

# **PRIMER OF EPILEPSY DIAGNOSIS AND TREATMENT**

revised 7/06

Nathan B. Fountain, MD

Associate Professor of Neurology  
Department of Neurology  
University of Virginia  
Box 800394  
Charlottesville, VA 22908

## DEFINITIONS

### **What is a seizure?**

Temporary alteration of brain function caused by paroxysmal, abnormal cerebral neuronal discharge

### **What is an ictus?**

A seizure

### **What is a convulsion?**

A seizure causing abnormal muscle contractions

### **What is epilepsy?**

Continuing tendency to spontaneous recurrent seizures, resulting from a persistent pathologic process

### **What is a seizure disorder?**

Synonymous with epilepsy

### **What is a provoked seizure?**

A seizure occurring in an otherwise normal brain as a result of some transient alteration, such as changes in glucose or sodium or drug effects

### **What is status epilepticus?**

Continuing or recurring seizures without return of normal consciousness

## SEIZURE CLASSIFICATION

### **What is the most common type of seizure?**

Complex partial seizures

### **On what basis are seizures classified?**

They are classified according to observable clinical manifestations by the International League Against Epilepsy (ILAE).

### **What are the two main categories of seizures?**

Generalized and partial (focal) seizures

### **What is the defining clinical difference between generalized and partial seizures?**

Consciousness is lost in generalized seizures and preserved in partial seizures

### **What is the pathophysiologic significance of this?**

Preservation of consciousness implies seizures arise from a *localized* area. Alteration of

consciousness implies that all or most of the cortex is involved.

**Name two categories of seizures that may make the patient unable to respond to questions.**

Generalized and complex partial

## PARTIAL SEIZURES

**What is another name for partial seizures?**

Focal seizures

**What are the subdivisions of partial seizures?**

Simple partial seizure (SPS)

Complex partial seizure (CPS)

**What characteristic distinguishes simple partial from complex partial seizures?**

Consciousness is normal in simple partial seizures. Consciousness is impaired, but not lost, in complex partial seizures - patients are awake but not normally interactive with the environment.

## SIMPLE PARTIAL SEIZURES

**How are simple partial seizures further subdivided?**

Based on whether symptoms are primarily motor, sensory, autonomic or psychic

**List 4 types of simple partial motor seizure.**

Repetitive jerking of a body part (e.g., face, arm, or leg), which may “march” up a limb due to involvement of the primary motor cortex.

Versive eye or head movements due to frontal eye field involvement.

Posturing of a limb due to supplementary motor involvement.

Phonatory from involvement of Broca's area.

**What is the localizing value of simple partial motor seizures?**

They imply involvement, and usually origin, in the frontal lobe.

**List 6 types of simple partial sensory seizures.**

Tingling of a body region from primary somatosensory cortex in the parietal lobe.

Visual hallucinations of vague descriptions from primary visual cortex in occipital lobe.

Auditory hallucinations of noises possibly from primary auditory cortex in temporal lobe.

Olfactory hallucinations, usually of an unpleasant odor, from primary olfactory cortex in uncus of temporal lobe (uncinate fits).

Gustatory sensations, usually of temporal lobe origin.

Vertigo or dizziness, usually from temporal lobe, but not very localizing.

**List 2 symptoms of autonomic simple partial seizures.**

Sympathetic overdrive, including tachycardia, sweating, pupillary dilatation.  
Abdominal or epigastric sensations, often poorly described as a “rising” sensation

**List 6 types of symptoms of psychic simple partial seizures.**

Aphasia/dysphasia, memory (déjà vu; jamais vu), cognitive (dreamy state), affective (fear, anger), illusions (macropsia), structured hallucinations.

**What is déjà vu?**

Feeling as though something has been seen or experienced before; literal French translation is “already seen”.

**What is jamais vu?**

Feeling of unfamiliarity in a familiar situation; literal French translation is “never seen”.

**What is an aura?**

A simple partial seizure occurring as the prelude to a more widespread seizure; the focal start of a seizure.

**What is the significance of an aura?**

It occurs only in seizures with a focal onset and may help localize the site of seizure onset.

**COMPLEX PARTIAL SEIZURES**

**Describe a typical complex partial seizure.**

Impaired alertness and responsiveness with amnesia for the event; sometimes preceded by an aura and followed by a postictal state.

**What are possible objective accompaniments to a complex partial seizure?**

Automatisms (confused purposeless behavior), especially lip smacking, vocalizations, swallowing, and fumbling.

**What is a postictal state?**

Temporary post-seizure neurologic deficit (most commonly lethargy), possibly secondary to neuronal exhaustion.

**What is a Todd's paralysis?**

A postictal state consisting of transient hemiparesis, reflecting the location of the most involved area of the brain.

**Name a seizure that originates in one brain area and subsequently spreads throughout the brain.**

Partial seizure with secondary generalization.

**GENERALIZED SEIZURES**

**Name 8 types of generalized seizure.**

1. Absence seizure (ABS; formerly called petit mal)
2. Atypical absence
3. Myoclonic seizure (MYO)
4. Tonic seizure
5. Clonic seizure
6. Generalized tonic-clonic (GTC; formerly called grand mal)
7. Atonic seizure
8. Infantile spasm

**Describe the essential features of a GTC seizure.**

Sudden generalized stiffness of a few seconds duration during the “tonic” phase, followed by rhythmic muscle contractions during the “clonic” phase, followed by post-ictal somnolence or confusion. It is truly a GTC seizure only when both tonic and clonic phases are present.

**What are other common accompanying symptoms?**

Injury during falling, tongue biting, stertorous respirations, urinary incontinence and drooling.

**Describe the essential features of an absence seizure.**

Sudden staring unresponsiveness of a few to several seconds duration which interrupts ongoing activities, with resumption of activity immediately upon termination of the seizure.

**What are other common accompanying symptoms?**

If it is prolonged (usually greater than about 14 seconds), it may be accompanied by automatisms, similar to a complex partial seizure.

**How do atypical absence seizures differ from typical absences?**

They consist of staring unresponsiveness, but often continue for prolonged periods of hours to days and usually are accompanied by static encephalopathy.

**Name an epilepsy syndrome in which atypical absence seizures are common.**

Lennox-Gastaut syndrome

**Describe a myoclonic seizure.**

A single sudden lightening-like jerk of the whole body or a group of muscles which may cause the patient to drop or throw something held in the hand, e.g. a fork while eating

**Name an epilepsy syndrome in which myoclonic seizures are common.**

Juvenile myoclonic epilepsy

**Describe a clonic seizure.**

Rhythmic muscle contractions, identical to the clonic phase of a GTC seizure

**How does this differ from a myoclonic seizure?**

Clonic seizures are multiple rhythmic jerks, while myoclonic seizures are single jerks, although several may occur in sequence arrhythmically.

**Describe a tonic seizure.**

Sudden sustained whole body muscle contraction of several seconds duration; typically the extremities, back and neck are pulled into extension. May be accompanied by an expiratory moan as air is forced out from thoracic muscle contraction.

**Describe an atonic seizure.**

Sudden loss of whole body muscle tone, associated with unprotected falling limp to the ground. Consciousness usually returns quickly.

**Name a childhood epilepsy syndrome in which atonic seizures are common.**

Lennox-Gastaut syndrome.

**Describe an infantile spasm.**

Sudden contraction of the trunk and arms, flexing the trunk forward and pulling the arms into extension. Also called a “salaam” attack.

**Name a childhood epilepsy syndrome in which infantile spasms are common.**

West’s syndrome.

**PSEUDOSEIZURE**

**What is a pseudoseizure?**

A nonepileptic event mimicking an electroconvulsive seizure

**What are 2 other names for pseudoseizures?**

Psychogenic seizures and nonepileptic seizures.

**What are 4 common causes of pseudoseizures.**

Conversion reaction, depression, adjustment disorder, malingering.

**What are 4 clinical characteristics that may help differentiate a pseudoseizure from a seizure.**

Bizarre behavior, pelvic thrusting, obvious purposeful behaviors, long duration. However, these characteristics may also occasionally occur during CPSs, especially of frontal lobe origin.

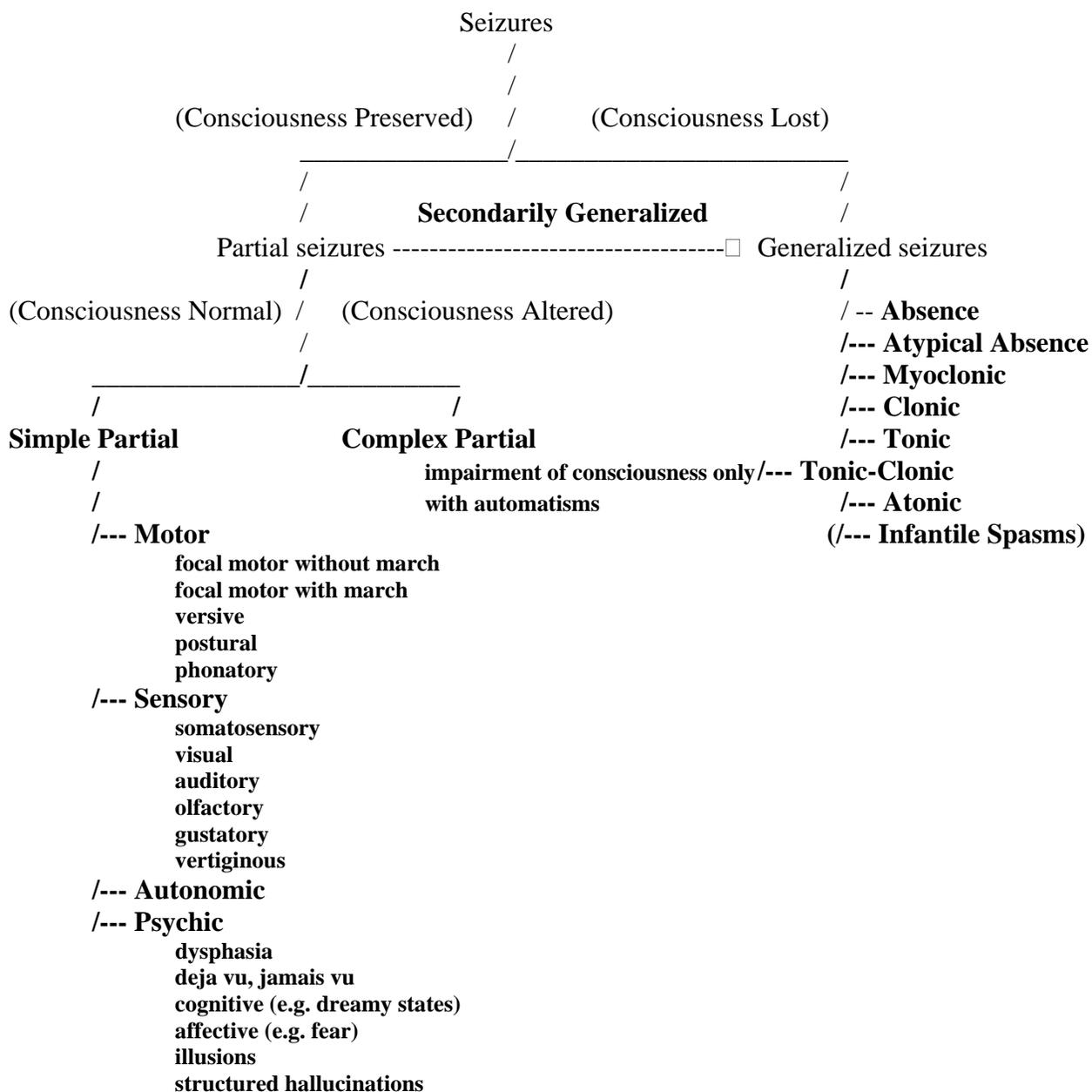
**What other historical factors, if present, may be useful?**

Lack of response to AEDs, obvious psychopathology.

**How do prolactin levels help differentiate them?**

Prolactin is almost always elevated after a GTC and frequently elevated after a CPS (especially temporal lobe seizures), but not after a pseudoseizure. If a prolactin level drawn 10 minutes after an event is elevated this strongly suggests that the event was a seizure, however, lack of elevation does not exclude a CPS.

## FLOWCHART OF SEIZURE CLASSIFICATION



## EPILEPSY SYNDROMES

### **What is the difference between *seizures* and *epilepsy syndromes*?**

Seizures are symptoms. Epilepsy is a disease. Seizures are a symptom of brain dysfunction analogous to cough as a symptom of respiratory dysfunction.

### **What is the advantage of using epilepsy syndromes, rather than only seizure type, to characterize patients?**

It is more informative. Patients with a given epilepsy syndrome have a similar natural history, response to treatment, and presumably share the same pathophysiology.

### **What is the prevalence of epilepsy?**

As much as 10% of the population experiences a seizure sometime in life, but only about 3-5% of the population has epilepsy.

### **How are epilepsy syndromes categorized into groups by the ILAE classification?**

They are fundamentally based on whether a localization-related (also called partial or focal) or generalized pathologic process is present and also whether the process is idiopathic, symptomatic or cryptogenic.

See Table "Epilepsy Syndromes."

### **What determines whether an epilepsy syndrome is categorized as symptomatic, cryptogenic or idiopathic.**

*Symptomatic epilepsies*- result from a known histopathologic abnormality in the brain.

*Cryptogenic epilepsies* - presumably have a structural basis because of their association with other neurologic symptoms, but that basis is not known.

*Idiopathic epilepsies* - usually are inherited and presumably are due to abnormalities of neurotransmission without associated structural abnormalities.

### **On what six characteristics are epilepsy syndromes based?**

1. Type of seizure
2. EEG (interictal and ictal)
3. Age at onset
4. Neuroimaging
5. Physical exam
6. Natural history

### **What are the "idiopathic generalized epilepsies?"**

Childhood absence, juvenile absence, juvenile myoclonic and GTCs on awakening. They share many clinical characteristics which occasionally makes distinguishing between them difficult and suggests some overlap between them.

### **What is a "mixed seizure disorder?"**

Term used to describe an epilepsy syndrome characterized by both partial and generalized seizures, in which it can't be determined whether the primary pathology is

focal or generalized. The pathology is probably most commonly presumed to be multifocal.

**What is the most common epilepsy syndrome?**

Temporal lobe epilepsy (TLE)

TEMPORAL LOBE EPILEPSY

**What type of epilepsy syndrome is TLE?**

Localization-related symptomatic epilepsy syndrome

**What is the main seizure type present in this syndrome?**

Complex partial seizures

**What is the most common interictal EEG finding?**

Spikes or sharp waves originating in the temporal region of the head

**What is the most common associated MRI abnormality?**

Atrophy and high T2 signal intensity of the hippocampus and other mesial temporal lobe structures; another term for this type of TLE is “mesial temporal lobe epilepsy” because it affects structures in the mesial portion of the temporal lobe

**What is the most common histopathologic finding in the temporal lobe?**

Mesial temporal sclerosis, consisting of neuronal loss and gliosis in the hippocampus, specifically cell loss in CA3, CA1 and dentate.

**What is the cause of mesial temporal sclerosis?**

Unknown. It may be acquired from febrile convulsions, status epilepticus, head trauma and CNS infection. It also may be congenital, but is not expressed until adolescence or early adulthood.

**What is “lateral TLE?”**

Structural disease in other areas of the temporal lobe. When the lateral temporal cortex is involved it is termed lateral temporal lobe epilepsy or neocortical epilepsy. However, it may also be associated with mesial temporal sclerosis, in which case there is “dual pathology” present.

**What is the most common etiology of lateral TLE?**

Tumors (especially ganglioglioma and other glial tumors) and hamartomas.

BENIGN ROLANDIC EPILEPSY OF CHILDHOOD (BREC)

**What type of epilepsy syndrome is BREC?**

Localization-related idiopathic epilepsy syndrome

**What is the age of onset?**

80% have onset between 5 and 10 years old with peak at 9 years old.

**What is the associated family history?**

Autosomal dominant, but variable penetrance, so that it is not clinically apparent in the appropriate percentage of family members (i.e. less than 50% of sibs).

**Why is it considered benign?**

Seizures almost universally abate by 14 years old.

**What is the classic EEG finding?**

Spikes in the centro-temporal region of the head, which is why the ILEA name is “benign childhood epilepsy with centro-temporal spikes.” The Rolandic area is around the central sulcus, which contains the primary motor cortex. They may be present only during sleep.

**Describe a typical seizure due to BREC.**

Simple motor seizure arising in the face region of the motor cortex, consisting of drooling, inability to speak and clonic facial movements. It may secondarily generalize into a convulsion.

**Is there associated structural pathology in the motor cortex?**

No. It is presumably due to transient age-related changes in subcellular systems (?neurotransmitter systems).

CHILDHOOD ABSENCE EPILEPSY (CAE)

**What type of epilepsy syndrome is childhood absence epilepsy?**

Generalized idiopathic epilepsy syndrome

**What is the typical age of onset?**

4-10 years old, peak at 6-7 years old.

**What types of seizures occur, other than ABS?**

GTC

**What is the associated family history?**

Autosomal dominant with variable penetrance.

**What is the classic EEG finding?**

Generalized 3 Hz spike and wave as isolated asymptomatic brief discharges or more prolonged discharges associated with unresponsiveness.

**What is the fundamental pathophysiology that results in seizures?**

Inhibition drives recurrent circuits between the thalamus and the cortex, mediated by t-

type calcium channels.

**How long does childhood absence epilepsy persist?**

About 70% abates by 14 years old.

JUVENILE ABSENCE EPILEPSY (JAE)

**What is the main difference between the presentation of childhood and juvenile forms of absence epilepsy?**

The juvenile form starts later and is more often associated with GTCs.

**Why is it important to distinguish between them?**

Juvenile absence epilepsy may more often persist into adulthood. Also, they may be genetically and pathophysiologically different.

JUVENILE MYOCLONIC EPILEPSY (JME)

**What type of epilepsy syndrome is JME?**

Idiopathic generalized epilepsy syndrome

**What is the peak age of onset?**

12-18 years old, but patients may not come to medical attention until older.

**What are the two main types of seizures accompanying JME?**

Myoclonic jerks and GTCs

**What is the classic EEG finding?**

Generalized multiple-spike and wave discharges occurring as isolated asymptomatic discharges or with myoclonic jerks. May also have generalized simple spike and wave, but usually at faster frequencies, about 4.5 cps.

**What is the associated family history?**

Autosomal dominant with variable penetrance.

**How long do seizures persist?**

Throughout life, but they are often well-controlled.

GTCS ON AWAKENING

**What is the main clinical characteristic of this syndrome?**

GTCs that occur exclusively or preferentially upon awakening. It is unclear whether this represents a single syndrome with a single pathophysiology or a diverse group of primary generalized epilepsies which happen to share this characteristic.

WEST'S SYNDROME

**What type of epilepsy syndrome is West's syndrome?**

Generalized cryptogenic epilepsy syndrome, because it is associated with static encephalopathy but the offending histopathology is not identifiable. However, in many cases the etiology is known, e.g. perinatal asphyxia, in which case it is actually a symptomatic epilepsy.

**What is West's syndrome?**

Infantile spasms occurring with developmental delay and a hypsarrhythmia EEG pattern

**What is the difference between infantile spasms and West's syndrome?**

Infantile spasms refer only to a type of seizure that may occur in different epilepsy syndromes. West's syndrome refers specifically to infantile spasms occurring with developmental delay.

**What is the typical age of onset?**

6 months to 2 years old. Onset after 2 is very rare.

**What EEG pattern often precedes Infantile spasms?**

Multifocal spikes.

**How long does West's syndrome persist?**

Infantile spasms abate in early childhood, but static encephalopathy and other seizure types persist throughout life.

**What epilepsy syndrome often evolves from West's syndrome?**

Lennox-Gastaut syndrome

**LENNOX-GASTAUT SYNDROME (LGS)**

**What type of epilepsy syndrome is LGS?**

Cryptogenic generalized epilepsy, because it is associated with static encephalopathy but the offending histopathology is not identifiable. However, in many cases the etiology is known, e.g. perinatal asphyxia, in which case it is actually a symptomatic epilepsy.

**What are its two main clinical characteristics?**

Static encephalopathy (mental retardation) and seizures beginning in childhood

**What is the classic EEG finding in LGS?**

Slow spike and wave; it is slow because it is less than 3 Hz

**What seizure types often accompany LGS?**

Tonic, atonic (drop attacks), GTC, atypical absences.

**How long does LGS persist?**

Throughout life. Seizures may be difficult to control.

Summary of Epilepsy Syndrome Characteristics

Name	Age onset	Seizure types	EEG	Family History	Physical Exam	Neuro-imaging	Natural History
TLE	10-30	CPS, 2 <sup>o</sup> gen.	temporal spikes	Neg.	Normal, ?Psych.	Mesial temporal sclerosis	Persists
BREC	5-10	SPS (motor), CPS	Centro-temporal spikes, esp. during sleep	Auto. Dom., variable penetrance	Normal	Normal	Resolves by 14 y.o.
CAE	4-10	ABS, GTC	3 cps generalized spike and wave	Auto. Dom., variable penetrance	Normal	Normal	Resolves by 14 y.o. in 70%
JAE	10-17	ABS, GTC	as above	as above	as above	as above	More often persists
JME	12-18	MYO, GTC	gen. 4.5 cps multiple spike and wave	Auto. Dom., variable penetrance	Normal	Normal	Persists, but is often well-controlled
GTC on awakening	10-20	GTC, ABS, MYO	gen. epileptiform D/Cs	variable	Normal	Normal	Probably heterogeneous group.
West's	6 - 24 mo.	Infantile spasms	hypsarhythmia	Neg., depending on etiology	Static Encephalopathy	variable depending on etiology	Often evolves to LGS
Lennox-Gastaut	2-adult	Tonic, Atonic, Atypical ABS	gen. slow spike and wave (<3 cps)	Neg., depending on etiology	Static Encephalopathy	variable depending on etiology	Persists, difficult to control

## **DIAGNOSTIC TESTS**

### **Is EEG indicated in the evaluation of seizures?**

Yes, for almost all patients.

### **Why?**

To distinguish partial from generalized seizure disorders; to localize site of seizure onset in partial seizures; to characterize the epilepsy syndrome.

### **What is the characteristic EEG abnormality in seizure disorders?**

Spikes and sharp waves

### **What is the difference between a spike and a sharp wave?**

A spike is more pointed (20-70 msec. in duration), than a sharp wave (70-200 msec.)

### **What is the significance of a spike or sharp wave on EEG?**

Signature of a potentially "epileptogenic" area in the region of brain originating the spike

### **What is the most common EEG finding in complex partial seizures?**

Focal spikes recorded in the region of the scalp overlying the epileptogenic region

### **What percent of patients with complex partial seizures have a normal interictal EEG?**

20-40%

### **What percent of patients with generalized seizures have a normal interictal EEG?**

About 10%, but this varies greatly, depending on the epilepsy syndrome

### **What is the most sensitive and specific method to determine whether a spell is a seizure?**

Simultaneous video and EEG monitoring during a spell

### **What EEG findings during a spell suggest pseudoseizure?**

Normal EEG

### **Does lack of EEG change during a spell always exclude a seizure?**

No. Simple partial seizures (e.g. auras) are not usually accompanied by EEG changes and frontal lobe seizures may only have subtle changes.

### **When may intracranial monitoring be indicated in the evaluation of seizures?**

When considering surgery to resect an epileptogenic region.

### **List 2 common types of intracranial electrodes.**

Depth electrodes which are thin coated flexible wires that pierce into brain parenchyma, such as the hippocampus.

Subdural electrodes which lie on the brain surface. They may be strips of electrodes (typically 4 to 6 contacts) or grids of electrodes (as large as 8 x 8 contacts).

**When is neuroimaging indicated in the evaluation of seizures?**

In the evaluation of most types of partial seizures, especially when there is other evidence of neurologic dysfunction (e.g., hemiparesis) to suggest a symptomatic epilepsy. Seizures of adult onset always require neuroimaging.

**What neuroimaging study is most sensitive and specific?**

MRI

**What is the difference between positron emission tomography (PET) and single photon emission computed tomography (SPECT)?**

PET uses radionuclides, such as fluorodeoxyglucose (FDG), to detect regional glucose utilization which implies cellular metabolic activity. SPECT uses radionuclides, such as technetium 99 m-HMPAO, to detect regional perfusion.

**What interictal PET finding is helpful in localizing site of seizure onset?**

Focal hypometabolism. This is relatively more useful in lateralizing temporal lobe seizures.

**What ictal PET finding is helpful in localizing the site of seizure onset?**

Focal hypermetabolism, but logistically ictal PET is relatively difficult to obtain.

**What ictal SPECT finding is helpful in localizing the site of seizure onset?**

Focal hyperperfusion in the area originating the seizure. The radionuclide must be injected within 90 sec. of seizure onset.

**What interictal SPECT finding is helpful in localizing the site of seizure onset?**

Focal hypoperfusion. However, if an anatomic defect is present, it may result in hypoperfusion even if it is not the origin of the seizures.

## TREATMENT

**What is the generic name for each of the following brand name antiepileptic drugs (AEDs):**

**Cerebyx**

Fosphenytoin

**Dilantin**

Diphenylhydantoin or phenytoin

**Tegretol**

Carbamazepine

**Depakene**

Valproic acid

**Depakote**

Divalproex sodium

**Zarontin**

Ethosuximide

**Mysoline**

Primidone

**Neurontin**

Gabapentin

**Lamictal**

Lamotrigine

**Topamax**

Topiramate

**Valium**

Diazepam

**Ativan**

Lorazepam

**Phenobarbital**

There is no common brand name

**What is the treatment of a provoked seizure?**

Relief of the provoking factor, e.g. correction of metabolic abnormalities

**What is the treatment of a single seizure without an identifiable provoking factor?**

If the seizure is due to an epilepsy syndrome, then therapy may be initiated, depending on the natural history of the syndrome. If the etiology is unknown, then generally antiepileptic drugs are not started until after the second seizure, but this is controversial.

**Which AEDs are useful for simple partial and complex partial seizures as part of most epilepsy syndromes?**

All except ethosuximide.

**What is the efficacy of these drugs for control of complex partial seizures in TLE?**

About 30% of patients continue to have complex partial seizures despite maximal drug therapy.

**What curative surgery is available for some patients with temporal lobe epilepsy?**  
Resection of part of the temporal lobe, "anterior temporal lobectomy"

**Which AED is useful only for generalized seizures, especially absence seizures in childhood absence epilepsy?**  
Ethosuximide

**How effective is it?**

It renders most patients with childhood absence epilepsy seizure free.

**What other AED is useful for absence seizures?**

The valproic acid derivatives, Depakote and Depakene

**Which AED is most useful for both myoclonic jerks and convulsions in juvenile myoclonic epilepsy?**

The valproic acid derivatives, Depakote and Depakene

**Which AED is the drug of choice in patients with both partial and generalized seizures?**

The valproic acid derivatives, Depakote and Depakene

**What is the drug of choice for treatment of infantile spasms?**

Adrenocorticotrophic hormone (ACTH) initially; valproic acid for maintenance therapy

**What is the most important factor determining the risk of seizure recurrence after withdrawal of AEDs?**

Etiology. The risk of seizure recurrence is determined by the natural history of the epilepsy syndrome. For example, patients with JME are very well controlled with medications but almost universally will have seizures when medication is withdrawn.

**What is the risk of seizure recurrence after medication withdrawal?**

20-70%, even for patients who are good candidates for drug withdrawal.

**What factors portend a poorer prognosis after medication withdrawal?**

Known or suspected structural brain disease (especially if present since birth), less than 2 years seizure free, abnormal EEG