# Convulsive status epilepticus in adults: Classification, clinical features, and diagnosis

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## INTRODUCTION

Status epilepticus is a relatively common medical and neurologic emergency that requires prompt evaluation and treatment. There are many different status epilepticus syndromes, defined by clinical features and electroencephalogram (EEG) findings. Causes, prognoses, and treatments differ, and optimal evaluation and treatment requires an understanding of both the type of status epilepticus and the underlying cause. Some forms of status epilepticus are associated with an excellent prognosis, while others can have major morbidity or even mortality.

The clinical features and diagnosis of convulsive status epilepticus in adults are discussed here; treatment is reviewed separately. (See "Convulsive status epilepticus in adults: Management" and "Refractory status epilepticus in adults".)

Nonconvulsive status epilepticus and the diagnosis and management of status epilepticus in children are also discussed separately. (See "Convulsive status epilepticus in adults: Management" and "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis" and "Clinical features and complications of status epilepticus in children" and "Management of convulsive status epilepticus in children".)

## DEFINITION OF STATUS EPILEPTICUS

The duration of continuous seizure activity used to define status epilepticus has varied over time. Historically, the International League Against Epilepsy (ILAE) and others defined status epilepticus as a single epileptic seizure of >30 minutes duration or a series of epileptic seizures during which function is not regained between seizures in a 30-minute period [1].

Because of the clinical urgency in treating generalized convulsive status epilepticus (GCSE), however, a 30-minute definition is neither practical nor appropriate in clinical practice. Once seizures have continued for more than a few minutes, treatment should begin without further delay.

- **Operational definition** – Considering the need for rapid evaluation and intervention in GCSE to avoid cardiovascular morbidity and refractory status, an accepted operational definition of GCSE consists of the following [2-4]:
  - ≥5 minutes of continuous seizures, or
  - ≥2 discrete seizures between which there is incomplete recovery of consciousness
- **ILAE definition** – In 2015, the ILAE published a revised conceptual definition of status epilepticus that incorporates two time points, t1 and t2 [5].
  - The first, t1, is the time at which ongoing seizure activity should be regarded as abnormally prolonged, unlikely to stop spontaneously, and when treatment for status epilepticus should be started.
  - The second, t2, is the time after which the ongoing seizure activity poses a significant risk of long-term complications.

  The ILAE definition is as follows [5]: "Status epilepticus is a condition resulting from either the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms that lead to abnormally prolonged seizures (after time point t1). It is a condition that can have long-term consequences (after time point t2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures."

For GCSE, the ILAE proposal specifies that t1 and t2 are 5 and 30 minutes, respectively, based on the best available data from animal and clinical studies, and consistent with the operational definition discussed above [5]. The term "convulsive" is defined by the ILAE as designating "episodes of excessive abnormal muscle contractions, usually bilateral, which may be sustained,

or interrupted" [5,6]. Convulsive status epilepticus is characterized by the presence of prominent motor symptoms and impairment of consciousness [5].

For other types of status epilepticus, the most appropriate time intervals for t1 and t2 have not been well defined and are far more speculative, particularly for nonconvulsive status epilepticus. The ILAE suggests using a t1 and t2 of 10 and >60 minutes for focal status epilepticus with impaired consciousness (often labeled complex partial status epilepticus) and a t1 of 10 to 15 minutes for absence status epilepticus. There are no available data to suggest any particular t2 for absence status epilepticus.

## EPIDEMIOLOGY

The reported yearly incidence of status epilepticus ranges from 1.3 to 74 cases per 100,000 [7]. Most earlier population-based studies defined status epilepticus using a duration of at least 30 minutes.

The wide range of reported incidence rates is likely due to differences in case ascertainment and the populations being studied. In addition, some studies have included both convulsive and nonconvulsive status epilepticus (NCSE), while others have excluded NCSE. In a study that included only generalized convulsive status epilepticus, the reported annual incidence rate was 7 cases per 100,000 people [8].

The incidence of status epilepticus follows a U-shaped distribution, with relatively high incidence rates in children less than one year of age and then rising again in older adults over the age of 60 years [9]. Over a lifetime, up to 10 percent of adults with epilepsy and 20 percent of children with epilepsy will have one or more episodes of status epilepticus [10].

## ETIOLOGY

Most cases of status epilepticus in adults are due to an underlying structural brain lesion or a toxic or metabolic disturbance [11]. If the underlying medical or structural cause is of recent origin (<1 to 2 weeks), status epilepticus is referred to as acute symptomatic or "provoked." Many episodes come from a combination of an earlier lesion (ie, remote symptomatic) and a superimposed new metabolic, infectious, or pharmacologic stressor such as uremia or a medication change.

Status epilepticus also commonly arises in patients with an established diagnosis of focal or generalized epilepsy. Status epilepticus is occasionally the presenting manifestation of epilepsy

[12].

- **Common causes** – Common causes of convulsive status epilepticus vary by age. In children, febrile status epilepticus is the most common etiology, accounting for approximately one-third of cases. (See "Clinical features and complications of status epilepticus in children", section on 'Epidemiology and etiology'.)

  In adults, the most common etiologies are acute symptomatic, accounting for approximately half of all cases, followed by remote symptomatic and low antiseizure medication levels in a patient with known epilepsy [12-14]. Examples of some of the more common causes in adults include:

  - Acute structural brain injury (eg, stroke, head trauma, subarachnoid hemorrhage, cerebral anoxia or hypoxia), infection (encephalitis, meningitis, abscess), or brain tumor. Stroke is the most common, especially in older patients.
  - Remote or longstanding structural brain injury (eg, prior head injury or neurosurgery, perinatal cerebral ischemia, cortical malformations, arteriovenous malformations, and low-grade brain tumors).
  - Antiseizure medication nonadherence or discontinuation in patients with prior epilepsy.
  - Withdrawal syndromes associated with the discontinuation of alcohol, barbiturates, or benzodiazepines.
  - Metabolic abnormalities (eg, hypoglycemia, hepatic encephalopathy, uremia, hyponatremia, hyperglycemia, hypocalcemia, hypomagnesemia) or sepsis. (See "Evaluation and management of the first seizure in adults", section on 'Acute symptomatic seizures'.)
  - Use of, or overdose with, drugs that lower the seizure threshold, including theophylline, carbapenems (eg, imipenem), high-dose penicillin G, cefepime, quinolone antibiotics, metronidazole, isoniazid, tricyclic antidepressants, bupropion, lithium, clozapine, flumazenil, cyclosporine, lidocaine, bupivacaine, metrizamide, dalfampridine, and, to a lesser extent, phenothiazines, especially at higher doses.

- **Autoimmune causes** – An increasingly recognized cause of convulsive seizures and status epilepticus, and especially refractory status epilepticus, is autoimmune encephalitis, which sometimes has an underlying paraneoplastic etiology. Causes include autoantibodies against neuronal proteins, such as the anti-leucine-rich glioma inactivated 1 (LGI1) protein,

the N-methyl-D-aspartate (NMDA) receptor, the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor, and the B1 subunit of the gamma-aminobutyric acid B (GABA-B) receptor; others include multiple sclerosis, adult-onset Rasmussen encephalitis, Hashimoto encephalitis, and lupus vasculitis [15-17].

Clinical presentations can range from convulsive status epilepticus to confusional or amnestic states. Autoimmune cases are often more refractory to treatment compared with other causes of status epilepticus but may respond favorably to immunosuppressive therapy [18]. (See "Autoimmune (including paraneoplastic) encephalitis: Clinical features and diagnosis" and "Refractory status epilepticus in adults", section on 'Immunomodulatory therapy'.)

## CLASSIFICATION

Status epilepticus, like seizures, is categorized electroclinically according to whether seizure activity is focal or generalized. In many cases, however, generalized convulsive status epilepticus (GCSE) cannot be separated easily into cases with a primarily generalized onset versus those with focal onset and secondary generalization. Most GCSE has some evidence of a focal onset or focal lesion [13].

The distinction between focal and generalized onset has clinical implications:

- In cases with focal onset, a causative lesion must be sought
- In primary generalized epilepsies, certain antiseizure medications (eg, phenytoin, carbamazepine, and oxcarbazepine) should usually be avoided (see "Convulsive status epilepticus in adults: Management", section on 'Second- or third-line medications' and "Convulsive status epilepticus in adults: Management", section on 'Myoclonic status epilepticus')

Both focal and generalized status epilepticus can be further classified according to whether clinical seizure activity is convulsive or nonconvulsive ( table 1). Convulsive forms of status epilepticus are the focus of this topic; nonconvulsive status epilepticus is discussed separately. (See "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis".)

Classifying the type of status epilepticus is important because it is a major factor in determining morbidity and, therefore, the aggressiveness of treatment required. For the purposes of this topic, we consider forms of status epilepticus with significant motor (movement)

manifestations, including generalized, focal motor, myoclonic, and tonic seizures, to be convulsive.

## CLINICAL PRESENTATIONS

Patients with convulsive status epilepticus present with characteristic motor manifestations that vary according to the seizure type.

**Types of motor manifestations** — While patients with generalized convulsive status epilepticus (GCSE) have obvious bilateral tonic and/or clonic motor activity and loss of consciousness, patients with focal motor status epilepticus may have jerking movements restricted to one area of the body, usually with preserved consciousness. Myoclonic status epilepticus typically involves much more rapid, but lower amplitude, jerking muscle activity, but with marked variability. Tonic status epilepticus includes slower, more sustained maintenance of a posture, or slow movement.

Other forms of focal status epilepticus that do not involve motor manifestations, including focal-onset nonconvulsive status epilepticus with altered awareness (previously known as complex partial status epilepticus), are discussed separately. (See "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis", section on 'Electroclinical classification'.)

**Generalized convulsive status epilepticus** — GCSE is the most dramatic form of status epilepticus, with the potential for serious complications, morbidity, and even mortality. GCSE includes both primary generalized and secondarily generalized convulsive seizures, with the latter now officially referred to as focal to bilateral tonic-clonic seizures [19]. There is always impaired consciousness and bilateral tonic stiffening, followed by rhythmic jerking of the limbs (clonus) that is usually symmetric; the initial tonic phase may not be witnessed.

**Focal motor status epilepticus** — Focal status epilepticus has many clinical manifestations, largely depending on the location of the epileptogenic brain area. Focal motor status epilepticus is the most easily recognized. It may have progression along the homunculus of focal jerking activity of a limb (a "Jacksonian march") or widespread but unilateral jerking muscle activity, with or without impaired consciousness.

- **Focal lesions** – In almost all cases of focal status epilepticus, there is an associated focal lesion, although the lesion is not always evident on imaging. Examples of causative lesions include heterotopias (clusters of normal neurons in abnormal locations due to disordered neuronal migration), vascular or infectious lesions, and tumors. Occasionally, benign

idiopathic (usually genetic) focal epilepsies lead to status epilepticus of the same type. (See "Focal epilepsy: Causes and clinical features", section on 'Self-limited epilepsies of childhood'.)

- **Epilepsia partialis continua** – A particularly refractory focal motor status epilepticus with very prolonged and very regular jerking activity with retained awareness is called epilepsia partialis continua (EPC). EPC can be remarkably persistent, with epileptic focal repetitive jerking activity lasting days, weeks, or even decades [20,21]. Causes include heterotopias, inflammatory or infectious lesions (eg, tuberculosis, syphilis, and toxoplasmosis), vascular lesions, neoplasms, congenital malformations, Rasmussen encephalitis, and hyperosmolar nonketotic hyperglycemia. The jerking is often restricted to one part of the body, does not spread, and is often slower than in most other forms of focal motor status epilepticus.

  Rasmussen encephalitis, although rare, is a relatively common cause of EPC that occurs in children and adolescents. It is usually manifested by refractory, unremitting focal seizures, progressive cerebral hemiatrophy with contralateral hemiparesis, and progressive cognitive dysfunction. It is often associated with lateralized periodic (epileptiform) discharges on electroencephalogram (EEG). (See "Focal epilepsy: Causes and clinical features", section on 'Hemispheric syndromes'.)

  Hyperosmolar nonketotic hyperglycemia can also cause EPC. Although hyperglycemia and fluid and electrolyte disturbances provide a precipitant for seizures, there is usually an underlying focal cerebral lesion as well [22]. Blood glucose levels can be extremely high, often above 1000 mg/dL. The EPC associated with nonketotic hyperglycemia is usually readily treatable by correcting the metabolic abnormality [23]. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis".)

**Myoclonic status epilepticus** — Myoclonic status epilepticus (MSE) is characterized by frequent, generalized, or focal myoclonic jerks that can be rhythmic or arrhythmic. The EEG often shows rapid epileptiform discharges time-locked to the movements persuasive for an epileptic origin of the myoclonus. Many authors consider myoclonic seizures to become MSE after 30 minutes [24]. MSE has many causes, often divided into epilepsy syndrome-related causes ("true MSE" [25]) and those "symptomatic" of other neurologic or medical illnesses. It has remarkably varied manifestations and occurs in many syndromes, ranging from relatively benign to life-threatening.

Because the clinical features often fail to distinguish the forms of MSE, the EEG features are often crucial in distinguishing the different etiologies and types of MSE and to guide treatment.

(See 'Electroencephalography' below.)

The prognosis of MSE depends on that of the underlying etiology [21]. Following anoxia, it is often fatal; with metabolic encephalopathies, it is often reversible.

- **Genetic epilepsies** – Many cases of MSE arise in syndromes of primary generalized (genetic) epilepsy (ie, generalized epilepsies with a presumed genetic etiology, without structural lesions in the brain [26]). In the relatively benign MSE syndromes, EEGs have a normal background and patients usually have no developmental or cognitive deficits between seizures. Isolated myoclonus is common, but MSE itself is rare.

  - **Relatively benign genetic epilepsy** – The best recognized, relatively benign genetic epilepsy syndrome is juvenile myoclonic epilepsy (JME), in which patients have intermittent myoclonus and myoclonic seizures and sometimes absence seizures and generalized convulsions [27]. The myoclonic jerks of JME tend to be bilateral, especially in the arms, but not particularly rhythmic, and usually correlate with generalized sharp waves, spikes, or polyspikes on the EEG. As with most other genetic generalized epilepsy syndromes, consciousness is usually preserved during the MSE. MSE is often triggered by discontinuing earlier antiseizure medications or from the use of inappropriate antiseizure medications, typically sodium channel-based drugs such as phenytoin, carbamazepine, or oxcarbazepine [28]. Often, the MSE can be interrupted relatively easily by benzodiazepines and other drugs. (See "Juvenile myoclonic epilepsy".)

  - **Less benign genetic epilepsies** – In some less benign epilepsy syndromes, seizures are often refractory and accompanied by severe cognitive impairment. One example is severe myoclonic epilepsy of infancy, also known as Dravet syndrome, a form of epileptic encephalopathy caused by mutations in the SCN1A gene encoding voltage-gated sodium channels, often causing refractory seizures (although MSE itself is rare) [29]. (See "Dravet syndrome: Genetics, clinical features, and diagnosis" and "Dravet syndrome: Management and prognosis".)

    Another example is Lennox-Gastaut syndrome (LGS); patients with LGS typically have severe cognitive impairment and impaired responsiveness, and often have multiple seizure types, especially tonic seizures, but also atonic, absence, myoclonic absence, generalized convulsions, and focal retained awareness seizures. (See "Lennox-Gastaut syndrome".)

    Other genetic syndromes leading to MSE include myoclonic astatic epilepsy and epilepsy with myoclonic absences. In all these syndromes, MSE is much harder to treat.

- **Neurologic illnesses with encephalopathy** – MSE also occurs in neurologic illnesses in which a concomitant encephalopathy has cognitive deficits, which often causes the patient more impairment than does the seizure activity. One group of such illnesses is termed progressive myoclonus epilepsies, often manifesting with ataxia, action myoclonus, and severe, progressively worsening cognitive deficits and epilepsy [30]. They include storage diseases such as neuronal ceroid lipofuscinosis and Lafora body and Unverricht Lundborg diseases, as well as mitochondrial disorders such as mitochondrial encephalopathy with ragged red fibers (MERRF). This MSE may be interruptible, but the encephalopathy usually progresses. Later-onset myoclonic seizures can also be seen in adults with Down syndrome and Alzheimer disease [31-33]. The EEG often shows a very slow background indicative of a severe encephalopathy. Epileptiform discharges may be multifocal and irregular.

- **Non-neurologic illnesses** – MSE may also be symptomatic of illnesses not primarily neurologic, such as infections, inflammatory diseases, and metabolic derangements such as uremic or hepatic encephalopathy, hypercarbic respiratory failure, or multiple medical problems such as a combination of uremia and sepsis (a typical cause) [34]. Drug toxicity may cause myoclonus and myoclonic seizures; antiseizure medications pregabalin and tiagabine appear to have caused MSE in several cases [35]. An EEG is necessary to confirm status epilepticus in patients with metabolic derangements. The EEG frequently shows a very slow background indicative of a severe encephalopathy, and epileptiform discharges may be multifocal and irregular.

- **Anoxia** – The MSE due to anoxia is the sign of a particularly severe illness, often with a terrible prognosis. It can be extremely difficult to treat, and most patients do poorly even after the MSE resolves, as determined primarily by the effects of the anoxic episode itself. With anoxia, the EEG often shows a very low voltage or even "flat" background with irregular sharp wave discharges, not always correlating with the timing of the myoclonus. An EEG is necessary to confirm status epilepticus in patients with myoclonus after anoxia (See "Hypoxic-ischemic brain injury in adults: Evaluation and prognosis" and 'Electroencephalography' below.)

- **Persistent, nonepileptic myoclonus** – Not all episodes of persistent myoclonus are epileptic in origin; many are better labeled "status myoclonicus" rather than truly epileptic. They include prolonged, continuous, but frequently nonrhythmic, myoclonic jerking, usually of large amplitude, often involving the face, trunk, and limbs, but sometimes multifocal or asynchronous. The cause is usually an acute, severe encephalopathy, particularly anoxia [21,31], although metabolic disturbances are also common [21]. Most

patients are comatose [31]. The EEG typically shows widespread slowing indicative of an encephalopathy (and in the case of anoxia, a very low voltage or even "flat" background), and the myoclonic jerks do not correlate with spikes or sharp waves. (See 'Electroencephalography' below.)

**Tonic status epilepticus** — Tonic status epilepticus (TSE) is rare in adults. It consists of maintenance of a tonic posture, particularly of axial musculature, rather than frank convulsions [36]. It usually occurs in children with many different seizure types, particularly those who have major neurologic and cognitive deficits from birth or early childhood, such as Lennox-Gastaut syndrome. The EEG may show widespread fast activity or very rapid spikes but may also include periods of background suppression or attenuation. TSE can be difficult to abort with antiseizure medications [37]. Occasionally, benzodiazepines may exacerbate TSE [38,39]. (See "Lennox-Gastaut syndrome".)

## EVALUATION AND DIAGNOSIS

**Electroencephalography** — An urgent portable electroencephalogram (EEG) should be obtained if there is uncertainty regarding the presence of status epilepticus. For patients with status epilepticus whose seizure has appeared to stop clinically but the patient's mental status is not clearly improving clinically or returning to baseline, an EEG should be done quickly to look for nonconvulsive seizures. An EEG may not be necessary for patients with known epilepsy who return to baseline after an episode of status epilepticus.

Continuous EEG monitoring is necessary for the management of refractory status epilepticus. (See "Refractory status epilepticus in adults", section on 'Continuous EEG monitoring'.)

- **EEG in generalized convulsive status epilepticus** – During generalized convulsive status epilepticus (GCSE), the EEG recording is often obscured by muscle and movement artifacts, but it may show continuous spike and wave activity indicative of generalized seizure activity. In some cases of GCSE, a focal onset is evident on EEG, especially early in the episode, and this can help to focus the evaluation on an underlying focal cause. Once convulsions have ceased, EEG is crucial in determining whether status epilepticus has truly ended, or whether there is continuing seizure activity without convulsions, especially if the patient is not rapidly waking up after movements cease. (See 'Generalized convulsive status epilepticus' above.)

- **EEG in focal motor status epilepticus** – In many cases of focal motor status epilepticus, EEG evidence of seizure activity is subtle or absent [40]. This is generally thought due to a

small or deep seizure focus or orientation of the seizure discharges such that they are not evident on surface, scalp EEGs. The seizures of focal status epilepticus can also be intermittent and thereby absent on a short EEG recording. (See 'Focal motor status epilepticus' above.)

- **EEG in unresponsive patients** – Certain EEG patterns in unresponsive patients are diagnostic of status epilepticus, including patterns that show discrete or merged seizures with temporal and spatial evolution. The meaning of other patterns, such as lateralized periodic discharges (LPDs; previously referred to as periodic lateralized epileptiform discharges [PLEDS]) ( waveform 1), remains controversial, although aggressive pharmacologic treatment in a patient whose EEG shows only LPDs without evolution and whose examination shows no clinical seizures should generally be avoided [41]. Continuous EEG recordings may be helpful if the initial study is not diagnostic. (See "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis", section on 'Electroencephalography'.)

- **EEG in myoclonic status epilepticus** – In myoclonic status epilepticus (MSE), EEG features can help to distinguish among the different etiologic groups, in turn helping to direct management. The "primary" or "idiopathic" (usually genetic) generalized myoclonic epilepsy syndromes, especially the benign syndromes, often show generalized polyspikes on a relatively normal background. In the other, more severe myoclonic epilepsy syndromes, there may be background slowing and less rhythmic and broader spikes, sometimes with periodic discharges. Cases with acute or remote symptomatic causes may show focal slowing; many show more widespread background slowing, indicative of an encephalopathy. (See 'Myoclonic status epilepticus' above.)

  The background EEG rhythm in MSE generally correlates better with prognosis than do the clinical manifestations. Cases with the particularly ominous MSE due to anoxia may show a very disturbed, nearly flat background EEG, indicative of an extremely severe encephalopathy and predictive of a poor prognosis.

**Neuroimaging** — A neuroimaging study is essential when status epilepticus is the first presentation of epilepsy, when evaluating a patient with a suspected focal onset of status epilepticus, and when recovery from status epilepticus does not follow the expected course. A noncontrast computed tomography (CT) scan of the head may be performed in the emergency department setting (eg, to look for a cerebral hemorrhage or major structural lesion such as a tumor or large stroke), but magnetic resonance imaging (MRI) has superior yield for determining the underlying etiology.

Once the patient is stabilized, a head CT may be obtained, but MRI is preferred (if available) as the best test to show the structural lesions that may cause or precipitate status epilepticus. However, MRI is not necessary to diagnose status epilepticus and cannot be performed until a patient is stabilized and seizures have been controlled.

The neuroimaging evaluation of epilepsy is discussed in detail separately. (See "Neuroimaging in the evaluation of seizures and epilepsy".)

Aside from underlying structural lesions that may identify the underlying cause of seizures, MRI can show abnormalities due to recent prolonged seizures themselves; these are often reversible. Examples include areas of increased signal intensity on fluid attenuated inversion recovery, T2, or diffusion-weighted images; patchy contrast enhancement; and increased blood flow on perfusion-weighted imaging ( table 2). These findings are thought to represent seizure-induced cellular edema. They are most often seen in cortical and limbic structures, particularly the hippocampus or other deep structures such as the pulvinar. Many are reversible but may last for weeks or longer [42], especially if seizures are prolonged; they ultimately resolve or evolve into focal atrophy and sclerosis. It is not always easy to tell the difference between seizure-related findings and an underlying causative lesion, and repeat imaging may be necessary [43]. (See "Magnetic resonance imaging changes related to acute seizure activity", section on 'Local peri-ictal MRI findings'.)

**Diagnosis** — GCSE is a clinical diagnosis, confirmed in most cases by the presence on examination of sustained and generalized tonic and/or rhythmic clonic motor activity lasting for longer than five minutes or repetitive convulsive seizures without a return to baseline consciousness between seizures.

Although the diagnosis of GCSE is usually obvious, a detailed neurologic examination is important in making the diagnosis of more subtle or focal forms of status epilepticus. (See 'Clinical presentations' above.)

Particularly important are assessment of the level of consciousness, observation for automatic movements or myoclonus, and any asymmetric features on examination that may indicate a focal structural lesion. (See "The detailed neurologic examination in adults" and "Stupor and coma in adults", section on 'Neurologic examination'.)

Clinically obvious status epilepticus should be treated immediately; there is no need to wait for an EEG. An EEG is critical in the diagnosis of more subtle forms of status epilepticus, for distinguishing myoclonic status epilepticus from nonepileptic myoclonus, and in the aftermath of generalized convulsive status epilepticus to exclude ongoing nonconvulsive seizures. (See 'Electroencephalography' above and "Convulsive status epilepticus in adults: Management".)

## DIFFERENTIAL DIAGNOSIS

Few other conditions appear similar to generalized convulsive status epilepticus (GCSE).

- **Encephalopathies** – Many other conditions, mostly various causes of encephalopathies (eg, hypercarbic respiratory failure, other metabolic disorders), can cause unresponsiveness and abnormal movements; examples include irregular movements consistent with myoclonus, or regular movements consistent with inducible clonus, tremors, or shivering. These movements may be hard to distinguish from nonconvulsive status epilepticus, or even convulsive status epilepticus. The electroencephalogram (EEG) usually shows a very slow background indicative of a severe encephalopathy without epileptiform discharges; however, it may also show rhythmic or periodic discharges that require monitoring over time in order to distinguish them from seizure-related patterns. (See "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis", section on 'Electroencephalography'.)

- **Psychogenic nonepileptic seizures (PNES) and psychogenic status epilepticus** – Although relatively uncommon, psychogenic status epilepticus should be considered in situations where there are bilateral motor movements with at least some preservation of responsiveness. Some frontal-onset seizures can also cause bilateral movements with preserved alertness (and memory), but consciousness is not preserved in GCSE.

  Video and EEG monitoring are the best way to establish the correct diagnosis. Not all seizures show up on an EEG, but prolonged episodes of impaired awareness or behavior without any changes on EEG are unlikely to represent true status epilepticus (remembering that the EEG often remains normal during focal aware seizures as well, including focal aware status epilepticus).

  Psychogenic status epilepticus is important to recognize, because iatrogenic injury can occur through over-treatment with benzodiazepines. PNES and psychogenic status epilepticus are discussed separately. (See "Psychogenic nonepileptic seizures: Etiology, clinical features, and diagnosis".)

- **Movement disorders** – Some movement disorders occasionally mimic status epilepticus. An EEG at the time of the movements or examination by an experienced clinician will differentiate them from status epilepticus. Tremors and dystonic movements do not usually cause diminished responsiveness. However, dystonic posturing may occur with paroxysmal sympathetic hyperactivity in unresponsive patients with severe traumatic

brain injury or intracranial hemorrhage. (See "Paroxysmal sympathetic hyperactivity", section on 'Clinical features'.)

- **Basilar territory stroke** – Another very uncommon condition that can mimic (or trigger) seizures or status epilepticus is acute basilar artery stroke, with pontine, midbrain, or thalamic infarctions, or combinations of these, presenting with seizure-like motor activity [44-49]. In most reported cases, an EEG was not performed at the time of the convulsive movements, so their relationship to seizures was unknown. Some patients with bilateral paramedian thalamic or midbrain infarctions (or both) had seizures or status epilepticus (convulsive or nonconvulsive) confirmed by EEG [45,49]. Abnormal eye movements (eg, nystagmus, limited vertical gaze, ocular bobbing) or pupillary findings (eg, miosis as part of a Horner syndrome) were present in most of these cases. Basilar stroke is confirmed by neuroimaging, preferably with brain MRI, which is more sensitive than CT for detection of acute ischemic stroke; many brainstem strokes are too small to be detected by CT scan. (See "Posterior circulation cerebrovascular syndromes", section on 'Basilar artery'.)

## TREATMENT

Status epilepticus is a medical and neurologic emergency that requires prompt evaluation and treatment. The treatment of convulsive status epilepticus is summarized in the algorithm (algorithm 1) and discussed in detail separately. (See "Convulsive status epilepticus in adults: Management" and "Refractory status epilepticus in adults".)

## COMPLICATIONS AND OUTCOME

**Generalized convulsive status epilepticus** — The prognosis of status epilepticus depends most strongly on the underlying etiology, but there is some evidence that status epilepticus is independently associated with mortality and neurologic sequelae.

- **Mortality** – The mortality rate for adults who present with a first episode of generalized convulsive status epilepticus (GCSE) is roughly 10 to 20 percent [50-53]. Estimates vary widely, mainly as a function of the underlying etiology and whether status epilepticus following cerebral anoxia was included in the study [9,52]. The mortality for status epilepticus after anoxia ranges from 69 to 81 percent [54-57]. While etiology is the most important predictor of outcome, older age, medical comorbidity, and high initial APACHE-II scores (a prognostic scoring system for intensive care unit patients based on underlying disease, chronic conditions, and physiologic variables) are also independent risk factors

for mortality [52,58-61]. (See "Predictive scoring systems in the intensive care unit", section on 'Acute Physiologic and Chronic Health Evaluation (APACHE)'.)

- **Impact of underlying etiology** – Many of the underlying causes of GCSE (see 'Etiology' above) are associated with significant morbidity and mortality, even in the absence of seizures. In one series, 89 percent of deaths in patients with status epilepticus were attributed to the underlying etiology [62]. Another study found that acute symptomatic status epilepticus is associated with a sixfold increased risk of mortality compared with status epilepticus arising from chronic epilepsy [63]. Mortality is also lower in individuals who have previously survived an episode of status epilepticus (4.8 versus 15.6 percent in one study), again suggesting that the underlying etiology is a major determinant of outcome in status epilepticus [59,64]. In one report, patients who received mechanical ventilation had a threefold increase in mortality [52], likely due in large part to more refractory status epilepticus, underlying etiology, and medical comorbidity rather than an independent effect of ventilatory support.

- **Systemic consequences** – Systemic consequences of GCSE include cardiac arrhythmias, hypoventilation and hypoxia, fever, and leukocytosis [65]. Aspiration pneumonitis, neurogenic pulmonary edema, and respiratory failure may complicate status epilepticus. Cardiac injury due to massive release of catecholamines may also contribute to morbidity [66-68]. (See "Complications of stroke: An overview", section on 'Neurogenic cardiac damage'.)

- **Neurologic consequences** – Physiologically, there appear to be deleterious neurologic effects of status epilepticus that worsen after approximately 30 minutes in humans, at least for GCSE, and similar derangements may occur after nonconvulsive status epilepticus [69]. Longer seizure duration and status epilepticus in the setting of acute neurologic insult are risk factors for long-term neurologic disability. In some series, 10 to 50 percent of survivors are left with disabling neurologic deficits, particularly after prolonged refractory status epilepticus [63,70,71]. (See "Refractory status epilepticus in adults", section on 'Outcomes'.)

  Status epilepticus may also be epileptogenic. Approximately 10 percent of chronic epilepsy presents with status epilepticus [72]. Conversely, approximately 40 percent of patients with a first episode of status epilepticus develop subsequent epilepsy [73], four times the rate following a single acute symptomatic seizure. It could be, however, that patients more likely to have epilepsy in the future may begin with more severe seizures at the onset, ie, status epilepticus may represent a marker for a more severe epileptic process that has already begun [72].

Adult survivors of status epilepticus are at significant risk for recurrent seizures and status epilepticus [10]. In a population-based study that followed patients for ten years, status epilepticus recurred in approximately one-third of patients [73]. When patients with progressive neurologic disease were excluded, the risk was 25 percent and was similar among other etiologic subgroups. Female sex and a failure to respond to the first drug administered for status epilepticus were risk factors for recurrence.

- **Cognitive outcomes** – A number of studies of the cognitive consequences of status epilepticus have found minimal neuropsychologic morbidity [74,75], but most of these studies were pediatric and retrospective. Comprehensive neuropsychologic evaluations before and after status epilepticus are seldom available. It is difficult to control for many variables, and it is also often unclear whether the underlying illness or status epilepticus itself causes morbidity. Many neurologic deficits fluctuate due to the underlying illness, and patients with progressive illness will worsen, irrespective of any additional morbidity due to status epilepticus. Furthermore, it is difficult to control for many variables that affect cognition, including the influence of antiseizure medications. Medications, doses, serum levels, and drug interactions may change frequently in patients with refractory epilepsy, including at the time of testing.

- **Neuropathology** – Pathologic studies of the effects of status epilepticus in humans are scarce, in part because fatal cases are often associated with acute, severe brain-injuring illnesses such as ischemic stroke, hemorrhage, and encephalitis, all of which may cause damage independently.

  Experimentally, neuronal death can occur under certain circumstances after as little as 30 to 60 minutes of continuous seizure activity [76,77]. One pathologic correlate of this phenomenon, cortical laminar necrosis, may also be seen on brain magnetic resonance imaging (MRI) as a persistent, high-intensity lesion on T1 or diffusion-weighted images, which follows the gyral anatomy of the cerebral cortex [78,79]. This may have a clinical correlate in the increased neurologic morbidity that follows status epilepticus of longer duration, even after controlling for the effects of etiology [80].

**Focal motor status epilepticus** — The long-term prognosis of focal motor status epilepticus depends on the prognosis of the underlying lesion. Long-term morbidity in terms of weakness, sensory and visual loss, and language dysfunction can be substantial, and many patients have severe cognitive problems [81]. In one series, nearly half the patients died over a follow-up averaging three years, usually because of the underlying causative lesion [21].

**Myoclonic status epilepticus** — As with treatment, the prognosis of myoclonic status epilepticus (MSE) is strongly dependent upon the form of MSE. The more benign primary generalized epilepsy syndromes (such as juvenile myoclonic epilepsy) seldom lead to MSE. Rare occurrences of MSE caused by a primary generalized epilepsy syndrome typically respond well to treatment and resolve with no residual morbidity.

In other myoclonic epilepsy syndromes in which encephalopathy is more prominent than myoclonus interictally, status epilepticus is typically more refractory to antiseizure medications. The MSE can usually be brought under control, but underlying neurologic deficits may persist or worsen. The same is true for MSE in chronic or progressive neurologic illnesses, such as mitochondrial encephalopathies or storage diseases.

MSE in the setting of a new, acute encephalopathy, whether due to infection or metabolic disturbance, has the prognosis of the underlying encephalopathy. Patients with MSE due to multiple medical problems, such as a combination of uremia and sepsis, tend to have poor outcomes. If the encephalopathy can be treated successfully, however, the MSE is likely to resolve without major morbidity from the seizures.

The prognosis is poorest for patients with MSE due to an acute new illness, particularly when there has been a period of anoxia [82-84]. In such cases, the prognosis is determined by the anoxia, rather than by the seizures [85,86]. Rarely, patients recover from multifocal and irregular myoclonus after anoxia [87,88]. In a review of several studies including 134 cases of post-anoxic MSE, 89 percent of patients died, 8 percent remained in a state of unresponsive wakefulness (previously referred to as a persistent vegetative state), and 3 percent survived; only two had a good recovery [89]. The prognosis for MSE due to anoxia may be improved somewhat by targeted temperature management, but data are limited [90]. Patients with MSE due to multiple medical problems, such as a combination of uremia and sepsis, also tend to have poor outcomes. (See "Hypoxic-ischemic brain injury in adults: Evaluation and prognosis".)

**Refractory status epilepticus** — Refractory status epilepticus is defined as status epilepticus that does not cease with administration of two antiseizure medications (administered in appropriate and adequate doses; usually an intravenous benzodiazepine, followed, if necessary, by a longer-acting antiseizure medication).

Super-refractory status epilepticus is defined as status epilepticus persisting or recurring after at least 24 hours of highly sedating antiseizure drugs (often referred to as anesthetics), usually midazolam, pentobarbital, or propofol. (See "Refractory status epilepticus in adults", section on 'Definition and etiology'.)

The outcome of refractory status epilepticus is discussed elsewhere. (See "Refractory status epilepticus in adults", section on 'Outcomes'.)

## 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 5$^{th}$ to 6$^{th}$ 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 10$^{th}$ to 12$^{th}$ 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 topic (see "Patient education: Epilepsy in adults (The Basics)")

## SUMMARY AND RECOMMENDATIONS

- **Definition** – Generalized convulsive status epilepticus (GCSE) is operationally defined as ≥5 minutes of continuous seizure activity with prominent motor activity, usually bilateral, or more than one seizure without recovery in between. This establishes the critical point at which treatment must be initiated in order to avoid serious morbidity. (See 'Definition of status epilepticus' above.)

- **Epidemiology** – The incidence of status epilepticus follows a bimodal age distribution, with peak rates in children less than one year of age and adults over the age of 60 years. (See 'Epidemiology' above.)

- **Causes** – Etiologies of status epilepticus include acute brain injury or infection, noncompliance with antiseizure medication treatment, drug or alcohol withdrawal syndromes, and metabolic disturbances, among others. (See 'Etiology' above.)

- **Classification** – Classifying the type of status epilepticus is important because it is a major factor in determining morbidity and, therefore, the aggressiveness of treatment required. The four major forms of convulsive status epilepticus are generalized convulsive, focal motor, myoclonic, and tonic. Various forms of nonconvulsive status epilepticus are discussed separately. (See 'Classification' above and "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis".)

- **Clinical manifestations** – Patients with convulsive status epilepticus present with characteristic motor manifestations that vary according to the seizure type. While patients with generalized convulsive status have obvious bilateral tonic followed by clonic motor activity and loss of consciousness, patients with focal motor status may have jerking or other movements limited to one limb and many retain awareness. (See 'Clinical presentations' above.)

- **Diagnosis** – GCSE is a clinical diagnosis, confirmed in most cases by the presence on exam of sustained and/or rhythmic generalized or focal tonic and/or clonic motor activity lasting for ≥5 minutes. Electroencephalography (EEG) is often necessary in the aftermath of GCSE to exclude ongoing nonconvulsive seizures and is mandatory for managing prolonged and refractory status epilepticus. (See 'Diagnosis' above and 'Electroencephalography' above.)

- **Outcomes** – The prognosis of status epilepticus depends most strongly on the underlying etiology, but there is some evidence that status epilepticus is independently associated with mortality and neurologic sequelae. (See 'Complications and outcome' above.)

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Topic 2217 Version 39.0

## GRAPHICS

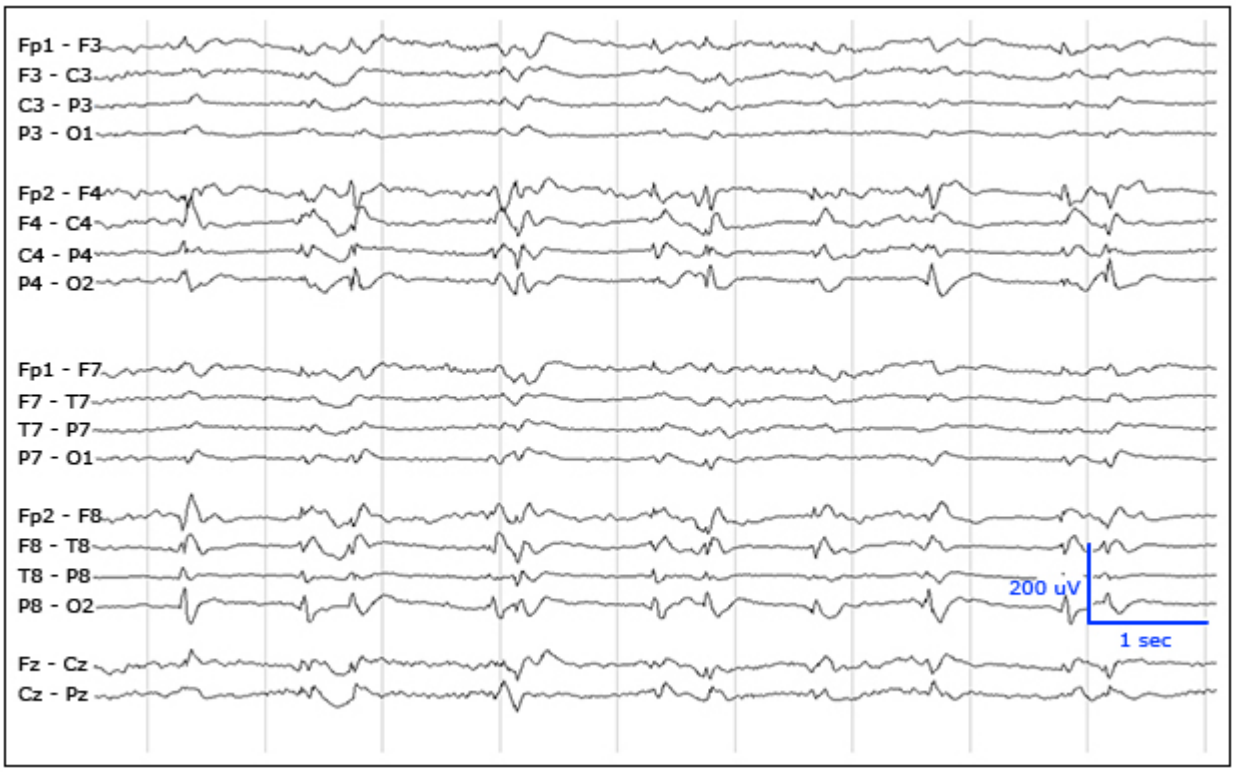
### Forms of status epilepticus

| Convulsive | |
|---|---|
| **Generalized** | **Focal** |
| Generalized convulsive status epilepticus<br>▪ Primary generalized convulsive SE<br>▪ Secondarily generalized convulsive SE (focal onset)<br>Myoclonic<br>Tonic (may also have focal onset)<br>Clonic (may also have focal onset)<br>Atonic (very rare for SE in adults; may also have focal onset) | Focal motor SE (includes epilepsia partialis continua) |
| **Nonconvulsive** | |
| Typical ("classic") absence NCSE<br>Other primary generalized NCSE<br>Atypical absence NCSE<br>Other generalized NCSE, with a focal onset | Focal-onset NCSE with impaired awareness<br>Focal-onset NCSE with nonmotor features (eg, cognitive or sensory) |

SE: status epilepticus; NCSE: nonconvulsive status epilepticus.

Graphic 97140 Version 5.0

## Lateralized periodic discharges (LPDs), previously known as periodic lateralized epileptiform discharges (PLEDs)




High-pass filter: 1Hz; low-pass filter: 70Hz; notch filter: off.

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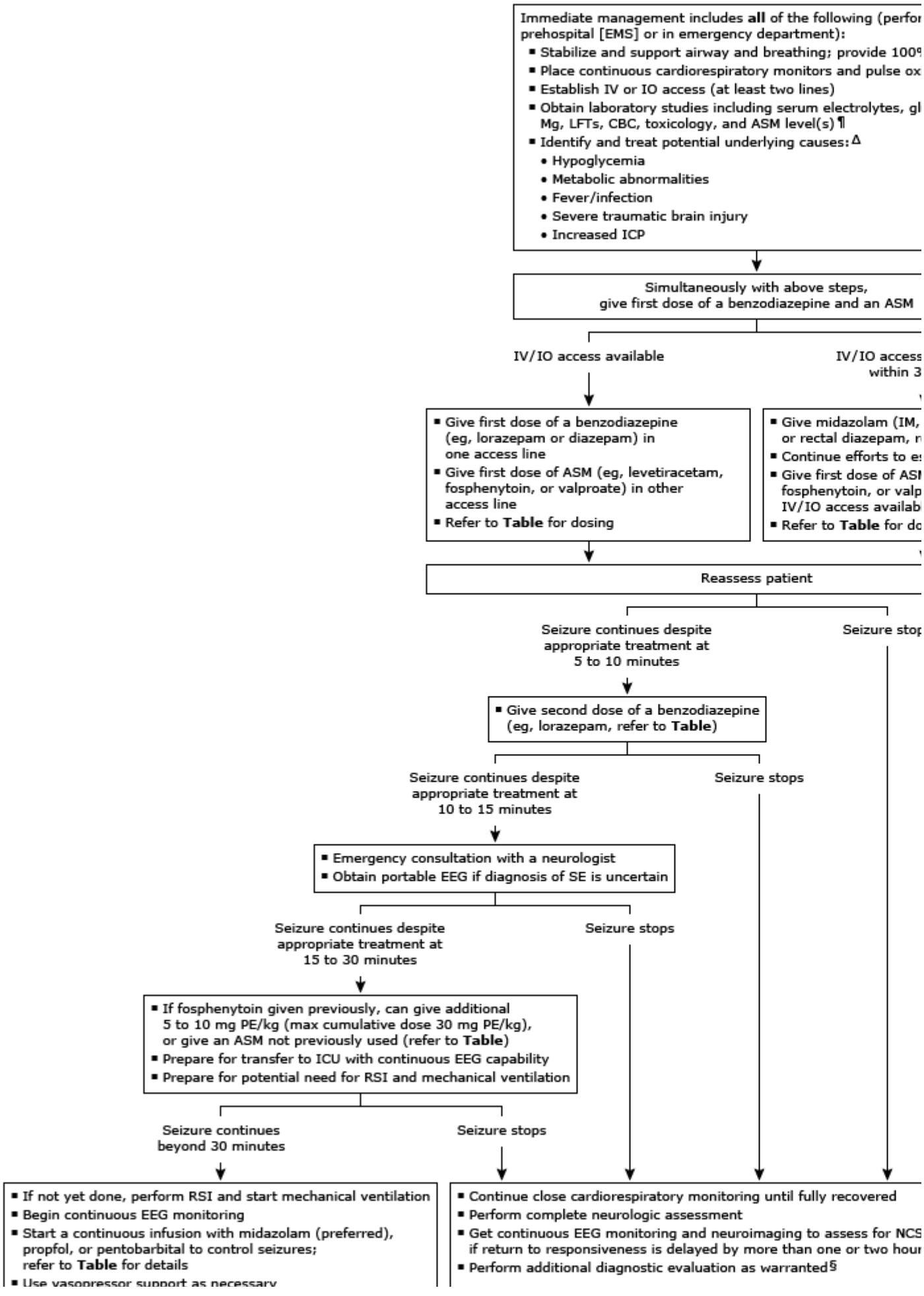
Graphic 94774 Version 3.0

## Periictal imaging abnormalities

| Local | Remote |
| --- | --- |
| ▪ Mass effect, sulcal effacement<br>▪ Hippocampal swelling<br>▪ Focal cortical lesions, increased T2 signal, restricted diffusion<br>▪ Migratory lesions<br>▪ Blood brain barrier breakdown, contrast enhancement<br>▪ Increased vessel caliber/flow<br>▪ Increased perfusion | ▪ Cerebellar diaschesis<br>▪ Unilateral/bilateral diencephalic lesions, most commonly in the pulvinar<br>▪ Splenium abnormalities<br>▪ Posterior leukoencephalopathy |

Graphic 59643 Version 4.0

# 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.

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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.

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