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Seizures

General Principles

Definition

- Seizure: stereotyped spells caused by abnormal electrical brain activity. A more complex definition is uncontrolled excessive electrical discharges in the brain that may produce a sudden change in brain function causing physical convulsion, minor physical signs, thought disturbances, or a combination of symptoms.
- Epilepsy is defined as a state of recurrent seizures.
- Status epilepticus is defined by >30 minutes of continuous seizure activity or recurrent seizures without full recovery between episodes. However, in practice, a seizure lasting >5 minutes in adults (>10 minutes in children) should be treated as status epilepticus. Generalized convulsive status epilepticus (GCSE) is a medical emergency.
- Nonconvulsive status epilepticus (NCSE) is defined by electrographic seizures with clinically absent or subtle motor activity and impairment or loss of consciousness. NCSE should be treated promptly to avoid irreversible cerebral injury.
- An aura is a simple partial seizure manifesting as sensory, autonomic, or psychic symptoms.
- A prodrome is a sensation or feeling that a seizure will soon occur. Distinguishing a prodrome from an aura can be clinically challenging.

Classification

- Partial seizures begin focally. Provided are both the classic nomenclature and, in parentheses, the 2010 updated nomenclature from the International League Against Epilepsy.
  - **Simple partial (focal seizure without impairment of consciousness):** Consciousness is not impaired. The symptoms can be motor (hand jerking), sensory (focal tingling, visual, auditory), autonomic (sensation of epigastric rising), or psychic (déjà vu).
  - **Complex partial (focal seizure with impairment of consciousness, or "dyscognitive" focal seizures):** Consciousness is impaired. The symptoms vary based on whether they involve the temporal (automatisms such as lip smacking or picking at clothes, staring, behavior arrest), frontal (hypermotor behaviors, bicycling, pelvic thrusting, and automatisms), or occipital lobes (unformed images, visual hallucinations). Frontal seizures are often misdiagnosed as nonepileptic seizures (i.e., pseudoseizures) due to their often complex, sometimes bizarre semiology and the frequent absence of electrographic seizure activity on standard EEG.
- Generalized seizures originate from bilateral hemispheres, and by definition, consciousness is lost.
  - May begin as generalized or as partial seizures with secondary generalization.
  - Include tonic, clonic, tonic-clonic, atonic, myoclonic, and absence.

Epidemiology

- Epilepsy is estimated to affect approximately 70 million people worldwide with the prevalence being twice as high in low-income countries relative to high-income countries.
- The median worldwide incidence of epilepsy is approximately 50 per 100,000 per year (Neurology 2011;77(10):1005 [PMID:21893672]).

Etiology

Etiologies for seizures include those listed in Table 27-3. For patients with a known seizure disorder presenting with an increase in seizure frequency, the most common causes are anticonvulsive medication noncompliance, subtherapeutic anticonvulsant levels, or infection.

Table 27-3: Etiologies of Seizures

• CNS infections • Fever

- Hypoxic brain injury
- Stroke (ischemic or hemorrhagic)
- Cerebral venous thrombosis
- Vascular malformations
- Tumors/carcinomatous meningitis
- Head injury
- Eclampsia
- Hypertensive encephalopathy/reversible posterior leukoencephalopathy
- Hyperthyroidism
- Congenital brain malformations
- Hereditary (Sturge-Weber, tuberous sclerosis, Dravet syndrome, and other channelopathies)
- Toxic metabolic (porphyria, uremia, liver failure)
- Drug withdrawal (alcohol, barbiturates, benzodiazepine, AEDs)
- Drug intoxication (TCAs, bupropion, clozapine, tramadol, cocaine, amphetamine)
- Electrolyte abnormalities/metabolic
  - Hyponatremia or hypernatremia
  - Hypocalcemia
  - Hypomagnesemia
  - Hypophosphatemia
  - Hypoglycemia/hyperglycemia

AEDs, antiepileptic drugs; CNS, central nervous system; TCAs, tricyclic antidepressants.

Diagnosis

Clinical Presentation

History

- Query for family history of epilepsy, developmental delay, trauma, medical historical information including preexisting medical conditions, current and recently discontinued medications, drug allergies, recreational drug use, and possible precipitating events.
- Ask the patient about any prodrome/aura. An eyewitness account of the event is critical, and a video of the event can be extremely helpful. Inquire about the temporal features (i.e., seizures are typically acute onset with a rapid crescendo), **incontinence**, **tongue biting**, and how the patient behaved after the event ended (e.g., confused?, somnolent? if so, for how long?).

Physical Examination

- Vital signs and blood sugar should be obtained immediately on all patients. As discussed previously, empiric thiamine should be given when treating hypoglycemia. Ictal and/or postictal fever can occur.
- Look for nuchal rigidity, rash, asterixis, or signs of trauma.
- Convulsive seizures are usually easily identified.
- Features of the seizure can aid in identifying the ictal focus (e.g., complex automatisms in frontal lobe seizures, lip smacking and postictal nose wiping in temporal lobe seizures, ictal laughter in hypothalamic seizures).
- Carefully observe for subtle signs of nonconvulsive seizures, such as automatisms, facial or extremity twitching, eye deviation, and periods of relatively preserved mental status alternating with periods of impaired consciousness.
- Patients may present during the postictal period, defined as the time between the end of the seizure and the return to baseline mental status. During this time, patients may act confused, obtunded, and have amnesia for events since the seizure. This period can typically last from minutes to hours or, rarely, days in the elderly and those with prior CNS injury.
- Postictal paresis (also called Todd paralysis) is a transient neurologic deficit that lasts for hours or, rarely, days after an epileptic seizure.

Differential Diagnosis

Alternate diagnoses that may mimic seizures include:

- Syncope, especially convulsive syncope in which seizure-like motor activity is observed. The Calgary Seizure Syncope score is a useful and reliable clinical tool in distinguishing these two entities (J Am Coll Cardiol 2002;40(1):142 [PMID:12103268]).
- Nonepileptic seizures (“pseudoseizures”) (see the following text).
- Transient ischemic attack.
- Complicated migraine.
- Toxic-metabolic encephalopathy.
- Tremors, dyskinesias (episodic movement disorders).

- Nonepileptic myoclonus following a hypoxic event.
- Sleep disorders.
- Rigors.

Diagnostic Testing

Laboratories

Initial laboratory studies should include blood glucose, electrolytes (sodium, calcium, magnesium, and phosphorus), CBC, urinalysis, urine drug screen, and AED levels if indicated.

Imaging

Neuroimaging is usually indicated to identify structural etiologies.

- Start with a head CT in the acute setting. The administration of contrast can assist in diagnosis of possible tumors.
- Brain MRI with and without contrast, protocolled to evaluate for an ictal focus, is almost always indicated in the evaluation of new-onset seizures and is certainly indicated in patients with recurrent unprovoked seizures.

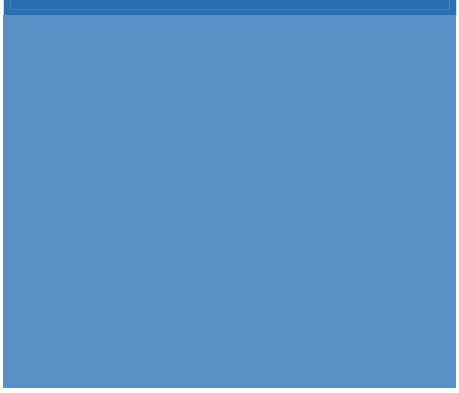
Diagnostic Procedures

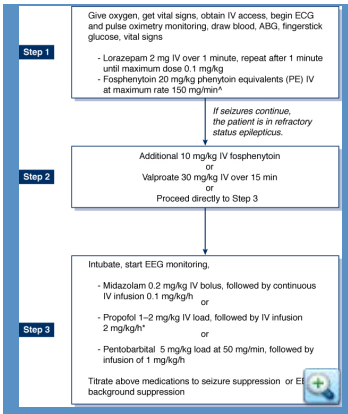
- LP should be done if there is concern for CNS infection. Send for routine CSF studies as well as HSV polymerase chain reaction (HSV-PCR). Save extra CSF for any additional testing, if later indicated.
- EEG is not required for initial diagnosis and management of GCSE. If mental status is not improving as expected after convulsive seizures stop, EEG may be necessary to exclude conversion to NCSE. Unless the patient is known to typically have an extraordinarily prolonged postictal period, NCSE should be considered in any patient who fails to return to baseline within an hour of a seizure. Approximately 50% of patients who present with GCSE will go on to develop NCSE within 24 hours of cessation of clinical seizure activity.
- Routine EEG is indicated for all new-onset seizures (Neurology 2007;69(18):1772 [PMID:17967993]).
- Video EEG is the gold standard test for the evaluation of suspected nonepileptic seizures. A significant (30–50% in some studies) number of patients with nonepileptic seizures ("pseudoseizures") will also have epileptic seizures.

Treatment

- **Initiation of AED therapy is usually not indicated after a single unprovoked seizure** because about two-thirds of patients who had a single seizure will not have seizure recurrence (N Engl J Med 1998;338(7):429 [PMID:9459646]). However, patients with a single unprovoked seizure and either an abnormal EEG or evidence of an ictal focus on head CT or brain MRI warrant initiation of AED therapy given a much higher likelihood of seizure recurrence.
- In general, AEDs should not be started in patients with provoked seizures.
- A diagnosis of epilepsy is made after two or more unprovoked seizures. AED treatment is generally started after the second seizure because the patient has a substantially increased risk (approximately 75%) for repeated seizures after two events.
- Treatment of status epilepticus must be prompt because efficacy of treatment decreases with increased seizure duration (Semin Neurol 2008;28(3):342 [PMID:18777481]) and GCSE carries an all-cause mortality of 30%. (See Figure 27-1 for treatment of status epilepticus.) Within 5–30 minutes of GCSE onset, the body's homeostatic mechanisms begin to fail and patients' risk of permanent brain injury increases, as does risk of systemic complications including hyperthermia, pulmonary embolism, cardiovascular and respiratory insufficiency, and other life-threatening complications. Prolonged NCSE will also result in brain injury but on a timescale of days as opposed to minutes (see Figure 27-2).

Figure 27-1. Treatment of status epilepticus.

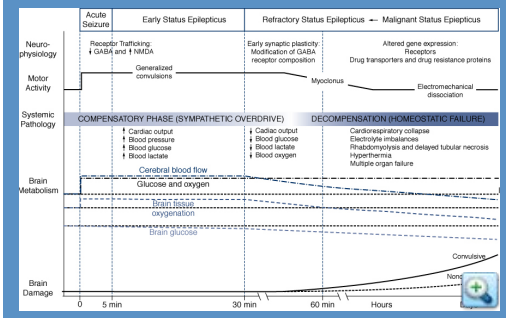




ABG, arterial blood gas; EEG, electroencephalogram.

(Modified from Arif H, Hirsch LJ. Treatment of status epilepticus. Semin Neurol 2008;28(3):342 [PMID:18777481].)

Figure 27-2. Brain and systemic pathology in prolonged convulsive and nonconvulsive status epilepticus.



(From Hirsch LJ, Gaspard N. Status epilepticus. Continuum 2013;19(3):767 [PMID:23739110].)

Medications

- The selection of a specific AED for a patient must be individualized according to the drug effectiveness for seizure type(s), potential adverse effects of the drug, interactions with other possible medications, cost, and mechanism of drug action (Epilepsia 2006;47:1094 [PMID:16886973]).
- About half of all patients with a new diagnosis of epilepsy will be seizure free with the first AED prescribed (Epilepsia 2001;42:1255 [PMID:11737159]).
- Treatment should be started with a single drug that can be titrated until adequate control or until side effects are experienced.
- **Combination therapy (polytherapy) should be attempted only after at least two adequate sequential trials of single agents have failed.** Failure to control epilepsy with adequate trials of two drugs meets criteria for treatment-resistant epilepsy, and a referral for presurgical evaluation should be considered (Epilepsia 2010;51(6):1069 [PMID:19889013]).

Lifestyle Modifications

- Patients should not start other medications (e.g., over-the-counter medications or herbal remedies) without contacting their physician because there may be drug interactions.
- Patients should keep a seizure calendar to identify possible seizure triggers. Screen patients for poor sleep hygiene. Females may have catamenial (perimenstrual) seizures.
- Women should ideally inform their physicians well in advance of any plans for pregnancy or at the very least immediately upon finding out they are pregnant given the teratogenicity associated with certain AEDs, the increased risk of teratogenicity with polytherapy versus monotherapy, and the potential need for medication adjustment during pregnancy.
- Patients should reduce alcohol intake because heavy consumption (three or more drinks per day) is associated with an increased risk of seizures.

Referral

Neurologic consultation may be helpful for managing status epilepticus and for evaluation and management of new-onset seizures.

Patient Education

Patients with epilepsy, especially those left untreated, have a small risk of sudden death in epilepsy (Lancet Neurol 2011;10(11):961 [PMID:21937278]). Patients with epilepsy should not swim unsupervised, bathe in a bathtub of standing water, use motorized tools, or be in position to fall from heights during a seizure (i.e., patients should avoid situations in which they could harm themselves or others if they were to have a seizure). Driver licensing requirements for patients with epilepsy vary from state to state. A complete listing of state laws can be found at https://www.epilepsy.com/driving-laws.

Monitoring/Follow-Up

- Regular follow-up visits should be scheduled to check drug concentrations, blood counts, and hepatic and renal function. Side effects after initiating AED should be monitored.
- Again, correctable causes for seizures (e.g., hyponatremia, drug toxicity, alcohol withdrawal) do not require long-term anticonvulsant therapy.

Outline

- Chapter 27: Neurologic Disorders
  - Alterations in Consciousness
  - Alzheimer Disease
  - **Seizures**
  - Multiple Sclerosis
  - Cerebrovascular Disease
  - Headache
  - Head Trauma
  - Acute Spinal Cord Dysfunction
  - Parkinson Disease
  - Neuromuscular Disease
    - Guillain-Barré Syndrome
    - Myasthenia Gravis
    - Other Neuromuscular Disorders
    - Neuromuscular Disorders with Rigidity