

Definition

An *epileptic seizure* is an episode of altered behavior resulting from abnormal, paroxysmal electrical discharge within the gray matter of the brain. *Epilepsy* consists of recurrent epileptic seizures in the absence of extraordinary provocation. Widespread, forceful, and repetitive contraction of the body musculature is termed a *convulsion*. Convulsions are not necessarily specific for epileptic seizures. Coordinated but involuntary motor activities occurring during the course of a seizure, usually with clouding of consciousness, are called *automatisms*.

Technique

Despite recent advances in electroencephalography and neuroradiology, the history remains preeminent in the diagnosis of epilepsy. Diagnosis often depends on the testimony of a witness even more than on that of the patient, and the description of a reliable witness should be avidly pursued at the time of the initial evaluation, by writing, or by long-distance telephone if necessary. If the patient is initially postictal, psychotic, or comatose, a third party may be the only one who can describe the most crucial events.

Begin with a general question that directs the patient to the matter of interest: "Tell me about your spells." AVOID categorizing them as "seizures" before you have had a real chance to think about what they are. Many laypeople do not consider that seizures are necessarily related to epilepsy, and others may have received an improper diagnosis. Determine the general conditions under which episodes occur. Is there more than one type? When did they begin? How often do they happen? Are spells related to time of day, position, food intake or deprivation, sleep or sleep deprivation, emotion, fever, pain, or fatigue? Can they be precipitated by flashing lights or other sensory stimuli? Are they associated with medications that have convulsant potential, such as theophylline; or do they follow withdrawal from alcohol or addictive drugs?

Specific details of attacks are essential for correct diagnosis and classification of seizure disorders (Table 56.1). What (if anything) is the first hint that a spell will occur? What happens next? If consciousness is lost, how long before it returns? What does the patient feel afterward? Find out from witnesses if the eyes were open or closed, if there was a motionless stare at outset, or if there were automatisms. What, exactly, were any movements of head and limbs? How long did they last, and what was their relationship to a period of unconsciousness? Determine whether there has been incontinence or tongue biting. Often the patient has not thought about such questions before the physician asks them; if the diagnosis is in doubt, the patient may have to take some time to consider them and be interviewed again later, or may have to keep a diary of what happens.

One of the most effective maneuvers for getting the "feel" of an episode is to have the patient or a witness imitate it physically in the office. Many patients show remarkable reluctance to assist the physician by imitating their spells; gentle encouragement may overcome this.

Table 56.1
International Classification of Epileptic Seizures

Partial (focal, local) seizures	
A.	Simple partial seizures (consciousness not impaired)
1.	With motor signs
a.	Focal motor without march
b.	Focal motor with march (Jacksonian)
c.	Versive
d.	Postural
e.	Phonatory (vocalization or arrest of speech)
2.	With somatosensory or special-sensory symptoms (simple hallucinations, e.g., tingling, light flashes, buzzing)
a.	Somatosensory
b.	Visual
c.	Auditory
d.	Olfactory
e.	Gustatory
f.	Vertiginous
3.	With autonomic symptoms or signs (including epigastric sensation, pallor, sweating, flushing, piloerection, and pupillary dilation)
4.	With psychic symptoms (disturbance of higher cerebral function). These symptoms rarely occur without impairment of consciousness and are much more commonly experienced as complex partial seizures.
a.	Dysphasic
b.	Dysmnestic (e.g., déjà vu)
c.	Cognitive (e.g., dreamy states, distortions of time sense)
d.	Affective (fear, anger, etc.)
e.	Illusions (e.g., macropsia, micropsia)
f.	Structured hallucinations (music, visual scenes)
B.	Complex partial seizures (with impairment of consciousness; may sometimes begin with simple symptomatology or be accompanied by automatisms)
C.	Partial seizures evolving to secondarily generalized seizures. (These may be generalized tonic-clonic, tonic, or clonic.)
Generalized seizures (convulsive or nonconvulsive)	
A.	1. Absence seizures
a.	Impairment of consciousness only
b.	With mild clonic components
c.	With atonic components
d.	With tonic components
e.	With automatisms
f.	With autonomic components
2.	Atypical absence (with more pronounced changes in tone, or with gradual onset or cessation)
B.	Myoclonic seizures
C.	Clonic seizures
D.	Tonic seizures
E.	Tonic-clonic seizures
F.	Atonic (astatic) seizures

Source: Abstracted from Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489-501.

Many of these questions relate directly to establishing the diagnosis. Tables 56.2 and 56.3 are reminders that epileptic seizures have a differential diagnosis, and very precise historical details may be needed to tell the possible entities apart. Eye closure during an attack, rotation of the head from side to side, prolonged motionless unresponsiveness, and very severe flailing movements are all quite unusual for epileptic seizures. Tongue biting and incontinence favor true epilepsy, but may be seen when a patient injures himself or herself in falling or even in hysterical attacks. Noticeable jerking can be seen with vasodepressor syncope or Stokes-Adams attacks and must be distinguished from sustained clonic activity. An aura of dizziness, a need to sit or lie down, nausea, and a wave of warmth over the body are common in vasodepressor syncope and rare in true epilepsies. Some symptoms associated with partial seizures are bizarre, and difficult for the patient to describe, but occur repeatedly in a stereotyped manner; such consistency argues against a hysterical or psychotic etiology and favors an epileptic disorder.

The past medical history should pay special attention to birth injuries, febrile convulsions in childhood, head trauma, malignancies, and central nervous system (CNS) infections. A review of systems must include a careful survey of other neurologic or cardiovascular complaints. The family history should screen for relatives with seizures, CNS tumors, aneurysms, or arteriovenous malformations.

Basic Science

The pathophysiology of epileptic seizures appears to involve two distinct mechanisms, which may overlap in the same patient, though seldom in the same seizure. The details of seizure initiation and propagation are still not completely understood, but the electrical abnormalities have been extensively delineated.

Corticoreticular is the current term for seizures characterized by spike-wave discharges that are generalized from onset. The classic clinical form of corticoreticular epilepsy is childhood absence; the classic laboratory model for corticoreticular seizures is generalized penicillin epilepsy in the cat. For many years, absence and other types of seizures generalized from onset were designated "centrencephalic"—the presumption being that they arose in the core gray structures of the brain, including the thalamus and midbrain, and that this site of origin explained their simultaneous appearance all over the cerebral cortex. This concept has now been generally abandoned for many reasons, the most salient being that (1) no anatomical correlate has ever been found in humans or experimental animals that would confirm seizure origin from the "centrencephalon"; and (2) no experimental manipulation confined

to the thalamus or midbrain has ever produced true spike-wave discharges characteristic of naturally occurring epilepsies. Instead, extensive work with the feline penicillin model has shown that both the cortex and core gray structures appear to be involved. The volleys of electrical activity that become spike and wave seem to originate in the thalamus, but the major perturbation is at the cortex, where otherwise normal thalamic outputs encounter abnormal excitability and are transformed into spike and wave. Application of penicillin to the cortex alone will produce generalized spike-wave; application to the thalamus or midbrain alone will not. The discharges of corticoreticular epilepsy travel along normal neuronal pathways by normal synaptic mechanisms; because of their widespread synchrony, they are spectacularly prominent on EEG, but they may have surprisingly little effect on external behavior in some patients, and are never followed by postictal confusion. The tendency to corticoreticular epilepsy is generally considered a familial trait with variable expression and is only rarely exacerbated by an anatomic lesion. However, individual seizures may be precipitated by specific factors including the alkalosis of hyperventilation, other metabolic imbalance, flashing lights, sleep deprivation, or emotional stress.

Seizures of focal origin and those secondarily generalized appear to have a different neurophysiology. The major underlying electrical abnormality is the paroxysmal depolarization shift (PDS), in which individual neurons or clusters of neurons undergo a striking, marked, and prolonged depolarization that may last for many seconds. The PDS is followed by an abnormal degree of hyperpolarization, which may persist for many minutes. During the PDS, the cell may produce action potentials at a very high rate; during the subsequent hyperpolarization, it does not react normally to synaptic inputs. In some experimental preparations, the PDS appears to be initiated by relatively normal synaptic mechanisms; but it may also lead to strikingly aberrant phenomena, such as retrograde conduction of an action potential backward across the synapse. The exact mechanisms leading to the PDS are unknown. Many researchers believe that they involve abnormal architecture of the cell body and dendrites, secondary to local cortical injury. Many convulsant agents, including several metals, will produce a PDS when applied directly to the cortex. The uptake of iron from hemosiderin may produce neuronal abnormalities, and provides one possible link between brain lesions and the later development of focal epilepsies.

Certain portions of the brain appear much more likely than others to produce an epileptic focus as a reaction to injury. In adults, the most susceptible areas are the motor cortex and the temporal lobe, especially the "limbic" structures of the hippocampus and the amygdala. Some neurons

Table 56.2
Differential Diagnosis of Generalized Seizures

Vasodepressor syncope
Orthostatic syncope
Cardiac arrhythmias
Hysteria
Hyperventilation
Sleep attacks, cataplexy
Epinephrine release: acute anxiety, panic disorder, hypoglycemia, pheochromocytoma

Table 56.3
Differential Diagnosis of Complex Partial Seizures

Absence seizures
Sleep attacks
Daydreaming
Hysterical or depressive dissociation, fugue states
Epinephrine release
Hyperventilation
Rage attacks
Transient global amnesia
Transient ischemic attacks

in the normal hippocampus have been shown to produce spontaneous bursts of action potentials that resemble the PDS. Furthermore, because of its proximity to the free edge of the tentorium and to the sharp bony margins that define the middle fossa of the skull, the temporal lobe is vulnerable to trauma from birth onward. These factors help to account for the relatively high incidence of temporal foci in partial epilepsies.

The interictal EEG spikes of experimental focal epilepsies are regularly associated with the PDS and closely resemble focal spikes in the EEGs of patients with clinical seizure disorders. The development of focal seizures and their occasional secondary generalization appears to involve spread of the PDS to larger and larger groups of neurons. This spread is seen most dramatically in *Jacksonian seizures*, which begin focally with movement of a single body part and march sequentially into larger and larger areas before generalizing. During the PDS, discharges can also be conducted backward across the synapse and retrograde to areas that normally project to the cortex, including the thalamus. From these structures, they may then be widely and rapidly disseminated.

During partial seizures or generalized tonic-clonic convulsions, normal neuronal processing is completely interrupted and remains abnormal throughout the duration of the hyperpolarization that follows. This probably explains the postictal state that usually follows focal or generalized tonic-clonic seizures. Occasionally a focal deficit of motor, sensory, or higher cortical function persists for several hours or more (Todd's paralysis). Seizures that are focal or secondarily generalized may begin at any age and have a high correlation with structural cerebral disease that may be static or progressive. This is in contrast to the corticoreticular epilepsies (primary generalized epilepsies), which usually begin in childhood or adolescence and are not associated with structural brain disease. Nonetheless, the distinction between these two basic mechanisms of the epilepsies is not absolute; many patients with classical absence also have tonic-clonic convulsions, and in a few patients the seizures may begin with generalized spike-wave characteristic of a corticoreticular discharge, evolving into convulsions characteristic of the PDS.

Given the existence of two different mechanisms for epileptic seizures, it might be anticipated that the anticonvulsants used to treat them could be divided into two different classes. Ethosuximide, until recently the undisputed first choice for childhood absence, is ineffective for focal or generalized major motor seizures. Phenobarbital, primidone, carbamazepine, and phenytoin are all effective against focal and generalized convulsive seizures, but have little if any usefulness for absence. Valproic acid is the only agent that appears effective for both categories of seizure. Valproic acid appears to augment the effect of GABA, an inhibitory neurotransmitter that is widely distributed in the cerebral cortex.

Until the recent advent of long-term monitoring techniques, the great majority of patients had seizures that were difficult to capture in the EEG laboratory; and a significant fraction lack interictal EEG abnormalities between seizures. For this reason, the International Classification of Epileptic Seizures is based on clinical and not the (presumed) electrical phenomena. The current scheme is given in Table

56.1. "Partial" is preferred over "focal," and simple partial seizures involve focal phenomena without alteration of consciousness. The category of complex partial seizures deserves special mention because of its high incidence and the different interpretations that have historically been placed on the word "complex." Though the term formerly referred to a variety of psychic phenomena, at present it implies merely that the patient lacks awareness or recall for all or part of the episode, with the presumption that the discharge has spread into areas affecting memory. The old terms *petit mal* and *grand mal* are now discouraged. The former was originally synonymous with absence, but has been popularly misused to mean almost anything else short of a convulsion. The latter is less useful than descriptive terms such as tonic-clonic or massive myoclonic seizures.

Clinical Significance

The clinical manifestations of epilepsy depend on the area of brain involved by the seizure plus the rapidity and extent to which it spreads. Many of the symptoms can be predicted from cortical anatomy, as implied in Table 56.1.

The most important distinction is between the primary generalized epilepsies (corticoreticular epilepsies) and those that are focal or generalize secondarily. Work-up, management, and therapy are strongly influenced by the classification of seizures. Primary generalized seizures require a search for environmental precipitants but seldom imply a progressive brain lesion. A CT scan on a healthy child with absence and 3-per-second spike-wave on EEG is a waste of time. Radiological work-up and close follow-up are usually indicated for seizures that have focal characteristics by history or EEG, that are acquired in adulthood, or that are suspected of being secondarily generalized even when this cannot be demonstrated from available history. The major exception to this requirement is for the common childhood disorder of Rolandic epilepsy, in which the EEG shows focal but highly characteristic spike discharges and there is no association with progressive disease.

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