epilepsy")
- Neurodegenerative dementia, including Alzheimer disease (see "Clinical features and diagnosis of Alzheimer disease", section on 'Seizures' and "Seizures and epilepsy in older adults: Etiology, clinical presentation, and diagnosis")

Most of the generalized epilepsy syndromes have an onset in infancy or childhood, but some syndromes, such as juvenile myoclonic epilepsy (JME), begin in adolescence and the diagnosis may be delayed. Patients with JME may have morning myoclonic jerks for years before

presenting with their first generalized seizure (see "Juvenile myoclonic epilepsy"). Late-onset idiopathic generalized epilepsy in adults has also been described [12-14].

DIFFERENTIAL DIAGNOSIS

Seizure is primarily a clinical diagnosis, and accurate diagnosis requires differentiating seizure from other common clinical events that can mimic seizure.

In adults, the primary conditions to consider in patients presenting with transient or paroxysmal neurologic events are (table 7):

- Syncope
- Transient ischemic attack (particularly in older adults)
- Migraine
- Panic attack and anxiety
- Psychogenic nonepileptic seizure
- Transient global amnesia (rare before the age of 50 years)
- Narcolepsy with cataplexy
- Paroxysmal movement disorders

The clinical features of these disorders and their differentiation from epileptic seizures are reviewed in the table (table 7) and discussed in detail separately. (See "Nonepileptic paroxysmal disorders in adolescents and adults".)

Events that occur during sleep or in the transition periods between sleep and wakefulness have a largely separate differential diagnosis that includes a variety of rapid eye movement (REM) and nonREM parasomnias (eg, REM sleep behavior disorder, sleepwalking, confusional arousals), as well as isolated sleep paralysis and psychiatric events (table 8). (See "Approach to abnormal movements and behaviors during sleep".)

INITIAL EVALUATION

Medical history — The diagnostic evaluation of a first seizure begins with the history. The goals of the history are to characterize the event as a seizure and rule out alternative diagnoses, determine whether similar events have happened in the past, and evaluate for underlying risk factors for seizures in the past medical history, family history, and medications.

Description of the event — An accurate description of the seizure may be difficult to obtain from the patient and witnesses; it is usually necessary to ask pointed questions about the circumstances leading up to the seizure, the ictal behaviors, and the postictal state.

Patients with focal seizures without impairment of consciousness can typically provide a complete description of the event, whereas patients with focal seizures with impairment of consciousness or generalized seizures typically cannot, or can only remember the early stages of the seizure.

Most seizures, whether focal or generalized, have a clear and abrupt clinical onset and rapid progression of symptoms over the course of seconds. The pace of progression is more rapid than migraine aura, for example, which increases in intensity over the course of 5 to 10 minutes.

The majority of seizures end spontaneously within two to three minutes; more prolonged symptoms may be a clue to alternative conditions such as migraine, transient ischemic attack, or psychogenic nonepileptic seizure (table 7).

Ictal behaviors are useful for localization, as well as to determine whether a seizure was focal or generalized. Generalized seizures are associated with immediate alteration of consciousness, whereas focal seizures are more variable. For focal seizures, some behaviors have localizing and/or lateralizing value. For example, versive head turning or eye deviation to the left suggests onset in the right frontal lobe, unilateral sensory disturbance suggests contralateral parietal lobe onset, and prominent dysphasia suggests involvement of the dominant hemisphere. (See 'Types of seizures' above and "Focal epilepsy: Causes and clinical features", section on 'Clinical features'.)

The timing of the seizure in relation to sleep is also important to determine. Events that occur during sleep, or in the transition periods between sleep and wakefulness, have implications for both differential diagnosis and risk of recurrence. (See 'Differential diagnosis' above and 'When to start antiseizure medication therapy' below.)

Postictal period — Following the end of a seizure, there is a period of transition from the ictal state back to the preseizure baseline level of awareness and function, referred to as the postictal period.

Manifestations of the postictal period typically include confusion and suppressed alertness [15]. Focal neurologic deficits may also be present, often referred to as Todd paralysis or postictal paresis. The classic example of postictal paresis is weakness of a hand, arm, or leg that appears following a focal motor seizure involving the one side of the body. The degree of weakness is

usually moderate but can be severe. Other focal postictal symptoms vary according the location of the seizure and may include aphasia, hemianopsia, or numbness.

The postictal state may last from seconds to minutes to hours, depending upon several factors including which part(s) of the brain were affected by the seizure; the length of the seizure; medications received, such as benzodiazepines; and age. As an example, young adults with focal seizures of frontal lobe origin may have postictal states that last only several seconds, while older patients with secondarily generalized seizures may have postictal confusion and sleepiness; confusion may persist for as long as several days to a week, particularly if there is underlying brain dysfunction or neoplasm [16].

Although there is a broad range, most patients begin to recover responsiveness and alertness within 10 to 20 minutes of a generalized seizure and show gradual, consistent improvement in postictal symptoms as time elapses. Patients with prolonged postictal symptoms should be evaluated for ongoing subclinical seizure activity with electroencephalography (EEG) and should undergo neuroimaging and lumbar puncture, as clinically indicated. (See 'Additional testing' below.)

In some cases, the postictal symptoms may be the presenting clinical feature, when the seizure itself is very brief, unwitnessed, or occurs during sleep. Particularly when the event is a first-time seizure, the clinical syndrome in these cases can be indistinguishable from that of acute stroke.

Seizure precipitants or triggers — A key element in the history is whether a particular environmental or physiologic precipitant or trigger immediately preceded the seizure. Some patients with epilepsy tend to have seizures under particular conditions, and their first seizure may provide a clue to their so-called seizure trigger. Triggers include (but are not limited to) strong emotions, intense exercise, loud music, and flashing lights [17,18]. These triggers are often experienced immediately before the seizure.

Other physiologic conditions such as fever, the menstrual period, lack of sleep, pregnancy, and stress can also precipitate seizures, probably by lowering seizure threshold rather than directly causing a seizure. As a result, the temporal relationship to the presenting seizure is often less clear. Triggers may also precipitate nonepileptic paroxysmal disorders, especially syncope.

However, the majority of patients with epilepsy have no identifiable or consistent trigger to their seizures. In addition, triggers are the sole cause of epileptic seizures in only a very small percentage of patients.

Photosensitivity is a relatively uncommon seizure trigger, although it occasionally receives heightened attention in relation to particular television shows or video games [17,19,20].

Children are more susceptible to photic-induced seizures and photoparoxysmal EEG changes than adults, and a tendency for photic-induced seizures may be inherited. Photoconvulsive seizures are usually generalized, but they may be focal.

Prior events — A substantial number of patients presenting for first evaluation of a seizure have had similar or related events in the past [21]. In a retrospective study of 220 adults referred to a first-seizure clinic, 41 percent of patients endorsed one or more events before their index seizure [22]. Delays in diagnosis were most common in patients with prior nonconvulsive events, although 28 percent of prior events were convulsive. Other studies have found similar results, with rates of prior seizure or probable seizure ranging from 20 to 60 percent in patients presenting with a "first seizure" [23-25].

In some cases, prior events are subtle and may only be recognized when patients are directly asked about them. Young adults in particular should be asked whether they have ever experienced sudden jerks in the arms or legs shortly after awakening in the mornings, as these may represent epileptic myoclonic jerks commonly seen in juvenile myoclonic epilepsy (JME) or other generalized epilepsy syndromes. (See "Juvenile myoclonic epilepsy", section on 'Seizures'.)

Additional examples of focal seizures or auras that may go unrecognized, unreported, or misattributed until patients experience a first-time (secondarily) generalized seizure include olfactory or gustatory hallucinations as a manifestation of temporal lobe epilepsy; brief episodes of fear, panic, or anxiety as a manifestation of temporal or frontal lobe epilepsy; and visual hallucinations as a manifestation of occipital-onset seizures. (See "Focal epilepsy: Causes and clinical features", section on 'Clinical features'.)

Medications and substances — There are a number of prescribed or over-the-counter medications that have been associated with iatrogenic seizures (table 6) [26,27]. For most drugs, the magnitude of risk is not well-characterized but is likely low unless medications are taken at supratherapeutic doses, in combination with other drugs that inhibit their metabolism, or in the setting of underlying liver or renal dysfunction. Focal-onset seizures are less likely to be drug-induced than generalized tonic-clonic seizures.

Alcohol intoxication or withdrawal and drugs of abuse should not be overlooked as a potential cause of seizure. Of note, however, a history of alcohol does not preclude other causes of seizure. In a study of 259 patients with first seizure suspected to be due to alcohol withdrawal, head computed tomography (CT) identified 16 patients (6 percent) with a clinically significant

lesion (eg, subdural hematoma), and the presence of altered mental status or focal deficits did not correlate with abnormal head CT results [28].

Hypomagnesemia is common in alcohol withdrawal and intake of large quantities of beer has been associated with hyponatremia.

Past medical history — There are a number of risk factors for epileptic seizures that should be addressed, including head injury, abnormal early neurologic development or intellectual disability, stroke, Alzheimer disease, history of intracranial infection, alcohol or drug abuse, immunosuppression, history of cancer, rheumatologic disorders such as systemic lupus erythematosus [29], and hematologic disorders including sickle cell disease, porphyria, and antiphospholipid syndrome [30].

Family history — A positive family history of seizures is a risk factor for epilepsy. In particular, absence seizures and myoclonic seizures may be inherited. Occasionally, a family member does not have seizures but has an abnormal EEG. One genetic epidemiology study suggests that while family history of seizures in siblings is reasonably accurate, seizures and epilepsy in parents are underreported [31].

Physical and neurologic examination — The physical examination is generally unrevealing in patients with epileptic seizures, but is important when central nervous system infection or hemorrhage are diagnostic possibilities. In addition, an examination directed at identifying any seizure-related trauma should be done. If new shoulder pain or limited motion is found, a posterior dislocation, which may be more difficult to see on plain radiographs, should be suspected.

The neurologic examination should evaluate for lateralizing abnormalities, such as weakness, hyperreflexia, or a positive Babinski sign, that may point to a contralateral structural brain lesion.

A tongue bite or laceration may be evident in a patient who has had a generalized tonic-clonic seizure; oral lacerations that occur with epileptic seizures tend to be on the side of the tongue [32], whereas lacerations on the tip of the tongue might be more likely to result from falls or trauma unrelated to seizure. Although tongue biting lacks sensitivity for the diagnosis (ie, it occurs in a minority of generalized tonic-clonic seizures), it does have high specificity in distinguishing epileptic events from psychogenic nonepileptic seizures and syncope [32]. In meta-analyses, the pooled sensitivity and specificity of tongue biting for a diagnosis of epileptic seizure are 20 to 33 percent and 96 to 100 percent, respectively [33,34]. By contrast, urinary incontinence has lower diagnostic utility (sensitivity and specificity of 38 and 57 percent) [35].

Laboratories — Rapid point-of-care glucose should be checked in all patients with a first seizure. Other laboratory evaluations that are appropriate for the evaluation of a first seizure include electrolytes, glucose, calcium, magnesium, complete blood count, renal function tests, liver function tests, urinalysis, and toxicology screens, although the likelihood of finding a relevant abnormality in unselected patients is low [36]. (See 'Acute symptomatic seizures' above.)

A pregnancy test in women of childbearing age is commonly performed as pregnancy may affect testing and treatment decisions.

Serum lactate can be helpful in patients with unwitnessed transient loss of consciousness or impaired consciousness, as an elevated lactate level within the first two hours after onset of the event suggests the cause was a generalized seizure rather than syncope or a psychogenic nonepileptic seizure [37-39]. Other laboratory abnormalities that may be present after a generalized convulsive seizure, such as elevated creatine phosphokinase (CPK), cortisol, white blood cell count, lactate dehydrogenase, and neuron-specific enolase [40-44], are nonspecific and not generally useful in the diagnostic evaluation of suspected seizure.

Serum prolactin assessment has limited utility as a diagnostic test for epileptic seizures and is not recommended as part of the routine evaluation [45]. In selected cases, an elevated serum prolactin may be useful in differentiating generalized tonic-clonic and focal seizures from psychogenic nonepileptic seizures in adults and older children [46]. A low serum prolactin does not exclude epileptic seizure, although it lowers the likelihood of an epileptic seizure if the event appeared to be a generalized tonic-clonic seizure. (See "Psychogenic nonepileptic seizures: Etiology, clinical features, and diagnosis", section on 'Serum testing'.)

Electrocardiogram — An electrocardiogram (ECG) should be performed in all patients with loss of consciousness, as cardiogenic syncope can manifest as a secondary hypoxic seizure. The purpose of the ECG is to identify features that may suggest cardiac arrhythmia as a cause of syncope, such as acquired or congenital long QT syndromes [47,48]. A prolonged QT interval can be an important early clue to serious drug intoxications, particularly the tricyclic antidepressants. (See "Syncope in adults: Clinical manifestations and initial diagnostic evaluation", section on 'Electrocardiogram'.)

ADDITIONAL TESTING

Additional testing in patients with a first seizure includes neuroimaging in all patients and electroencephalogram (EEG) and lumbar puncture in selected patients. The urgency with which

to obtain testing depends on the clinical history, examination, and suspicion for an underlying structural cause for seizure.

Lumbar puncture — Lumbar puncture should be performed if the clinical presentation is suggestive of an acute infectious process that involves the central nervous system or if neuroimaging studies raise concern for an alternative meningeal process such as leptomeningeal cancer or chronic meningitis [36]. In other circumstances the test is not likely to be helpful and may be misleading, since a prolonged convulsive seizure itself can cause transient, mild cerebrospinal fluid pleocytosis.

Lumbar puncture should only be performed after a space-occupying brain lesion has been excluded by appropriate neuroimaging studies. When there is a high clinical suspicion for bacterial meningitis or encephalitis, treatment with dexamethasone and antimicrobial agents should be given prior to neuroimaging studies. (See "Lumbar puncture: Technique, contraindications, and complications in adults".)

Electroencephalography — The EEG is an essential study in the diagnostic evaluation of epileptic seizures [36,49]. If abnormal, the routine, interictal EEG may aid in supporting the diagnosis of epileptic seizures and may also suggest whether a patient has generalized or focal seizures.

The timing of EEG should be individualized. Urgent EEG to evaluate for subclinical, nonconvulsive seizure activity should be performed in patients who fail to return to baseline within 30 to 60 minutes of a generalized convulsion and those with waxing and waning mental status or prolonged focal deficits unexplained by a structural cause on neuroimaging. (See "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis", section on 'Diagnosis'.)

In patients who have returned to baseline, outpatient EEG is appropriate and may be more representative of a patient's underlying risk for seizure recurrence than EEG performed immediately after a seizure, which may be confounded by medication effects and acute postictal changes.

Among adults presenting with a first seizure, routine EEG demonstrates epileptiform abnormalities in approximately 25 percent of patients [36]. This finding substantially increases the likelihood that the patient will experience a second seizure over the next two years [36,50]. (See 'When to start antiseizure medication therapy' below.)

Use of sleep deprivation and provocative measures during the test, such as hyperventilation and intermittent photic stimulation, increases the yield [51,52].

However, a normal EEG does not rule out epilepsy, and many EEG abnormalities are nonspecific. As an example, diffuse slowing may also occur with a wide variety of encephalopathies or in association with some medications, especially at high doses. Epileptiform abnormalities are usually more informative than less specific changes. (See "Electroencephalography (EEG) in the diagnosis of seizures and epilepsy".)

Neuroimaging — A neuroimaging study should be performed in all adults with a first seizure to evaluate for a culprit structural brain abnormality. In the absence of contraindications (eg, pacemaker, severe claustrophobia), magnetic resonance imaging (MRI) is preferred over computed tomography (CT) because it has superior sensitivity for detecting a variety of acute and remote causes of seizure and epilepsy, including infarcts, tumors, mesial temporal sclerosis, and cortical dysplasia. (See "Neuroimaging in the evaluation of seizures and epilepsy", section on 'Sensitivity' and "Neuroimaging in the evaluation of seizures and epilepsy", section on 'Epilepsy protocol for MRI'.)

The urgency with which to perform neuroimaging depends on the clinical context.

- Neuroimaging should be performed immediately when an intracranial lesion is suspected, and specifically in patients with a new focal deficit or persistent altered mental state, fever, persistent headache, focal-onset seizure, history of acute head trauma, malignancy, immunocompromise, alcoholism, anticoagulation, or bleeding diathesis. In such cases, a noncontrast head CT is often the most appropriate initial study, followed in most cases by MRI.

- Deferred outpatient MRI may be reasonable in patients evaluated in the emergency department who have returned to a normal baseline and have a normal neurologic examination, particularly if an initial head CT is normal and reliable follow-up can be ensured. To limit radiation exposure, an expedited outpatient brain MRI is preferred to obtaining a head CT in the emergency department for select (especially younger) patients who have fully recovered from the seizure.

These recommendations are consistent with guidelines from the American Academy of Neurology (AAN), the American College of Emergency Physicians, and others [36,49,53,54]. In some guidelines, an exception is made for patients who can be confidently diagnosed with a genetic generalized epilepsy syndrome (also called idiopathic generalized epilepsy); in practice, however, the majority of these patients do undergo neuroimaging at the time of a first seizure.

The yield of neuroimaging in patients with a first seizure varies by imaging modality, age, and other factors. A systematic literature review of 15 published reports concluded that a noncontrast CT scan performed in the emergency department changed acute management in 9

to 17 percent of adult patients presenting with a first seizure [55]. Relevant findings included intracranial hemorrhage, brain abscess, and tumor.

In young to middle-aged adults, common MRI findings are mesial temporal sclerosis, sequelae of head injury, congenital anomalies, brain tumors, cysticercosis, and vascular lesions. In older adults, MRIs often reveal strokes, cerebral degeneration, or neoplasms. However, over 50 percent of patients with epilepsy, regardless of age, have normal neuroimaging studies, and the likelihood of detecting an epileptogenic lesion is highest in those patients presenting with a focal seizure [56].

Importantly, while structural abnormalities on brain MRI or CT usually suggest a symptomatic, focal-onset epilepsy syndrome, these findings should not be interpreted in isolation. Many MRI findings are nonspecific and may be incidental to the index event [57,58].

The utility of brain MRI in individuals presenting with a seizure is discussed in detail separately. (See "Neuroimaging in the evaluation of seizures and epilepsy".)

MANAGEMENT

Early postseizure management — Most seizures remit spontaneously within two minutes and rapid administration of a benzodiazepine or antiseizure medication is not required. Nonetheless, intravenous access is typically secured by paramedics or in the emergency department setting for patients presenting acutely so that parenteral medications can be administered if the seizure is more prolonged or recurs.

For patients with acute symptomatic seizures, any underlying metabolic disturbances or infectious etiologies should be quickly identified and treated. Hypoglycemia should be treated with intravenous thiamine and dextrose. As stated above, care should be taken to avoid overly rapid correction of severe, chronic hyponatremia. (See "Overview of the treatment of hyponatremia in adults", section on 'Avoid overcorrection'.)

Seizures that last longer than 5 to 10 minutes or serial clinical seizures without an interictal return to baseline consciousness meet the definition of status epilepticus. The evaluation and management of status epilepticus (algorithm 1) are discussed separately. (See "Convulsive status epilepticus in adults: Classification, clinical features, and diagnosis" and "Convulsive status epilepticus in adults: Management".)

When to start antiseizure medication therapy — The decision whether to start antiseizure medication therapy immediately after a first seizure depends on multiple factors, including the

probability that the event represented a seizure, the suspected or confirmed cause of the seizure based on the initial evaluation, the stability of the patient, and the estimated risk of recurrent seizure.

In critically ill patients with an acute symptomatic seizure, an antiseizure medication that can be loaded intravenously to obtain rapid plasma levels is typically administered, with the goal of preventing recurrent seizures and further destabilization while the underlying condition is treated. Commonly used drugs in this setting include levetiracetam, fosphenytoin/phenytoin, and valproic acid. (See "Management of acute moderate and severe traumatic brain injury", section on 'Intensive care management'.)

Similarly, patients with seizures provoked by metabolic derangements are generally not felt to be at risk for future epilepsy but they may be at risk for seizure recurrence in the acute setting if the underlying disturbance is severe or prolonged, thus warranting short-term antiseizure medication therapy (algorithm 2). This was illustrated by a retrospective study of 218 patients with hospital-onset seizures that included 43 patients whose seizures were provoked by an underlying metabolic disturbance; of these patients, 21 (49 percent) had seizures on multiple days during the index hospitalization [59].

The decision to initiate therapy with antiseizure medications is more complex in patients presenting with a first unprovoked seizure who have returned to baseline (algorithm 3). In the emergency department, the decision to start an antiseizure medication should be made in consultation with neurology. Approximately one-third of patients will have a recurrent seizure within five years [60-62], and the risk is increased 2- to 2.5-fold in association with any of the following factors (see "Initial treatment of epilepsy in adults", section on 'Risk of seizure recurrence'):

- Epileptiform abnormalities on interictal electroencephalogram (EEG)
- Remote symptomatic cause, as identified by clinical history or neuroimaging (eg, brain tumor, brain malformation, prior central nervous system infection)
- Abnormal neurologic examination, including focal findings and intellectual disability
- A first seizure that occurs during sleep

In patients with any of these risk factors, the risk of a recurrent seizure approaches or exceeds 60 percent over the next 10 years, thereby meeting criteria for epilepsy according to the current International League Against Epilepsy (ILAE) definition [6]. Initiation of antiseizure medication therapy is suggested in most of these patients, either at the time of initial evaluation in the

emergency department or in consultation with a neurologist as soon following the index event as possible [53,63]. Drug selection and multiple other aspects of the initial treatment of epilepsy in adults are reviewed separately. (See "Initial treatment of epilepsy in adults", section on 'When to start antiseizure medication therapy'.)

In patients without any of these risk factors, the decision should be individualized, weighing the risk of seizure recurrence against adverse effects of antiseizure medications and considering patient preferences [62]. In many cases, antiseizure medication therapy can be reasonably deferred until the occurrence of a second unprovoked seizure. (See "Initial treatment of epilepsy in adults", section on 'First-time unprovoked seizure'.)

Indications for hospitalization — Hospitalization may be required for patients who have a first seizure associated with a prolonged postictal state, incomplete recovery, or serious seizure-related injury. Other indications for hospitalization include status epilepticus, the presence of a neurologic or systemic illness or insult requiring additional evaluation and treatment, or questions regarding compliance.

Most patients with a first unprovoked seizure who have returned to their clinical baseline and have normal initial studies can be discharged from the emergency department with close outpatient follow-up. This practice is supported by a clinical policy statement of the American College of Emergency Physicians [53,63]. Decisions should be individualized, however, and additional factors including reliability of follow-up and access to outpatient testing may affect discharge planning.

Data on the need for hospitalization after a first seizure and outcomes associated with early discharge from an emergency department are somewhat limited. One study included 1025 patients admitted to two emergency departments with provoked or unprovoked seizures, one-third of which were first seizures [64]. The mean time to early seizure recurrence was 121 minutes, and more than 85 percent of early seizures recurred within six hours. Nonalcoholic patients with first-time seizure had the lowest early seizure recurrence (9 percent); predictors of increased risk included age ≥40 years, hyperglycemia, and abnormal Glasgow Coma Scale.

Indications for referral — The majority of patients with a first-time seizure should be evaluated by a neurologist, unless the seizure was obviously provoked and initial studies are otherwise unremarkable. Some institutions have first-seizure clinics or other pathways to facilitate timely access to specialty consultation after an index event. As many as 50 percent of patients referred to first-seizure clinics have had prior clinical events or EEG findings commensurate with a diagnosis of epilepsy [22,23].

In addition to review of the medical history and consideration of alternative causes of the event (see 'Medical history' above), neurology consultation typically includes further risk stratification through review of outpatient EEG, coordination of seizure protocol magnetic resonance imaging (MRI) if one was not obtained at the time of the index event, and discussion of the risks and benefits of antiseizure medication therapy.

Patient education — Newly diagnosed patients with seizure and epilepsy may suffer a number of losses, including loss of independence, employment, insurance, ability to drive, and self-esteem. As the treatment plan is formulated, these psychosocial issues should be explored with patients so that appropriate referrals for additional help and counseling can be initiated.

Seizure precautions — Patients with a first seizure should be aware of common seizure triggers or precipitating factors, including sleep deprivation, alcohol, certain medications (table 6), and infection or systemic illness.

Patients should be advised to avoid unsupervised activities that might pose danger with sudden loss of consciousness, including bathing, swimming alone, working at heights, and operating heavy machinery. The bathtub is the most common site of seizure-induced drowning, and patients with epilepsy should be told to take showers instead of baths.

Individuals with epilepsy are at increased risk for personal injury, accidental death, and drowning as well as psychiatric comorbidity, suicidal deaths, and sudden unexpected death in epilepsy. (See "Comorbidities and complications of epilepsy in adults".)

Driving — States and countries vary in driver licensing requirements for patients with an episode of loss of consciousness, including from seizures and epilepsy, as well as the responsibilities of clinicians to notify state authorities [65]. Most if not all require at least some period of abstinence from driving after a seizure or other event associated with loss or alteration of consciousness.

Patients should be appropriately counseled about driving restrictions prior to discharge from the emergency department, and written discharge instructions should document any driving limitations. In one study, only 64 percent of patients referred to a first-seizure clinic had received documented driving advice in the emergency department [66].

This topic is discussed in more detail elsewhere. (See "Driving restrictions for patients with seizures and epilepsy".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Seizures and epilepsy in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Seizures (The Basics)" and "Patient education: EEG (The Basics)")
- Beyond the Basics topics (see "Patient education: Seizures in adults (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Goals of evaluation** – The primary objectives of the medical evaluation of the first seizure are to establish whether the event was a seizure, and if so, whether it resulted from a correctable systemic process or whether the patient is at risk for developing further unprovoked seizures (epilepsy). (See 'Causes of seizures' above and 'Differential diagnosis' above.)
- **Definitions** – Seizures are typically referred to as either acute symptomatic seizures or unprovoked seizures depending on the clinical circumstances at the time of the event.
    - **Acute symptomatic seizure** – An acute symptomatic seizure is a seizure that occurs in the setting of acute medical (eg, hypoglycemia, hyponatremia) or neurologic illness or injury (eg, stroke, traumatic brain injury, meningitis, anoxic encephalopathy). Such

seizures may recur during the index illness but generally carry a low risk of future epilepsy compared with unprovoked seizures. (See 'Acute symptomatic seizures' above.)

- **Unprovoked seizure** – An unprovoked seizure refers to a seizure of unknown etiology as well as one that occurs in relation to a preexisting brain lesion or progressive nervous system disorder. Approximately one-third of adults with a first unprovoked seizure will have a recurrent seizure (ie, epilepsy) over the next five years. (See 'Unprovoked seizure' above.)

- **Epilepsy** – Epilepsy refers to the tendency for recurrent, unprovoked seizures. (See 'Epilepsy' above.)

- **Focal versus generalized onset** – Seizures are further categorized as either focal or generalized according to whether the onset of electrical activity involves a focal region of the brain or the entire cortex simultaneously. The clinical manifestations of seizures vary based on the location of the seizure in the brain and the amount of cortex that is involved. (See 'Types of seizures' above.)

- **Causes** – The causes of epilepsy can be broadly categorized as genetic, structural, metabolic, immune, infectious, and unknown. While a significant proportion of epilepsy in childhood has a genetic, metabolic, or congenital structural basis, epilepsy diagnosed in adults is more likely to be due to an acquired vascular, degenerative, or neoplastic etiology. (See 'Causes of seizures' above.)

- **Differential diagnosis** – Seizure is only one cause of transient neurologic symptoms with or without alteration of consciousness. Other common causes of paroxysmal neurologic symptoms in adults are syncope, transient ischemic attack, migraine, and psychogenic nonepileptic seizures (table 7). (See 'Differential diagnosis' above and "Nonepileptic paroxysmal disorders in adolescents and adults".)

- **Diagnostic evaluation** – Seizure is largely a clinical diagnosis made by history, physical and neurologic examinations, and selected additional tests to identify an underlying cause:

  - A detailed description of the seizure should be obtained from the patient and witnesses and should include the circumstances leading up to the seizure, including possible triggers or precipitants, the ictal behaviors (table 2 and table 4), and the postictal state (table 3). (See 'Description of the event' above and 'Postictal period' above and 'Seizure precipitants or triggers' above.)

- Prior similar events including subtle myoclonus or auras should not be overlooked in the history. Other items in the past medical history and a physical and neurologic examination are also important in the evaluation of a first seizure. (See 'Prior events' above and 'Medications and substances' above and 'Physical and neurologic examination' above.)

- Testing should include laboratory studies (electrolytes, glucose, calcium, magnesium, complete blood count, renal function tests, liver function tests, urinalysis, and toxicology screens), an electrocardiogram (ECG), an electroencephalogram (EEG) (urgently when impaired sensorium is persistent), and a neuroimaging study. Depending on the clinical situation, a lumbar puncture may also be indicated. (See 'Laboratories' above and 'Electrocardiogram' above and 'Additional testing' above.)

- **Seizure duration** – Most seizures remit spontaneously within two minutes and rapid administration of a benzodiazepine or antiseizure medication is not required. Nonetheless, intravenous access is typically secured by paramedics or in the emergency department setting for patients presenting acutely so that medications can be administered if the seizure is more prolonged or recurs. Diagnosis and management of status epilepticus are reviewed separately. (See "Convulsive status epilepticus in adults: Management".)

- **When to start antiseizure medication** – Antiseizure medications are not always indicated after a first seizure (algorithm 2 and algorithm 3). The decision whether to start antiseizure medication therapy depends on multiple factors, including the probability that the event represented a seizure, the suspected or confirmed cause of the seizure based on the initial evaluation, the stability of the patient, and the estimated risk of recurrent seizure. (See 'When to start antiseizure medication therapy' above.)

- **Indications for hospital admission** – Most patients with a first unprovoked seizure who have returned to their clinical baseline and have normal initial studies can be discharged from the emergency department with close outpatient follow-up. Hospitalization may be required for patients who have a first seizure associated with a prolonged postictal state or incomplete recovery. Other indications for hospitalization include status epilepticus, the presence of a systemic or neurologic illness or injury requiring additional evaluation and treatment, and questions regarding compliance. (See 'Indications for hospitalization' above.)

- **Driving restrictions and other precautions** – All patients should be counseled about driving restrictions and other seizure precautions. Although specific regulations vary, the majority of states and countries require at least some period of abstinence from driving

after a seizure or other event associated with loss or alteration of consciousness. (See 'Patient education' above and "Driving restrictions for patients with seizures and epilepsy".)

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Topic 2219 Version 50.0

GRAPHICS

International League Against Epilepsy (ILAE) classification of seizure types

Generalized onset seizures	
Motor	**Nonmotor (absence)**
▪ Tonic-clonic ▪ Clonic ▪ Tonic ▪ Myoclonic ▪ Myoclonic-tonic-clonic ▪ Myoclonic-atonic ▪ Atonic ▪ Epileptic spasms	▪ Typical ▪ Atypical ▪ Myoclonic ▪ Eyelid myoclonia
Focal onset seizures	
Motor onset	**Nonmotor onset**
▪ Aware ▪ Impaired awareness ▪ Unknown awareness	▪ Aware ▪ Impaired awareness ▪ Unknown awareness
▪ Automatisms ▪ Atonic* ▪ Clonic ▪ Epileptic spasms* ▪ Hyperkinetic ▪ Myoclonic ▪ Tonic	▪ Autonomic ▪ Behavior arrest ▪ Cognitive ▪ Emotional ▪ Sensory
▪ Focal to bilateral tonic-clonic	▪ Focal to bilateral tonic-clonic
Unknown onset seizures	
Motor	**Nonmotor**
▪ Tonic-clonic ▪ Epileptic spasms	▪ Behavior arrest
Unclassified seizures¶	

ILAE: International League Against Epilepsy.

* Degree of awareness usually is not specified.

¶ Due to inadequate information or inability to place in other categories.

Adapted from: Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia 2017.

Graphic 91409 Version 4.0

Symptoms of focal seizures without impairment of consciousness (also called simple partial seizures or auras)

Black out	Psychic experience
Body size or weight alteration in perception	Racing thoughts
Breathing difficulty	Rising epigastric sensation
Chewing movements	Running
Confusion	Shaking
Convulsion	Skin color changes
Deja-vu	Sound perception distortion
Dizziness	Spacial perception distortion
Drooling	Spacing out
Electric shock feeling	Spinning feeling
Eyelid fluttering	Staring
Eyes rolling up	Stiffening
Falling down	Swallowing
Foot stomping	Sweating
Hand waving	Talking difficulty
Heart racing	Teeth clenching/grinding
Inability to move	Tightness
Incontinence	Time perception distortion
Jamais vu	Tingling feeling
Lightheadedness	Tongue biting
Lip smacking	Tremors
Loss of consciousness	Twitching movements
Making sounds	Undressing
Memory loss	Urge to urinate or defecate
One side of body different than other	Visual distortion
Out-of-body experience	Visual loss or blurring
Oversensitivity to stimulation	Walking

Graphic 55996 Version 5.0

Common postictal symptoms

Confusion
Depression
Difficulty talking
Embarrassment
Exhaustion, sleep
Fear
Frustration
Headache
Loneliness
Memory loss
Nausea
Pain
Perceptual alterations
Psychosis
Thirst
Weakness

Graphic 59341 Version 1.0

Phases of tonic-clonic seizures

Aura (None)
Tonic phase (10 to 20 seconds)
Sudden loss of consciousness
Loss of posture with high risk of self injury depending on activity
Brief flexion of arms, eyes deviated upward
Extension of back, neck, arms, and legs
Involuntary crying out from contraction of respiratory muscles
Shallow respiration, cyanosis may occur
Ends with tremors that gradually slow and merge with clonic phase
Clonic phase (30 to 90 seconds)
Brief, violent, generalized flexor contractions alternating with progressively longer muscle relaxation
Cyanosis
Possible cheek or tongue biting
Foamy salivation
Possible loss of bowel or bladder control
Ends with deep inspiration, sustained muscle relaxation
Postictal phase (Minutes to several hours)
Headache, mild confusion
Muscles sore
Fatigue, patient may sleep and awake refreshed
Other features
Fast heart rate
Elevated blood pressure
Respiratory and metabolic acidosis
Dilated pupils
Risk of vertebral fracture, pneumonia

Graphic 54942 Version 2.0

Causes of provoked seizures

Alcohol & drug withdrawal
Drug intoxication
Hyponatremia, hypernatremia
Hypomagnesium
Hypocalcemia
Hypoglycemia
Nonketotic hyperglycemia
Uremia
Hypoxia
Hyperthyroidism
Dialysis disequilibrium syndrome
Porphyria

Graphic 61807 Version 5.0

Medications associated with seizures

Category	Examples
Analgesics	▪ Opioids (eg, meperidine, tramadol)
Anticancer drugs*	▪ Busulfan ▪ Chlorambucil ▪ Cytarabine ▪ Doxorubicin ▪ Etoposide ▪ Fluorouracil ▪ Interferon alfa ▪ Methotrexate ▪ Mitoxantrone ▪ Nelarabine ▪ Platinum-based drugs (eg, cisplatin) ▪ Vinblastine ▪ Vincristine
Antimicrobials¶	▪ Carbapenems (eg, imipenem) ▪ Cephalosporins (fourth generation) ▪ Fluoroquinolones (eg, ciprofloxacin) ▪ Isoniazid△ ▪ Penicillins
Hypoglycemic agents	▪ Potentially any antidiabetic agent that can cause hypoglycemia
Immunosuppressants	▪ Azathioprine ▪ Cyclosporine ▪ Mycophenolate ▪ Tacrolimus
Psychiatric medications	▪ Antipsychotics◇ ▪ Atomoxetine ▪ Bupropion ▪ Buspirone ▪ Lithium ▪ Monoamine oxidase inhibitors§ ▪ Selective serotonin reuptake inhibitors¥ ▪ Serotonin norepinephrine reuptake inhibitors¥ ▪ Serotonin modulators ▪ Tricyclic antidepressants (eg, amoxapine, clomipramine, maprotiline)

Pulmonary drugs	▪ Aminophylline ▪ Theophylline
Stimulants	▪ Amphetamines ▪ Methylphenidate
Sympathomimetics and decongestants	▪ Anorexiants (eg, diethylpropion, phentermine, nonprescription diet aids) ▪ Phenylephrine ▪ Pseudoephedrine

The magnitude of risk of seizure for various categories and individual agents is not well established. Factors that may contribute to the risk of seizure with medications include overdose, alcohol abuse, organ dysfunction, drug interactions, older age, and a history of seizures. Illicit drugs use, herbs/natural remedies (eg, guarana), nonprescription supplements, and abrupt withdrawal from chronic alcohol use and certain prescription medicines (eg, antiseizure medications, baclofen, benzodiazepines) are also associated with seizure.

This table is not all-inclusive. For detailed prescribing information, including reported adverse effects, readers should refer to the individual drug information topics within UpToDate. Comprehensive information on drug interactions can be determined using the drug interaction program included within UpToDate.

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* For more details and additional anti-cancer drugs that have been associated with seizures, refer to UpToDate topic reviews on the neurologic complications of anticancer therapies.

¶ Among antibiotics, evidence for an association is strongest for unsubstituted penicillins, fourth-generation cephalosporins, imipenem, and ciprofloxacin in combination with renal dysfunction, brain lesions, and epilepsy[1].

Δ Seizures are a manifestation of pyridoxal-5-phosphate deficiency; they respond to pyridoxine and benzodiazepine treatment. Refer to UpToDate topic review on isoniazid poisoning.

◇ Clozapine has a higher risk of seizure than most other antipsychotics[2]; refer to UpToDate topic review on guidelines for prescribing clozapine in schizophrenia for more information.

§ Monoamine oxidase inhibitors include: furazolidone, isocarboxazid, linezolid, moclobemide, pargyline, phenelzine, procarbazine, rasagiline, selegiline, tranylcypromine.

¥ Selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors do not increase seizure risk in patients with epilepsy when used in therapeutic doses, but may be proconvulsant at toxic doses[3,4].

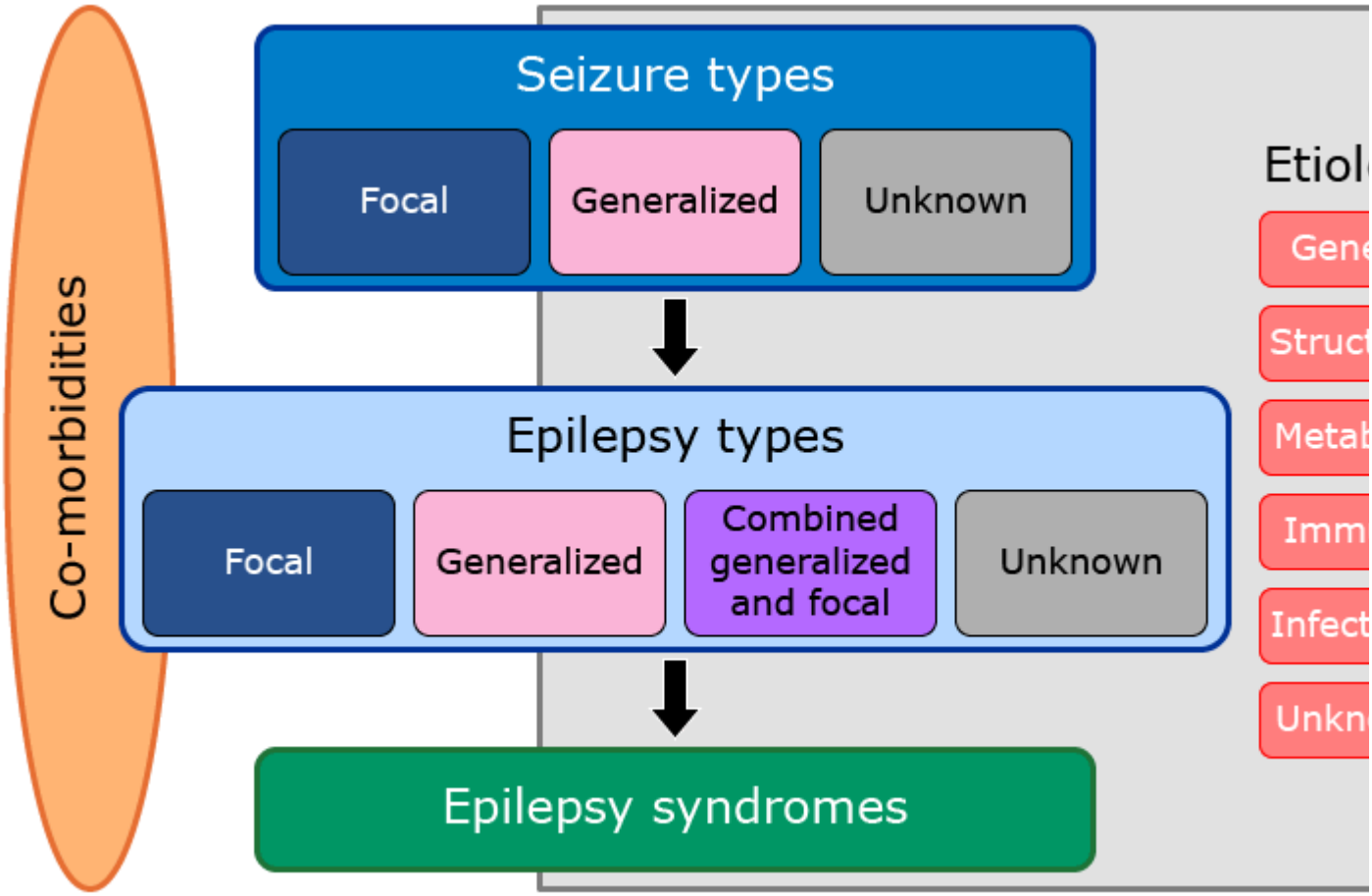
References:

1. *Sutter S, Ruegg S, Tschudin-Sutter S. Seizures as adverse events of antibiotic drugs: A systematic review. Neurology 2015; 85:1332.*
2. *Hitchings AW. Drugs that lower the seizure threshold. Adverse Drug React Bull 2016; 298:1151.*
3. *Kanner AM. Most antidepressant drugs are safe for patients with epilepsy at therapeutic doses: A review of the evidence. Epilepsy Behav 2016; 61:282.*

4. *Landmark CJ, Henning O, Johannessen SI. Proconvulsant effects of antidepressants – What is the current evidence? Epilepsy Behav 2016; 61:287.*

Graphic 106961 Version 11.0

International League Against Epilepsy (ILAE) framework for seizure and epilepsy classification



Graphic 112425 Version 1.0

Clinical features of seizures, syncope, and other paroxysmal neurologic events in adults

	Clinical features	Duration	Recall of the event	Diagnostic tools
Focal seizure	Initial symptoms depend on location in brain; motor and visual symptoms usually "positive" (eg, shaking, jerking, flashing lights, or visual distortion); may have anatomic "march" over seconds; some progress rapidly to GTC	Usually <2 minutes; can be difficult to distinguish ictal from postictal phase	Variable depending on whether consciousness is impaired	EEG may show interictal spikes (poor sensitivity); ambulatory EEG if episodes are frequent enough; MRI may show structural lesion
Generalized seizure	Sudden alteration or loss of consciousness without warning; some have myoclonic jerks or staring; tongue-biting and urinary incontinence may occur (for GTC)	<5 minutes (for GTC); <1 minute for absence	Complete amnesia; patient may recall initial focal symptoms	EEG may show generalized spike-and-wave characteristic of specific syndrome MRI usually normal for generalized epilepsy syndromes, may show structural lesion if focal onset
Psychogenic nonepileptic seizure	Fluctuating, asynchronous motor activity, often with eye closure, side-to-side head or body movements, pelvic thrusting; most occur in front of a witness; fully or partially alert	Rarely <1 minute; often prolonged (>30 minutes)	Variable	Video-EEG monitoring

	despite bilateral motor activity; tongue-biting is rare			
Syncope	Transient loss of consciousness resulting in loss of postural tone; prodrome of lightheadedness, warm or cold feeing, sweating, palpitations, pallor; myoclonic jerks or tonic posturing may occur, especially if patient is kept upright; no or minimal post-event confusion	1 to 2 minutes	Patient can recall prodromal symptoms, if present; lack of warning may suggest cardiac source	ECG; echocardiography if structural cardia disease is suspected; ambulatory ECG monitoring if arrhythmia is suspected; orthostatic blood pressure measurements
Transient ischemic attack (TIA)	Rapid loss of neurologic function due to interrupted blood flow; symptoms depend on vascular territory but are typically "negative" (eg, weakness, numbness, aphasia, visual loss); intensity is usually maximal at onset; consciousness usually preserved	Several minutes to a few hours	Usually complete unless language areas involved	MRI/MRA, CTA, vascular risk factors
Migraine aura	Positive and/or negative neurologic symptoms, most often visual and sensory, evolving gradually over ≥5	Up to 1 hour	Complete	Personal or family history of migrain

	minutes (slower onset than TIA or focal seizure); slow spread of positive followed by negative symptoms, if present, is very characteristic; usually followed by headache			
Panic attack	Palpitations, dyspnea, chest pain, lightheadedness, sense of impending doom; associated hyperventilation may result in perioral and distal limb paresthesias	Minutes to hours	Complete	History of anxiety or depressive symptoms, triggering events or stressors
Transient global amnesia	Prominent anterograde amnesia (inability to form new memories) and variable retrograde amnesia; patient is disoriented in time, asking repetitive questions; other cognitive and motor functions spared; rare in adults younger than 50 years	1 to 10 hours (mean 6 hours)	Complete amnesia for the main episode; retrograde amnesia resolves within 24 hours	Clinical diagnosis; negative MRI and toxicology screens

GTC: generalized tonic-clonic; EEG: electroencephalography; MRI: magnetic resonance imaging; ECG: electrocardiogram; MRA: magnetic resonance angiography; CTA: computed tomography angiography.

Complex movements during sleep: Distinguishing clinical features

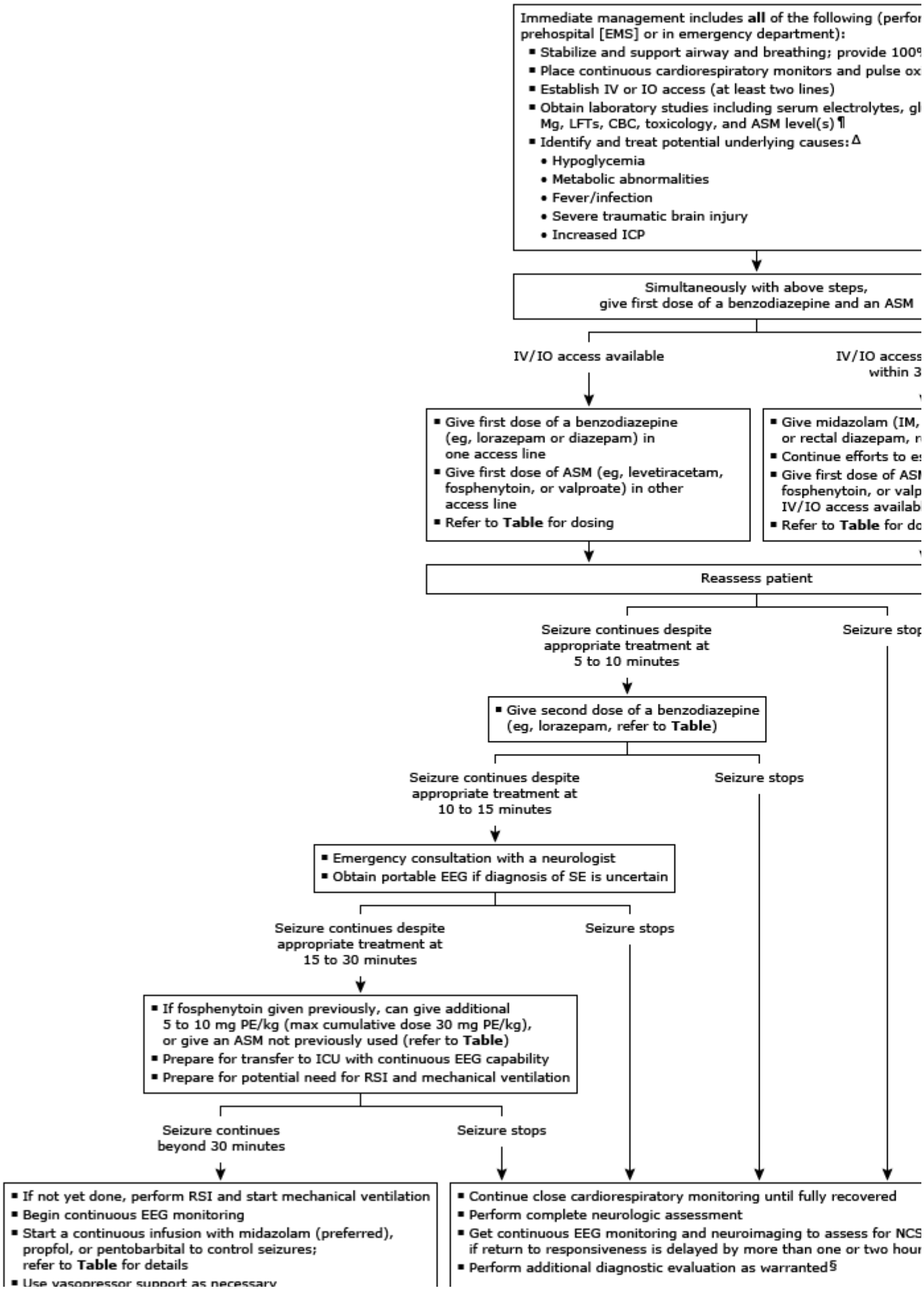
	Disorders of arousal	Sleep-related eating disorder	REM sleep behavior disorder	REM nightmares	Recurrent isolated sleep paralysis	
Behavior	Confused, semi-purposeful movement with eyes open	Eating high caloric or unusual foods with eyes open	Sometimes combative, violent dream enactment with eyes closed	Vivid, disturbing dreams, may end with a sudden jolt or jerk	Inability to move with preservation of eye and diaphragmatic movement	Varia pani symp
Age of onset	Childhood or adolescence	Variable	Older adults	Childhood or adulthood	Variable	Adol adul
Family history	Yes	Unknown	No	No	No	No
Time of occurrence	First third of night	First half of night	During REM sleep	Second half of the night most common (during REM sleep)	Upon awakening	Any t
Frequency	Once per night but not every night	Variable	Variable; a few times per month to nightly	May be nightly	Variable, less than weekly	Varia
Duration	Minutes	Minutes	Seconds to a minute	Movement lasts seconds	Seconds to a minute	Varia minu
Memory of event	Usually none	Usually none, or	Fragmentary to full dream recall	Yes	Yes	Non

		limited				
Stereotypical movements	No	No	No	No	No	No
PSG findings	Arousals from slow-wave sleep	Arousal from NREM sleep	Excessive EMG tone during REM sleep	Awakening out of REM sleep appearing distressed	Arousal from REM sleep	Occu state
Associated clinical findings	May indicate another problem causing arousals (eg, sleep apnea)	Morning anorexia, unexplained weight gain, comorbid RLS	May be associated with parkinsonism, narcolepsy, or medications (antidepressants)	May be associated with stress, psychological trauma, or medication effect	None (benign)	Othe unde diso anxi

REM: rapid eye movement; PSG: polysomnogram; NREM: non-REM; EMG: electromyography; RLS: restless legs syndrome.

Graphic 103634 Version 2.0

Approach to the treatment of convulsive status epilepticus in adults


Immediate management includes **all** of the following (perfor
prehospital [EMS] or in emergency department):
▪ Stabilize and support airway and breathing; provide 100%
▪ Place continuous cardiorespiratory monitors and pulse ox
▪ Establish IV or IO access (at least two lines)
▪ Obtain laboratory studies including serum electrolytes, gl
Mg, LFTs, CBC, toxicology, and ASM level(s) ¶
▪ Identify and treat potential underlying causes: Δ
• Hypoglycemia
• Metabolic abnormalities
• Fever/infection
• Severe traumatic brain injury
• Increased ICP
Simultaneously with above steps,
give first dose of a benzodiazepine and an ASM
IV/IO access available
IV/IO access
within 3
▪ Give first dose of a benzodiazepine
(eg, lorazepam or diazepam) in
one access line
▪ Give first dose of ASM (eg, levetiracetam,
fosphenytoin, or valproate) in other
access line
▪ Refer to **Table** for dosing
▪ Give midazolam (IM,
or rectal diazepam, r
▪ Continue efforts to es
▪ Give first dose of ASM
fosphenytoin, or valp
IV/IO access availabl
▪ Refer to **Table** for do
Reassess patient
Seizure continues despite
appropriate treatment at
5 to 10 minutes
Seizure stop
▪ Give second dose of a benzodiazepine
(eg, lorazepam, refer to **Table**)
Seizure continues despite
appropriate treatment at
10 to 15 minutes
Seizure stops
▪ Emergency consultation with a neurologist
▪ Obtain portable EEG if diagnosis of SE is uncertain
Seizure continues despite
appropriate treatment at
15 to 30 minutes
Seizure stops
▪ If fosphenytoin given previously, can give additional
5 to 10 mg PE/kg (max cumulative dose 30 mg PE/kg),
or give an ASM not previously used (refer to **Table**)
▪ Prepare for transfer to ICU with continuous EEG capability
▪ Prepare for potential need for RSI and mechanical ventilation
Seizure continues
beyond 30 minutes
Seizure stops
▪ If not yet done, perform RSI and start mechanical ventilation
▪ Begin continuous EEG monitoring
▪ Start a continuous infusion with midazolam (preferred),
propfol, or pentobarbital to control seizures;
refer to **Table** for details
▪ Use vasopressor support as necessary
▪ Continue close cardiorespiratory monitoring until fully recovered
▪ Perform complete neurologic assessment
▪ Get continuous EEG monitoring and neuroimaging to assess for NCS
if return to responsiveness is delayed by more than one or two hour
▪ Perform additional diagnostic evaluation as warranted §

- Maintain therapeutic ASM level (levetiracetam, valproate, fosphenytoin, phenytoin, or other) ◇
- Titrate infusion to electroclinical seizure suppression for 24 to 48 hours, then attempt slow wean

This algorithm summarizes our suggested approach to antiseizure treatment for convulsive status epilepticus (CSE) in adults. CSE is defined as a single unremitting seizure lasting >5 minutes or frequent clinical seizures without an interictal return to the baseline clinical state. Along with immediate antiseizure therapy, patients with CSE require simultaneous, rapid initiation of monitoring, including supportive care of airway, breathing, and circulation, and rapid recognition and treatment of hypoglycemia, electrolyte disturbance, poisoning, central nervous system infection, sepsis, and traumatic brain injury. The goal of therapy is to achieve seizure freedom (ie, cessation of clinical and electrographic seizures using continuous EEG). Refer to UpToDate topics on adult CSE for additional details.

EMS: emergency medical services; IV: intravenous; IO: intraosseous; LFT: liver function test; CBC: complete blood count; ASM: antiseizure medication; ICP: intracranial pressure; IM: intramuscular; EEG: electroencephalogram; SE: status epilepticus; ICU: intensive care unit; RSI: rapid sequence endotracheal intubation; RSE: refractory status epilepticus; NCSE: nonconvulsive status epilepticus; CSE: convulsive status epilepticus; PE: phenytoin equivalents; LP: lumbar puncture.

* Rapid sequence intubation should be performed if airway, ventilation, or oxygenation cannot be maintained, or if the seizure becomes prolonged.

¶ Refer to UpToDate topics on SE in adults for a complete list of ancillary studies.

Δ Common causes of CSE are listed here. For further discussion of causes of CSE in adults, refer to UpToDate topics on adult CSE.

◇ Usually the ASM used for initial or second therapy, unless an alternative ASM can be tailored to clinical circumstances.

§ Additional evaluation may include neuroimaging if CSE is the first presentation of epilepsy or if there are new focal neurologic findings, signs of head trauma, suspicion for infection, concern for increased ICP, or prolonged duration of depressed consciousness (ie, for >1 to 2 hours after the episode). If there is concern for infection, blood cultures should be obtained and empiric antimicrobials should be started prior to brain imaging, and LP should be performed after a space-occupying brain lesion has been excluded by imaging. For additional details regarding the diagnostic evaluation in patients with CSE, refer to UpToDate topics on adult CSE.

¥ There is no definite maximum cumulative dose of lorazepam; clinicians should be guided by the clinical effect (including on blood pressure) and seizure control.

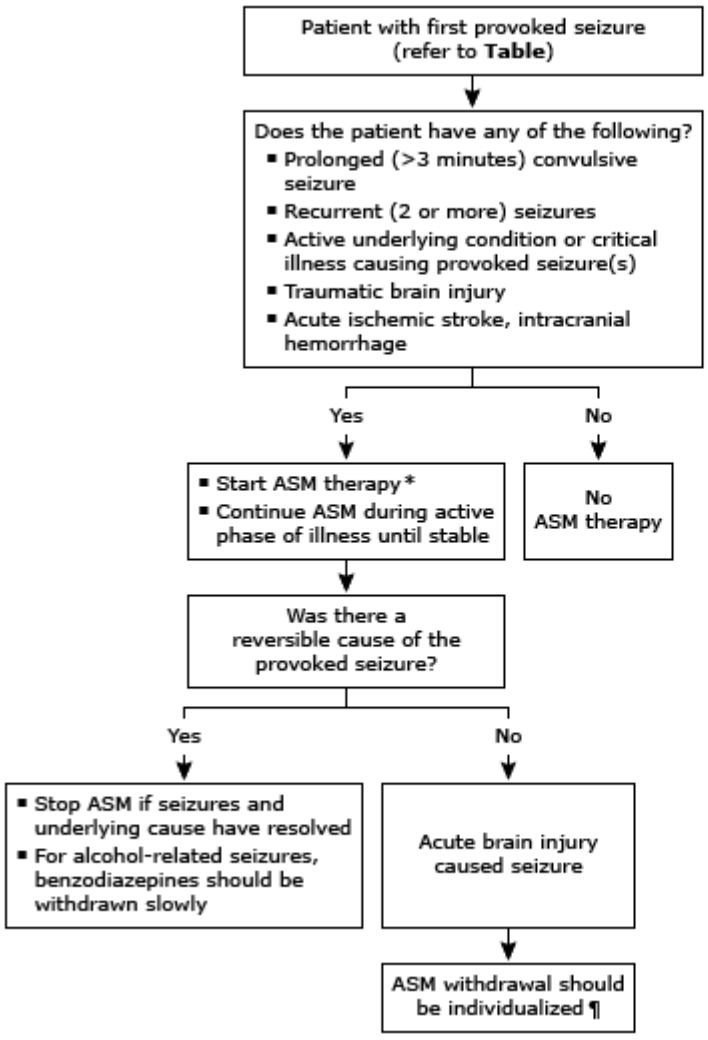
‡ If IO administration is necessary, levetiracetam may be preferred, based upon clinical experience.

† Phenytoin and fosphenytoin may be less effective for the treatment of seizures due to toxins or drugs and may intensify seizures caused by cocaine, other local anesthetics, theophylline, or lindane. In such cases, levetiracetam, valproate, or phenobarbital should be used. Other clinical considerations in choice may apply (eg, for patients currently receiving an antiseizure medication); refer to UpToDate topics on adult CSE.

** If fosphenytoin is not available, IV phenytoin may be used (20 mg/kg IV; do not exceed 1 mg/kg per minute; maximum rate: 50 mg per minute). Both fosphenytoin and phenytoin require cardiac monitoring.

Graphic 74649 Version 20.0

Management of first provoked seizure in an adult



Table

Provoked (acute symptomatic) seizure:
- Occurs at the time of a systemic insult or in close temporal association with a documented brain insult
- Seizures may recur during the index illness
- Low risk of future epilepsy, especially with reversible causes

Examples:
- Reversible causes of seizure:
  - Metabolic derangements (eg, hypoglycemia, hyponatremia, hypomagnesemia)
  - Drug or alcohol withdrawal
  - Drug intoxication, poisoning, or overdose
- Acute brain injury causing seizure:
  - Acute stroke
  - Encephalitis, meningitis
  - Traumatic brain injury

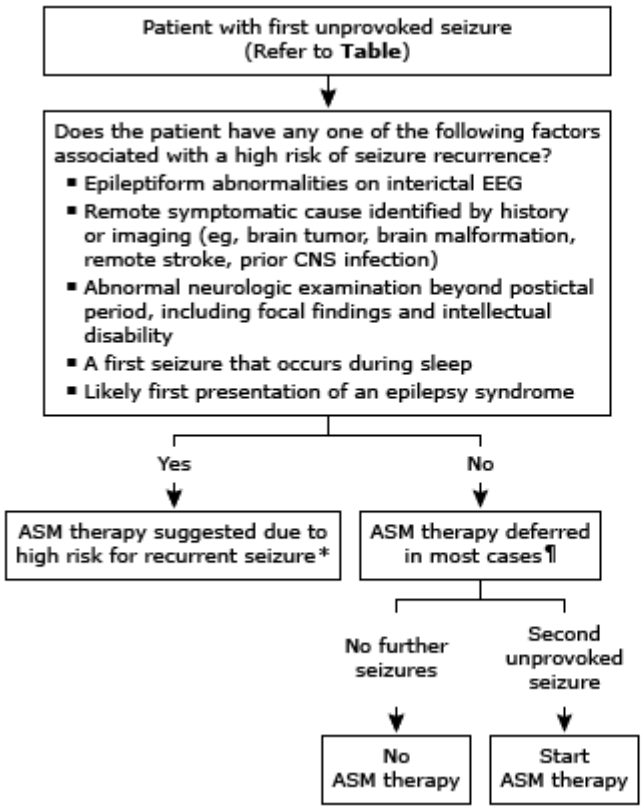
ASM: antiseizure medication.

* ASM started in consultation with neurology; treatment should be individualized.

¶ Consult with neurologist; continued ASM treatment may be warranted for patients with a higher risk of recurrent seizure (eg, those with encephalitis, hemorrhagic stroke, or other acute intracranial lesions).

Graphic 134332 Version 1.0

Management of a first unprovoked seizure in an adult



Table

Unprovoked (remote symptomatic) seizure related to:

- Unknown etiology

  or

- Preexisting brain lesion (eg, brain tumor, prior CNS infection, remote stroke)

  or

- Progressive nervous system disorder (eg, Alzheimer disease, other neurodegenerative disorders)

Unprovoked seizures have a high risk for future epilepsy

Epilepsy is defined by any of the following:

- At least two unprovoked seizures occurring more than 24 hours apart
- One unprovoked seizure and a high risk of further seizures similar to the general recurrence risk after two unprovoked seizures (≥60%) occurring over the next 10 years; this may be the case with remote structural lesions (eg, stroke, CNS infection, or traumatic brain injury)
- Diagnosis of an epilepsy syndrome

CNS: central nervous system; EEG: electroencephalography; ASM: antiseizure medication.

* Coexisting medical conditions likely to be worsened by a seizure (eg, osteogenesis imperfecta, shoulder reconstruction) may warrant treatment for low-risk patients.

¶ ASM decision made in consultation with neurology; treatment should be individualized; patient preference may reasonably lead high-risk patients to defer ASM until they have a second seizure.

Graphic 134331 Version 1.0