Clinical Epilepsy

American Epilepsy Society
I. Definitions and Epidemiology

A. Seizure

A seizure is the manifestation of an abnormal, hypersynchronous discharge of a population of cortical neurons. This discharge may produce subjective symptoms or objective signs, in which case it is a clinical seizure, or it may be apparent only on an electroencephalogram (EEG), in which case it is an electrographic (or subclinical) seizure. Clinical seizures are usually classified according to the International Classification of Epileptic Seizures (Table 1). Although all classification schemes have limitations, this is the best one currently available. The incidence of new-onset seizures in the general population is approximately 80 per 100,000 per year; approximately 60% of these patients will have epilepsy, a tendency toward recurrent unprovoked seizures. The diagnosis of a particular seizure type, and of a specific type of epilepsy (epilepsy syndrome), directs the diagnostic workup of these patients and their initial therapy. (Slide 2 & 3)
TABLE 1. ANNOTATED INTERNATIONAL CLASSIFICATION OF EPILEPTIC SEIZURES

<table>
<thead>
<tr>
<th>I. Partial seizures (seizures beginning locally)</th>
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<tbody>
<tr>
<td>A. Simple partial seizures (consciousness not impaired)</td>
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<tr>
<td>1. with motor symptoms</td>
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<td>2. with somatosensory or special sensory symptoms</td>
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<td>3. with autonomic symptoms</td>
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<td>4. with psychic symptoms</td>
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<tr>
<td>B. Complex partial seizures (with impairment of consciousness)</td>
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<tr>
<td>1. beginning as simple partial seizures and progressing to impairment of consciousness</td>
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<tr>
<td>a. without automatisms</td>
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<tr>
<td>b. with automatisms</td>
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<tr>
<td>2. with impairment of consciousness at onset</td>
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<tr>
<td>a. without automatism</td>
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<tr>
<td>b. with automatism</td>
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| C. Partial seizures (simple or complex), secondarily generalized |   |

<table>
<thead>
<tr>
<th>II. Generalized seizures (bilaterally symmetric, without localized onset)</th>
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<tbody>
<tr>
<td>A. Absence seizures</td>
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<tr>
<td>1. true absence (‘petit mal’)</td>
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<tr>
<td>2. atypical absence</td>
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<tr>
<td>B. Myoclonic seizures</td>
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<td>C. Clonic seizures</td>
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<tr>
<td>D. Tonic seizures</td>
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<tr>
<td>E. Tonic-clonic seizures (‘grand mal’)</td>
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<tr>
<td>F. Atonic seizures</td>
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| III. Unclassified seizures |   |
1. Partial Seizures

Partial seizures are divided into two main types, depending on whether or not consciousness is fully preserved. During simple partial seizures, consciousness is preserved; the person is alert, can respond to questions or commands, and can remember what occurred during the seizure. Simple partial seizures with subjective symptomatology are often referred to as auras. During complex partial seizures, consciousness is altered or lost; the ability to pay attention or respond to questions or commands is thus impaired or lost. Often, there is no memory of what happened during all or part of the complex partial seizure. The distinction between simple and complex partial seizures is critical, because activities such as driving and operating dangerous machinery must be restricted in patients with uncontrolled complex partial seizures; restrictions for people with only simple partial seizures depend on the specific seizure manifestations (and, for driving, on regulations in a particular state). Partial onset seizures may progress to secondarily generalized seizures. (Slide 4)
1a. Simple Partial Seizures

The diverse range of simple partial seizures gives rise to diagnostic challenges. For example, paresthesias (tingling sensations) in the fifth finger spreading to the forearm can result from a seizure, migraine, transient ischemic attack, or ulnar nerve disorder. Sudden abdominal discomfort may be produced by a gastrointestinal disorder as well as by a seizure arising from brain structures subserving autonomic or visceral function. When occurring in isolation, these symptoms may not be recognized as seizures by the patient or doctor.

Motor seizures alter muscle activity. Localized tonic posturing (stiffening) or clonic movements (twitching, jerking) can occur. Abnormal movements may be restricted to one body part or involve gradual spread to adjacent areas on the same side of the body (Jacksonian seizure) or both sides of the body with loss of consciousness (secondarily generalized seizure).

Although ictal weakness, rather than stiffening or jerking, of one or more body parts is rare during partial motor seizures, postictal weakness in the affected region is common after a partial seizure; this is a Todd’s paralysis. Todd’s paralysis usually lasts minutes to hours, but even more prolonged postictal paralysis can occur, especially in patients with structural lesions such as tumor or stroke. Although initially described as a postictal hemiparesis, the term “Todd’s paralysis” has been used more loosely to describe any postictal focal deficit, such as somatosensory, visual, or language impairment.

Epileptic discharges that occur in the sensory cortex may produce sensory seizures that manifest as hallucinations or illusions, for example; a sensation of something that is not there or distortion of a true sensation. Hallucinations may remain restricted to one area (e.g., paresthesias in a finger) or spread to other areas (e.g., entire upper extremity or entire side in a Jacksonian sensory march). Hallucinations and illusions can involve any sensory modality, including touch (e.g., pins and needles, electrical sensations), smell or taste (e.g., chemical or metallic sensations, often unpleasant), vision (e.g., flashing lights, complex scene), and hearing (e.g., buzzing, person’s voice).

Autonomic seizures are common, evoking changes in autonomic activity (e.g., altered heart or breathing rate, sweating) or visceral sensations (e.g., in abdomen or chest). (Slide 5)
Psychic seizures affect how we feel, think, and experience things. Patients may report a “dreamy state,” transitional between waking and unconsciousness. Psychic seizures can alter language function, perception or memory. They can also evoke spontaneous emotions (e.g., fear, anxiety, or depression), altered perceptions of time or familiarity (time slowing down or speeding up; deja vu—new experiences appear familiar, jamais vu—familiar things appear foreign), depersonalization (feeling one is not oneself), derealization (the world seems unreal, dream-like), or autoscopy (viewing one’s body from outside).

Auras are simple partial seizures that may precede loss of consciousness (progression to a complex partial or secondarily generalized seizure). People with particularly vivid or disabling complex partial seizures may also use this term to refer to the earliest and mildest ictal symptoms. Many patients recognize the aura as a ‘warning’ that a larger seizure is about to occur. The aura may allow the patient to avoid injury or embarrassment by seeking a safe place to sit or lie down before the larger seizure occurs.

1b. Complex Partial Seizures

Complex partial seizures impair consciousness and occur in all age groups. Typically, staring is accompanied by impaired responsiveness, cognitive function, and recall, although some degree of responsiveness may be preserved (e.g., orienting toward a stimulus). Automatic movements (automatisms) are common and involve the mouth (e.g., lip smacking, chewing, swallowing), upper extremities (e.g., fumbling, picking), vocalization/verbalization (e.g., grunts, repeating a phrase), or complex acts (e.g., shuffling cards). More dramatic automatisms occasionally occur (e.g., screaming, running, disrobing, pelvic thrusting). Complex partial seizures usually last from 15 seconds to 3 minutes. After the seizure, postictal confusion is common, usually lasting less than 15 minutes, although other symptoms, such as fatigue, may persist for hours. (Slide 6)

1c. Secondarily Generalized Seizures

Partial seizures can spread to become tonic-clonic seizures (see 2e), or secondarily generalize. Patients may recall an aura, and witnesses may first observe a complex partial seizure that progresses to a tonic clonic seizure. Once a partial seizure secondarily generalizes into a tonic clonic seizure, it is generally impossible to differentiate from a primarily generalized seizure. The electroencephalogram (EEG), neurologic exam (especially postictally), and neuroimaging tests (CT or MRI) often help distinguish these seizure types. (Slide 7)

The EEG in partial seizures is variable. During simple partial seizures, scalp-recorded EEG may be normal, or show quite localized or lateralized abnormal rhythmic activity (Slide 8 & 9 same seizure). During complex partial seizures, bilateral, often asymmetric, rhythmic activity is usually seen. During secondarily
generalized seizures, rhythmic activity is usually high amplitude and diffuse, although it is usually obscured by artifact from the abundant muscle activity characterizing these seizures.

2. Generalized Seizures

The principal types of generalized seizures are absence, atypical absence, myoclonic, atonic, tonic, and tonic-clonic.

2a. Typical and Atypical Absence

Absence (petit mal) seizures are brief episodes, usually lasting 3-20 seconds, of staring with impairment of awareness and responsiveness. Seizures begin and end suddenly. There is no warning before the seizure, and immediately afterward the person is alert and attentive. This lack of a postictal period is a key feature that allows one to distinguish between absence and partial complex seizures. If duration is >10 seconds, there are often accompanying motor phenomena (e.g., eye blinks, brief automatic mouth or hand movements, changes in muscle tone). These spells usually begin between ages 4 and 14 years, and usually resolve by age 18. Absence seizures are often provoked by hyperventilation, an effective means of reproducing seizures in the office or during the EEG. The EEG signature of absence epilepsy is the generalized 3 Hz spike-wave discharge (Slide 10). Children with typical absence seizures usually have normal development and intelligence.

Atypical absence seizures also occur predominantly in children, usually beginning before 6 years of age. Atypical absences may begin and end gradually (over seconds), usually last 5-30 seconds, and are not generally provoked by rapid breathing. The child stares, but the reduction in responsiveness is usually incomplete. Eye blinking or slight twitching movements of the lips may be seen. Because atypical absence seizures often occur in children with global cognitive impairment, the seizures may be difficult to distinguish from the child’s usual behavior. The EEG usually shows generalized “slow spike-wave” complexes (i.e., <2.5 Hz). Atypical absence seizures usually arise during childhood, but may persist into adulthood. Atonic and tonic seizures often occur in patients with atypical absence seizures.

2b. Myoclonic Seizures

Myoclonic seizures involve a brief, shock-like jerk of a muscle or group of muscles. Benign myoclonus occurs in healthy people (e.g., while falling asleep). This is not a myoclonic seizure. Pathologic myoclonus can result from epileptic and nonepileptic causes. Epileptic myoclonus usually causes bilateral, synchronous jerks most often affecting the neck, shoulders, upper arms, body, and upper legs. Consciousness does not usually seem to be impaired, although this is difficult to verify given the brief duration of <1 second; if
several occur in rhythmic succession, this may be termed a clonic seizure, and may be associated with altered awareness. EEG during a myoclonic seizure typically shows a poly-spike-and-slow-wave discharge. Myoclonic seizures occur in a variety of epilepsy syndromes; rarely they are part of a progressive, degenerative condition (i.e., progressive myoclonus epilepsy).

2c. Atonic Seizures

Atonic seizures consist of a sudden loss of postural tone, often resulting in falls, or, when milder, head nods or jaw drops. Consciousness is usually impaired and significant injury may occur. Duration is usually several seconds, rarely more than 1 minute. EEG typically shows generalized slow spike-wave or poly-spike-and-slow-wave complexes. It should be noted that epileptic drop attacks may occur not just with atonic seizures, but also with myoclonic or tonic seizures if the legs are involved.

2d. Tonic Seizures

Tonic seizures, like atypical absence and atonic seizures, are most common in people with other neurologic abnormalities in addition to epilepsy. They often occur during sleep, and are characterized by flexion at the waist and neck, abduction and flexion or extension of the upper extremities, and flexion or extension of the lower extremities. Typical duration is 5-20 seconds. In contrast to partial motor seizures, tonic seizures are generalized, involving bilateral musculature in a symmetric or nearly symmetric manner. EEG usually shows generalized, low-voltage, fast polypsikes.

2e. Tonic-Clonic Seizures

Primary generalized tonic-clonic (also called grand mal or convulsive seizures) seizures cause loss of consciousness associated with an initial tonic phase of stiffening, a fall, and often a cry evoked by air forced through contracted vocal cords. Legs are usually extended, and arms may be extended, flexed, or each in succession. The subsequent clonic phase consists of jerking of the extremities which gradually slows before stopping. Tonic-clonic seizures usually last 30-120 seconds. There may be drooling or foaming resulting from lack of swallowing and excessive salivation; biting of the tongue, cheek, or lip, causing bleeding; and bladder or bowel incontinence. Postictal lethargy and confusion often last minutes to hours, and may be followed by transient agitation. The EEG shows generalized polyspike, but these are usually obscured by muscle artifact. Postictally, there is background suppression and then diffuse slowing.
B. Epilepsy

At least two unprovoked seizures are required for the diagnosis of epilepsy. In the past, physicians were reluctant to make this diagnosis even after repeated seizures, because of the adverse consequences including social stigmatization and limitations on driving and employment. Despite advances in public understanding of the condition, these issues remain active. The euphemism seizure disorder has been frequently employed to avoid the term epilepsy, and may also be used to refer to situations characterized by recurrent seizures where each is provoked by an identifiable stimulus; for example, febrile convulsions. The current definition of epilepsy is the tendency to have repeated seizures (at least two) as a consequence of a brain disorder, that is, unprovoked by an acute systemic or brain insult. This definition stresses that the problem is one of brain function, and that the patient has the potential for more seizures. This definition excludes seizures due to exogenous factors, such as ethanol or sedative drug withdrawal, or to metabolic disorders, such as nonketotic hyperglycemia.

Estimates of the annual incidence of epilepsy in the general population range from 30 to 57 per 100,000. These rates vary with age, being high in infants and young children, then decreasing throughout adulthood until approximately age 60, when they again begin to increase. The overall prevalence of epilepsy is approximately 6 per 1000.

Epilepsy is an umbrella term, under which many types of diseases and syndromes are included. The current classification of the epilepsies and epileptic syndromes attempts to separate these disorders according to their putative brain origins, that is, whether they arise in a circumscribed portion of the brain (partial), or appear to begin diffusely in the cortex and its deeper connections (generalized) (Table 2). The syndrome is idiopathic when the disorder is not associated with other neurologic or neuropsychologic abnormalities; symptomatic indicates that such an abnormality is present and the cause is known. Cryptogenic refers to syndromes that are presumed to be symptomatic but the cause in a specific patient is unknown. Many idiopathic epilepsies occur in children and adolescents, and often remit in adolescence or adulthood. There is evidence that most or all of these syndromes have a genetic basis, and that when this basis becomes known, they will move from the idiopathic to the symptomatic category. (Slide 11)

Some authors distinguish between epilepsies and epileptic syndromes, depending on whether seizures are the only neurologic disorder (an epilepsy) or are one of a group of symptoms (an epileptic syndrome). Some of the epilepsies (e.g., juvenile myoclonic epilepsy) have well-defined genetics, clinical courses, and responses to medication. Others (e.g., temporal lobe epilepsy) have natural histories which are highly variable, and which reflect differences in pathology as well as in host response to that pathologic process and to the treatments administered. (Slides 12, 13 & 14)
### TABLE 2. ANNOTATED PROPOSAL INTERNATIONAL CLASSIFICATION OF EPILEPSIES AND EPILEPTIC SYNDROMES

<table>
<thead>
<tr>
<th>1. Localization-Related (Local, Focal, Partial) Epilepsies and Syndromes</th>
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</thead>
<tbody>
<tr>
<td><strong>1.1 Idiopathic</strong> (with age-related onset)</td>
</tr>
<tr>
<td>• benign childhood epilepsy with centrotemporal spikes (‘rolandic epilepsy’)</td>
</tr>
<tr>
<td>• childhood epilepsy with occipital paroxysms</td>
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<tr>
<td><strong>1.2 Symptomatic</strong></td>
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<tr>
<td>• chronic progressive epilepsia partialis continua of childhood (e.g., ‘Rasmussen’s encephalitis’)</td>
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<tr>
<td>• frontal lobe epilepsies</td>
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<tr>
<td>• occipital lobe epilepsies</td>
</tr>
<tr>
<td>• parietal lobe epilepsies</td>
</tr>
<tr>
<td>• syndromes characterized by specific modes of precipitation</td>
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<tr>
<td>• temporal lobe epilepsies</td>
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<tr>
<td><strong>1.3 Cryptogenic</strong></td>
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<table>
<thead>
<tr>
<th>2. Generalized Epilepsies and Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.1 Idiopathic</strong> (with age-related onset)</td>
</tr>
<tr>
<td>• benign neonatal familial convulsions</td>
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<tr>
<td>• benign neonatal convulsions</td>
</tr>
<tr>
<td>• benign myoclonic epilepsy in childhood</td>
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<tr>
<td>• childhood absence epilepsy (pyknolepsy)</td>
</tr>
<tr>
<td>• juvenile absence epilepsy</td>
</tr>
<tr>
<td>• juvenile myoclonic epilepsy</td>
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<tr>
<td><strong>2.2 Cryptogenic or Symptomatic</strong></td>
</tr>
<tr>
<td>• West syndrome</td>
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<tr>
<td>• Lennox-Gastaut syndrome</td>
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| 3. Epilepsies and Syndromes Undetermined Whether Focal or Generalized |
II. Evaluation After the First Seizure

The initial evaluation after a single seizure should: 1) determine whether a seizure actually occurred, or whether the patient experienced some other transient event; 2) search for evidence of partial onset; 3) search for evidence of underlying central nervous system dysfunction; 4) search for evidence of systemic or metabolic disorders that could have precipitated the seizure; 5) attempt to classify the patient’s seizure and condition according to the schemata of Tables 1 and 2; 6) determine what diagnostic studies are appropriate; and 7) determine whether drug therapy should be instituted, and if so, with what agent. (Slide 15)

Often, the patient is amnestic for the events surrounding the seizure, and the description must be obtained from relatives, friends, or bystanders. Observers may report behavior consistent with a complex partial seizure immediately preceding a convulsion. In other cases, the patient may recall localized motor activity, suggesting a simple partial motor seizure before losing consciousness. At times, the only evidence of partial onset may be a brief subjective event consistent with an aura; in this case it is important to determine whether the identical aura ever occurred before.

One or more precipitating factors can contribute to the patient’s seizure. The discovery of a precipitant does not obviate the need to search for intracranial pathology or a genetic predisposition toward seizures, but may lead to a non-epilepsy diagnosis (e.g., alcohol withdrawal seizure), and is very useful in counseling the patient. Common precipitants include metabolic and electrolyte imbalance (such as low blood glucose, low sodium, low calcium or low magnesium), antiepileptic medication reduction or inadequate AED treatment, hormonal variations, stress, infection, severe sleep deprivation, withdrawal from alcohol or other sedative agents, and administration of drugs with proconvulsant properties, such as central nervous system stimulants including cocaine, anticholinergics (including over-the-counter antihistamines), almost all dopamine blocking agents, newer antipsychotics (particularly clozapine), antidepressants (especially bupropion), immune suppressants such as cyclosporine, and antibiotics such as quinolones or imipenem-cilastatin. (Slides 16, 17 & 18)

The examination of the patient who has experienced a seizure is often most revealing when conducted as soon after the seizure as possible, and should be frequently repeated to determine whether or not any observed deficits are transient. Postictal weakness, aphasia, or sensory dysfunction provide powerful lateralizing and sometimes localizing information. Upper motor neuron signs which are briefly present postictally (e.g., a transient unilateral Babinski sign) also provide important data. Signs which are not transient may indicate a pre-existing structural lesion (e.g., tumor) or a new condition (e.g., stroke), and
may lead to the diagnosis of an acute symptomatic seizure, that is, a seizure resulting from a new brain insult, which does not necessarily imply the existence of epilepsy (although epilepsy may later develop). (Slide 19)

There are no pathognomonic physical signs proving that an event was a seizure, but there are many useful associations. Bites on the side of the tongue or cheek, and urinary and/or fecal incontinence, are more common after seizures than after loss of consciousness from other causes. The general physical examination is otherwise most useful when it uncovers evidence of a precipitant for an acute symptomatic seizure (e.g., meningitis), or of a genetic predisposition to seizures, such as a neurocutaneous syndrome (e.g., tuberous sclerosis).

The laboratory evaluation of a patient after a single seizure depends on the circumstances surrounding the event. Blood tests should be tailored to the patient’s age and clinical circumstances. Routine blood tests can indicate problems such as hypo- or hyperglycemia; sodium, calcium or magnesium deficiency; compromised cardiorespiratory, liver or kidney function; or infection. Any suspicion of meningitis or encephalitis mandates lumbar puncture (after assessing potential for brain herniation), but otherwise this procedure is generally not necessary. Because many illicit drugs can cause seizures, toxic screens of blood and/or urine should be performed, especially in adolescents and young adults.

Patients who have had a new-onset seizure should undergo an electroencephalogram (EEG) and, with certain definable exceptions, magnetic resonance imaging (MRI). A CT scan is useful if an acute process is suspected (e.g., intracerebral hemorrhage), but is inadequate to exclude small tumors or vascular malformations, hippocampal atrophy, and cortical dysplasia. Some common exceptions to the need for neuroimaging are children with uncomplicated febrile convulsions or with firm clinical and EEG findings consistent with well-defined idiopathic syndromes such as childhood absence epilepsy or benign epilepsy with centrotemporal spikes.

The EEG is most useful for classifying the seizure type and, in many cases, the epilepsy syndrome. A normal EEG does not exclude the diagnosis of epilepsy. The EEG is only a very brief time sample of the patient’s brain electrical activity and will miss intermittent or transient abnormalities. In evaluating a patient suspected to have had a seizure, an EEG showing interictal (between seizures) epileptiform activity provides corroborating evidence, but is not proof, unless the patient has a seizure during the EEG (in which case the epileptiform activity is ictal rather than interictal).

Epileptiform activity includes spikes, sharp waves, electrographic seizures, and some other stereotyped phenomena which are strongly associated with seizures. Spikes and sharp waves are interictal epileptiform events. Background abnormalities indicate localized or diffuse cerebral dysfunction, and may reflect a transient postictal disturbance or the underlying process responsible for the seizure. (Slide 20)
III. TREATMENT

A. Single seizure: deciding whether or not to treat

Whether therapy with antiepileptic drugs (AEDs) should be initiated after a first seizure is controversial. Within 5 years after a single, unprovoked seizure, 16–62% of patients have another seizure. Recurrence is more likely if there has been an earlier neurologic injury sufficient to cause seizures; a structural abnormality on neuroimaging; an abnormal, particularly epileptiform, EEG; or a family history of epilepsy. Most studies also suggest that partial (including secondarily generalized) seizures are more likely to recur than primarily generalized tonic-clonic seizures. Treatment can reduce (perhaps by 50%) but not eliminate the risk of a second seizure. The treatment decision must be made individually for each patient, considering the potential physical, psychological, and vocational consequences of further seizures and of AED therapy. (Slide 21)

B. Drug Choice

Before treatment is instituted, the clinician must decide whether the patient’s seizures are partial or generalized in onset. The drug of choice should have the best efficacy (ability to stop seizures) and lowest likelihood of adverse effects. Several comparison studies have shown minimal differences in efficacy of the standard AEDs. Thus, differences in expected adverse effect profile, and pharmacokinetic profile, as well as expense, should guide AED choice. Most patients can be optimally managed on a single AED. One must be sure that a given drug has failed before moving on to an alternative drug or a two-drug combination. If the patient has persistent seizures but no adverse effects, the dose can be increased as tolerated or until seizure control is obtained (Slide 22). The “therapeutic range” of serum concentrations is only a guideline—the patient’s clinical state determines the appropriate dose.

In partial onset seizures with secondary generalization, carbamazepine, phenytoin, valproate, phenobarbital, and primidone are usually effective (Table 3). In partial seizures without generalization, phenytoin and carbamazepine may be slightly more effective. These conclusions are based on direct randomized comparison studies of these medications. Felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide are new antiepileptic drugs approved by the FDA since 1993. These drugs mark the beginning of new treatment options for epilepsy, and several new AEDs are likely to be approved within the next few years. After randomized clinical trials, all eight drugs received
**TABLE 3. COMMONLY USED ANTIEPILEPTIC DRUGS**

### Partial Seizures (with or without secondary generalization)

- carbamazepine
- phenytoin
- valproate
- phenobarbital
- primidone
- felbamate
- lamotrigine
- gabapentin
- lamotrigine
- levetiracetam
- oxcarbazepine
- topiramate
- tiagabine
- zonisamide

### Generalized Seizures

#### Absence
- ethosuximide
- valproate
- lamotrigine
- topiramate
- levetiracetam

#### Myoclonic
- valproate
- clonazepam
- lamotrigine
- topiramate
- levetiracetam
- zonisamide

#### Tonic-clonic
- valproate
- phenytoin
- carbamazepine
- felbamate**
- lamotrigine
- topiramate
- levetiracetam
- zonisamide

* **for tonic-clonic seizures associated with the Lennox-Gastaut syndrome**
FDA approval for adjunctive treatment in patients with partial onset seizures. Lamotrigine has also been approved as monotherapy in adults with partial seizures after failure of an enzyme-inducing AED such as phenytoin or carbamazepine. Felbamate and oxcarbazepine have also been approved for monotherapy, and the recent American Academy of Neurology AED recommendations include topiramate monotherapy for refractory partial seizures. (Slide 23)

In patients with generalized-onset seizures, the AED choice depends on the specific epileptic syndrome, and particularly the different types of generalized seizures associated (Table 3). In generalized epilepsies characterized by tonic-clonic seizures, myoclonic seizures, and/or absence seizures, or in photosensitive epilepsy, valproate is usually considered the drug of choice; AEDs discussed above for partial seizures, such as phenytoin and carbamazepine, are effective for tonic-clonic but not for other types of generalized seizures. In children with only absence seizures (no tonic-clonic seizures), ethosuximide and valproate are equally effective. Valproate has the advantage of protecting against the tonic-clonic seizures which may develop later; because of the risk of rare but potentially fatal valproate-induced hepatotoxicity, however, ethosuximide is considered safer. This valproate risk is maximal in children under age 2 years, especially those under age 6 months or with congenital metabolic disorders, who are treated with multiple AEDs. Clonazepam and phenobarbital or primidone can be useful in generalized seizures but often have greater sedative and behavioral effects than other AEDs. Clonazepam, a benzodiazepine, may lose some of its effectiveness after six months or less, due to the development of tolerance. Lamotrigine, topiramate, and zonisamide may be effective against some primarily generalized seizures, such as tonic-clonic, absence, and tonic seizures. Carbamazepine may exacerbate some generalized-onset seizures including absence and myoclonic seizures. This underscores the need for appropriate seizure classification for adequate selection of the AED. (Slides 24, 25 & 26)

Many AEDs are associated with potential teratogenic effects. Both valproate and carbamazepine may cause neural tube defects, which may result in spina bifida and anencephaly. These birth defects may be prevented by folic acid supplementation. Folic acid supplementation (0.4 mg/day) is recommended by the CDC for all women of childbearing age. Most neurologists prescribe a larger dose of folic acid (1 mg/day) for women with epilepsy. For women with a history of neural tube defects, or those taking carbamazepine or valproate, neurologists generally prescribe an even higher dose (4-5 mg/day).
C. **Practical Pharmacology of AEDs**

Different AEDs have widely different dose ranges, pharmacokinetics, therapeutic ranges of blood concentrations, and adverse effects (Table 4).

For example, phenytoin, one of the most commonly used AEDs, has unusual and somewhat difficult pharmacokinetic characteristics. It exhibits nonlinear kinetics because the metabolic enzymes saturate at commonly used doses. Thus, small dose changes can produce large changes in serum concentration; these changes get even larger as serum concentrations increase. Helpful clinical rules for phenytoin include: 1) if the initial serum concentration is below 7 mg/l and the dose needs to be increased, increase the daily dose by 100 mg; 2) if the serum concentration is between 7 and 11, and the dose needs to be increased, increase the daily dose by 50 or 60 mg (using the 50 mg tablet or two 30 mg capsules); 3) if the serum concentration is above 11 and the dose needs to be increased, increase the daily dose by 30 mg.

The new AEDs have several unique features. Gabapentin and levetiracetam undergo no hepatic metabolism or protein binding, and therefore have no important pharmacokinetic interactions with other AEDs, an advantage for combination therapy. Lamotrigine is also generally well tolerated, but is associated with rash, and must be titrated slowly. Topiramate, tiagabine, zonisamide and oxcarbazepine must also be titrated slowly to minimize cognitive side effects; topiramate and zonisamide, in addition, have a 1-2% incidence of renal stones. Felbamate was approved as monotherapy as well as adjunctive therapy for partial seizures, and for generalized seizures in children with Lennox-Gastaut syndrome (a severe epileptic syndrome; see Pediatric Epilepsy section). After release and exposure to over 100,000 patients, however, more than 40 cases of aplastic anemia or hepatic failure were reported, and the FDA recommends using this drug only when the potential benefits outweigh the risks. The place of these new AEDs in seizure treatment is evolving, and we need further studies and experience to determine whether the new AEDs will become first-line agents.

Most epilepsy patients are best managed with a single drug. **Monotherapy** can simplify treatment regimens, reduce adverse effects, and often improve seizure control. Only after one or more attempts to achieve a simplified regimen should one conclude that a given patient requires polytherapy. Patients on multiple AEDs should be considered for conversion to monotherapy, because even those with uncontrolled seizures may have equivalent or improved seizure control as well as fewer adverse effects by using high doses of a single AED rather than drug combinations. The clinician should first determine whether the patient has had an adequate trial of a first-line agent—i.e., whether seizures persisted even when the AED was gradually increased until troublesome adverse effects developed. When converting patients to
## TABLE 4: INFORMATION ON COMMON ANTIEPILEPTIC DRUGS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Daily Adult Dose (mg)</th>
<th>Half-Life (Hours)</th>
<th>Initial Target Range of Plasma Concentrations (µg/ml)</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbamazepine</td>
<td>600-1800</td>
<td>8-24*</td>
<td>4-12</td>
<td>Drowsiness, blurred vision, diplopia, dysequilibrium, leukopenia, hepatic failure</td>
</tr>
<tr>
<td>ethosuximide</td>
<td>500-1000</td>
<td>60</td>
<td>40-100</td>
<td>Gastrointestinal upset, mood changes, lethargy, hiccups, headache</td>
</tr>
<tr>
<td>felbamate</td>
<td>2400-3600</td>
<td>23</td>
<td>40-100</td>
<td>Nausea, insomnia, headaches, anorexia, aplastic anemia, hepatic failure</td>
</tr>
<tr>
<td>gabapentin</td>
<td>1200-2400</td>
<td>5-7</td>
<td>4-16</td>
<td>Ataxia, dizziness, somnolence, fatigue, nystagmus</td>
</tr>
<tr>
<td>lamotrigine</td>
<td>100-250 (w/valproate) 300-500</td>
<td>24-31†‡‡</td>
<td>2-20</td>
<td>Rash, dizziness, diplopia, ataxia, somnolence</td>
</tr>
<tr>
<td>levetiracetam</td>
<td>1000-3000</td>
<td>6-8±</td>
<td>20-60</td>
<td>Somnolence, infection, headache</td>
</tr>
<tr>
<td>oxcarbazepine</td>
<td>1200-2400</td>
<td>2+</td>
<td>5-50 (MHD)</td>
<td>Dizziness, diplopia, headache, blurred vision, somnolence, nausea</td>
</tr>
<tr>
<td>phenobarbital</td>
<td>90-180</td>
<td>100</td>
<td>10-40</td>
<td>Sedation, depression, loss of concentration, mental dulling, hyperactivity</td>
</tr>
<tr>
<td>phenytoin</td>
<td>300-500</td>
<td>10-30‡</td>
<td>5-25</td>
<td>Ataxia, dysarthria, gingival hypertrophy, hirsutism, acneiform eruption, hepatic failure, osteomalacia</td>
</tr>
<tr>
<td>primidone</td>
<td>750-1250</td>
<td>10-20**</td>
<td>5-12</td>
<td>Sedation, dizziness, nausea, ataxia, depression</td>
</tr>
<tr>
<td>tiagabine</td>
<td>32-56</td>
<td>5-8</td>
<td>5-70</td>
<td>Dizziness, nervousness, abnormal thinking</td>
</tr>
<tr>
<td>topiramate</td>
<td>200-400 (with inducer)</td>
<td>21</td>
<td>2-25</td>
<td>Fatigue, psychomotor slowing, dizziness, weight loss, renal stones (1-2%)</td>
</tr>
<tr>
<td>valproate</td>
<td>1000-3000</td>
<td>10-20</td>
<td>50-150</td>
<td>Gastrointestinal upset, weight gain, hair loss, tremor, thrombocytopenia, liver failure, pancreatitis</td>
</tr>
<tr>
<td>zonisamide</td>
<td>200-600</td>
<td>63</td>
<td>10-40</td>
<td>Dizziness, ataxia, confusion, anorexia, nausea</td>
</tr>
</tbody>
</table>

*The half-life of carbamazepine is considerably longer when the drug is first introduced, before the autoinduction of microsomal enzymes in the liver.

**Primidone is metabolized, in part, to phenobarbital; the values given are for the parent compound.

†Half-life is variable and depends on serum concentration (range 7-140 hours)

††Half-life is reduced to 15 hours when used with inducer (phenytoin or carbamazepine) and prolonged to 30-100 hours when combined with valproate.

+Half-life of active metabolite, MHD, is 9 hours.

±Half-life of clinical effectiveness is considerably longer.
monotherapy, one should try to first eliminate more sedating drugs (barbiturates and benzodiazepines). These should be withdrawn slowly, usually over several months. Though monotherapy is preferred, some patients with epilepsy require polytherapy. (Slide 27)

Antiepileptic drugs that are highly bound to serum proteins (e.g., phenytoin, valproate, and tiagabine) may be displaced from binding sites by other highly protein bound drugs (e.g., aspirin, warfarin, phenothiazines). In these cases, the serum concentration may not accurately reflect the unbound proportion of drug. Unbound (free) serum concentrations can be helpful in patients taking these drugs with other highly protein bound drugs, or in patients with significant renal disease or hypoalbuminemia.

Most AEDs are metabolized by hepatic enzymes, and may either induce or inhibit hepatic metabolism of other drugs. The exceptions are gabapentin and levetiracetam which have no measurable hepatic metabolism. Induction of hepatic enzymes by AEDs such as carbamazepine, phenytoin and phenobarbital may cause increased metabolism and decreased serum concentrations of many other drugs, such as steroid hormones (i.e., oral contraceptives) or warfarin. Felbamate and valproate are metabolic inhibitors and can increase serum concentrations of other hepatically metabolized drugs. Conversely, other drugs (e.g., erythromycin or fluoxetine, potent inhibitors) may inhibit the metabolism of AEDs. It is sometimes difficult to predict what type of interaction will occur when two AEDs or an AED and another drug are used together. (Slide 28)

The “therapeutic range” of AED serum concentrations are those that are often associated with seizure control without significant toxicity, and have been derived from population studies. This range is a useful guide, but cannot substitute for assessing the individual patient’s clinical response to an AED. Many patients can experience excellent seizure control and no adverse effects with serum concentrations above or below the therapeutic range. Further, some patients experience troublesome side effects with levels within or even below this range. Clinicians should not rigidly adhere to a therapeutic AED range but rather use serum concentrations to aid in balancing AED efficacy and toxicity. (Slides 29 & 30)
Pharmacokinetic factors should also be considered when interpreting AED serum concentrations. Most drugs need five half-lives to reach steady state. Drugs with long half-lives, such as phenytoin, phenobarbital, and zonisamide may require two weeks or more to reach steady-state. Thus, serum concentrations drawn too soon after drug initiation or dose change may not accurately reflect the steady-state. Conversely, serum concentrations of drugs with short half-lives may be significantly affected by the time interval between the last dose and the serum sample.

D. Dose Initiation and Monitoring

Before starting an AED, the patient should be informed about adverse effects and the realistic probability of efficacy. For example, fewer than 50% of adults with partial-onset seizures remain seizure-free for more than 12 months after starting first-line monotherapy. Patients should record seizure frequency and type and adverse effects on a calendar, so that efficacy can be quantitated and compared among AEDs. Potential provocative factors such as menses can also be charted. Most AEDs should be introduced slowly to minimize adverse effects. (Slide 31)

In addition, before starting AEDs, and at intervals during the first months of use, it is reasonable to check CBC, electrolytes, liver function tests, and serum drug concentrations.

E. Evaluation After Seizure Recurrence

When a seizure recurs, the major issues to consider include: 1) whether this is a manifestation of progressive pathology, such as a tumor or a neurodegenerative disorder; 2) whether there was a precipitant which could be avoided in the future; 3) if the patient was receiving an AED, a) whether compliance or some other pharmacokinetic factor (i.e. absorption, metabolism) is at issue, or b) whether the dose or the medication should be altered; and 4) if the patient was not taking medication, whether this recurrent seizure is an indication to institute treatment. (Slide 32)

In general, patients with partial seizures (with or without secondary generalization) who experience a change in seizure pattern, especially a change in the initial manifestation, should be evaluated for a progressive lesion with a neurologic exam, and possibly a repeat MRI and EEG.
For patients receiving AEDs, a recurrent seizure may be an indication to obtain a serum concentration of the drug. This is especially true of a patient whose seizures have been under good control for some period of time. If the serum concentration of an AED has fallen, one must determine the cause of the fall and attempt to re-establish the previously effective level. Conversely, if the patient has frequent seizures with serum concentrations in the “therapeutic” range, further measurements may not be useful and a change in management strategy may be indicated.

**F. Discontinuing Antiepileptic Drugs**

Antiepileptic drugs can eventually be withdrawn successfully in more than 60% of patients who remain free of seizures. Most neurologists require patients to be seizure free for 2 to 4 years before discontinuing AEDs, and the drugs are generally discontinued over a 2 to 6 month period. The underlying epileptic syndrome also may influence the success of antiepileptic drug withdrawal. For example, the success rate for drug discontinuation in juvenile myoclonic epilepsy is only about 20%, whereas in benign epilepsy with centrotemporal spikes, it is nearly 100%. The best prognosis for eventual withdrawal of AEDs is in patients with idiopathic generalized epilepsy (but not juvenile myoclonic epilepsy), a normal neurologic exam, and no structural brain lesion; even with these favorable factors, however, there is never a guarantee of remaining seizure free. (Slide 33)

For more information on AEDs, go to the pharmacology section.
IV. Non-Drug Treatments of Epilepsy

Although AEDs are the mainstay of treatment, alternative treatment modalities have varying degrees of clinical and experimental support. Lifestyle modifications, particularly avoidance of alcohol and sleep deprivation, can be very important in certain syndromes and individuals. Relaxation, biofeedback, and other behavioral techniques can help a subset of patients, especially those with a reliable aura preceding complex partial or secondarily generalized seizures. (Slide 34) Dietary supplements are of unproven value, except for pyridoxine (vitamin B6), which is crucial for treating rare pyridoxine dependency of neonates and infants and for seizures due to antituberculous therapy with isoniazid.

The ketogenic diet has been used for more than 80 years in children with severe seizure disorders, and is undergoing something of a revival. It is based on the observation that ketosis and acidosis have anti-seizure effects. Because of risks of severe metabolic abnormalities during and after the initial fasting period, this diet is initiated in the hospital. Strict protein, calorie, and especially carbohydrate restriction in the setting of a high fat diet is needed for ketosis, and may be difficult to maintain. In a minority of patients with intractable epilepsy, staying on this diet for months or years can result in a sustained improvement in seizure control, rarely even allowing withdrawal of AEDs. (Slide 35)

The vagus nerve stimulator (VNS), a device that provides intermittent electrical stimulation of the vagus nerve, was shown in several studies to be effective in reducing the frequency of complex partial seizures, and received FDA approval in 1997. The stimulator is similar to a cardiac pacemaker and is surgically implanted subcutaneously. Intermittent stimulation is delivered every 0.3-10 minutes for 7-30 seconds, but patients who experience a seizure warning can trigger the device manually. The mechanism by which stimulation reduces seizures is not well established. Adverse effects include hoarseness, throat pain, or a feeling of dyspnea during stimulation; these are generally mild. Central nervous system side effects typical of AEDs are not present. The stimulator has been studied only in combination with AED treatment, but in this setting, efficacy against medication-resistant partial seizures was comparable to that of some of the new AEDs. The cost of the device and its implantation may be limiting factors. (Slide 36)

Clinical trials show 26% effective and <5% seizure free.

The FDA has approved the device for partial onset seizures. VNS has a responder rate of 40% (i.e. 40% of patients have a 50% or more decrease in their seizures.)
V. Epilepsy Surgery

Most cases of epilepsy are well controlled with AEDs. However, 20 – 30% are not. Surgical therapy is worth considering in patients in whom seizures and/or medication side effects significantly impair quality of life. Surgical treatment is indicated in such patients if seizures arise from an area that can be removed without causing unacceptable neurological deficits. Candidacy for surgery is determined by a constellation of tests including video/EEG monitoring, neuroimaging, and neuropsychometric studies. In some cases, palliative surgical procedures are performed to reduce seizure frequency or severity even though there is a low expectation of cure. (Slide 37)

These procedures typically involve disconnections, such as cutting the corpus callosum, rather than removing brain tissue.

B. Evaluation

Overall, the most important determinant of a successful surgical outcome is patient selection. This requires detailed pre-surgical evaluation to characterize seizure type, frequency, and site of onset; neuropsychological, psychiatric, and psychosocial functioning; and degree of disability.

History and physical examination are performed to determine, if possible, the etiology, course, and functional impact of the patient’s epilepsy. Details of ictal events can provide important localizing information, such as an autonomic or psychic-cognitive aura suggesting mesial temporal lobe origin. Adequacy of previous, unsuccessful AED trials should be assured. (Slide 38)

Neuroimaging studies, particularly high-resolution MRI, should be performed. MRI is particularly useful in evaluating foreign tissue lesions (e.g., tumors), cortical dysplasia and other developmental abnormalities, gliosis, and neuronal loss as manifested by focal atrophy. Hippocampal atrophy, and sometimes signal abnormalities suggesting gliosis, are the hallmarks of mesial temporal sclerosis, the pathologic substrate of many cases of temporal lobe epilepsy successfully treated surgically.

Analysis of interictal as well as ictal EEG activity can provide evidence of localized cortical dysfunction, particularly if epileptiform activity (spikes, sharp waves, electrographic seizures) is seen. EEG activity at seizure onset is most important in localizing the seizure focus. Video/EEG monitoring can continuously record the EEG over hours, days, or even weeks, allowing careful inspection during any symptomatic event. In some cases, electrodes are surgically implanted in the brain (depth electrodes) or on the surface of the brain (subdural electrodes) when noninvasive studies do not sufficiently localize the site of seizure onset.
Formal neuropsychological testing can reveal specific focal or multifocal cognitive deficits that can at times be correlated with the neuroimaging and EEG data. This testing may help localize an abnormally functioning brain area and also serve as a baseline for post-surgical evaluation.

Psychiatric and psychosocial evaluation are vital to assess current level of functioning and to ensure that the patient and family have realistic goals and attitudes. This assessment also establishes a relationship that may be helpful in dealing with complicated adjustment issues that may occur even after successful epilepsy surgery.

Sodium amobarbital injections during carotid angiography accompanied by language and memory testing, the so-called Wada test, reveal critical information regarding lateralization of language and memory, which is necessary to assess whether the patient can tolerate epilepsy surgery.

C. Procedures

Epilepsy surgical procedures include anterior temporal lobectomy, which may be performed in a standardized or customized fashion. Temporal lobectomy is the most common surgical procedure for epilepsy, and can be performed in either the dominant or non-dominant hemisphere without significant language impairment. Among highly selected patients, more than 80% are free of complex partial or secondarily generalized seizures following surgery, though many remain on medications. Extra-temporal resections, most commonly in the frontal lobe and less often in the parietal or occipital regions, are performed mainly in patients with structural lesions or developmental abnormalities, and less often in cryptogenic focal epilepsies. Rare cases involving seizures arising from large parts of a cerebral hemisphere, associated with fixed hemispheric deficits, can be treated in children with a so-called anatomic or functional hemispherectomy. Palliative procedures such as corpus callosotomy may be performed in patients with intractable drop or atonic seizures as well as tonic-clonic and other generalized seizures. (Slide 39)

D. Results

The results of surgical intervention in appropriately selected candidates are generally positive, but vary with the specific operation performed. (Slide 40)

For more information go to Epilepsy Surgery Section.
VI. Status Epilepticus

Status epilepticus is defined as: 1) an episode of more than 30 minutes of continuous seizure activity, or 2) two or more sequential seizures spanning this period without full recovery between seizures. Clinically, however, most seizures last less than 5 minutes, and those persisting longer are unlikely to stop spontaneously. Therefore, one should initiate treatment for the seizures lasting longer than 5 minutes. (Slide 41)

The incidence of status epilepticus is at least 60,000 cases/year in the U.S., with higher rates among the very young and very old. Status epilepticus is an emergency because of its morbidity and mortality, and any seizure type may manifest as status epilepticus. The outcome of convulsive status epilepticus largely depends on etiology, but prompt treatment can improve outcome. (Slide 42)

From a practical standpoint, status epilepticus may be divided into convulsive and nonconvulsive forms. The convulsive forms may be generalized or partial. The nonconvulsive forms are difficult to classify on clinical grounds, but are often divided electroencephalographically into absence status (in which the EEG demonstrates generalized spike-wave activity) and complex partial status (in which the EEG may show a variety of localized rhythmic discharges).

Table 5 is based on a treatment protocol suggested by the Epilepsy Foundation. (Slides 43, 44 & 45)

Other treatment modalities include intravenous valproate instead of, or with phenytoin or phenobarbital, propofol instead of pentobarbital or midazolam, and epilepsy surgery if pharmacologic treatments are ineffective.
### TABLE 5. TIMETABLE FOR THE TREATMENT OF STATUS EPILEPTICUS

<table>
<thead>
<tr>
<th>Time (Min.)</th>
<th>Drug and Non-drug Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Ensure adequate respiration—intubation may be necessary and low flow oxygen should be started.</td>
</tr>
<tr>
<td>2-3</td>
<td>Start I.V. with normal saline. First draw blood for anticonvulsant levels, glucose, hepatic and renal function, CBC with diff., electrolytes, Ca, Mg, blood gases and toxicology screen. Obtain urine for routine U/A.</td>
</tr>
<tr>
<td>5</td>
<td>Start second I.V. line. Lorazepam 4 mg (.1mg/kg) or diazepam 10 mg (.2mg/kg)—infuse I.V. over 2 min. with saline for simultaneous administration of second medication and I.V. fluids.</td>
</tr>
<tr>
<td>7-8</td>
<td>Thiamine 100 mg, 50% D5W 25cc I.V. push. Phenytoin or fosphenytoin - 20 mg/kg (between 1000 and 2000 mg in most adults), I.V. push. Dilute in saline and infuse at a rate of no more than .75 mg/min/kg of body weight (no more than 50 mg/min phenytoin or 150 mg/min phenytoin equivalents of fosphenytoin in adults). In children less than 18 mo. of age pyridoxine 100-200 mg I.V. Monitor EKG and Blood Pressure.</td>
</tr>
<tr>
<td>10</td>
<td>Benzodiazepine—may be repeated.</td>
</tr>
<tr>
<td>30-60</td>
<td>Start continuous EEG monitoring unless status has stopped and the patient is waking up.</td>
</tr>
<tr>
<td>40</td>
<td>Phenobarbital—20 mg/kg (between 1000 and 2000 mg in most adults). Dilute in saline and infuse at a rate of no more than .75 mg/min/kg of body weight (50 mg/min in adults).</td>
</tr>
<tr>
<td>70</td>
<td>Pentobarbital—load with 3-5 mg/kg given over 3-5 minutes. Then start continuous infusion at 1 mg/kg/hr and increase continuous infusion with additional smaller loading doses until EEG burst/suppression. (Alternative is midazolam at a loading dose of 0.15-0.20 mg/kg followed by infusion of 0.05-0.30 mg/kg/hr. EEG should be monitored and infusion stopped at least temporarily after 12 hrs. to check for seizure recurrence.)</td>
</tr>
</tbody>
</table>
VII. Neonatal Seizures

Neonatal seizures can be a concerning neurological sign. The significance of neonatal seizures lies in their association with a high rate of mortality and neurologic morbidity. The clinical and electrographic manifestations of neonatal seizures differ from those in older, more neurologically mature individuals. This reflects the functional differences such as a lesser degree of myelination in the developing brain.

The reported incidence of neonatal seizures varies enormously, from 3% to 25%. Some of this variation probably reflects difficulties in diagnosis. (Slide 46)

Neonatal seizures are associated with increased rates of mortality and chronic neurologic morbidity, with sequelae in as many as 50% to 70%. Neonatal seizures may help identify a treatable disorder that can cause permanent brain damage. For example, hypoglycemia and bacterial meningitis can cause neonatal seizures. In such circumstances, quick and appropriate treatment may halt further progress of the disease and prevent additional damage to the brain.

The diagnosis of neonatal seizures has historically been based on visual inspection. A simple classification gradually evolved, including clonic, myoclonic, tonic and “subtle” neonatal seizures. There is relatively little problem associated with recognizing clonic, tonic or myoclonic seizures. Subtle seizures are more difficult. Although clinical behaviors such as apnea, tongue thrusting, sucking movements, and ocular nystagmus can be part of clinical seizure, when these occur in isolation, they do not necessarily imply seizures. Rather these events are termed “automatisms” or “brainstem release signs.” (Slide 47)

Video-EEG monitoring has helped define a more rational classification of neonatal seizures. Focal clonic, tonic, and myoclonic seizures are usually time-locked to changes on the EEG whereas, most generalized tonic, many generalized myoclonic and most subtle seizures are not time-locked to changes on EEG.

The evaluation of the infant with neonatal seizures should not await EEG confirmation. Management of suspected neonatal seizures pursues a simultaneous triple course: 1) confirm the diagnosis with EEG, 2) evaluate the infant for the cause(s) of the seizures, emphasizing treatable etiologies, and 3) initiate antiepileptic drug (AED) therapy. Many infants with neonatal seizures have underlying medical or neurologic illnesses that cause the seizure, i.e., acute, symptomatic seizures, not an intrinsically “lowered seizure threshold” constituting the substrate of epilepsy. (Slide 48)

Phenobarbital remains the most commonly used drug for neonatal seizures. Alternatives include phenytoin and benzodiazepines (Slide 49).
Some neonates subsequently develop chronic seizure disorders, often including refractory conditions such as West or Lennox-Gastaut syndromes. The reported frequency with which chronic epilepsy develops after neonatal seizures varies from 4% to 56% of those surviving the neonatal period.

One of the most difficult tasks in the holistic management of the neonate with seizures is a frank, accurate, realistic discussion of prognosis with the infant’s parents. Neonatal seizures are a sign of danger, and the risks of subsequent death, cerebral palsy, mental retardation, epilepsy, attention/hyperactivity disorders, behavioral disturbances and other related, CNS-based disorders must be carefully assessed and communicated.
VIII. Selected Pediatric Epilepsy Syndromes

Epilepsy syndromes may be classified according to whether the associated seizures are partial or generalized, and whether the etiology is idiopathic or symptomatic/cryptogenic. Several important pediatric syndromes can be further grouped according to age of onset and prognosis. These may be divided into the epileptic encephalopathies of infancy and early childhood, febrile convulsions, and benign partial and generalized syndromes of later childhood and adolescence.

A. Catastrophic Epilepsy Syndromes of Infancy and Early Childhood

These epileptic encephalopathies characteristically are present in early life, and can result from a variety of underlying disturbances. While the age of onset differs among the various syndromes, their common etiologic basis and overlap in clinical and EEG features suggests that they form a spectrum.

1. West Syndrome typically begins in the first year of life, usually between 3 and 8 months, and presents a distinct electroclinical triad of infantile spasms, hypsarrhythmic EEG (chaotic, high voltage activity with multifocal spikes) and psychomotor delay. Flexor spasms are typical, but extensor postures and focal motor features are common. These usually last several seconds each but occur in clusters lasting several minutes or longer. Prenatal and perinatal brain injury, metabolic, degenerative disorders, and neurocutaneous disorders and cerebral malformations are frequently identified.

Factors associated with poor prognosis include onset before age 3 months, symptomatic etiology, and multiple seizure types. Neurodevelopment is normal in only 10-15% of affected patients. Pharmacologic agents used to treat West Syndrome include the benzodiazepines, valproate and corticosteroids or corticotropin. More recently, vigabatrin (an inhibitor of the GABA-catabolic enzyme GABA transaminase, not currently available in the U.S.) has been introduced with success, especially in patients with tuberous sclerosis. West Syndrome associated with focal cortical dysplasia has been treated by resective surgery.

2. Lennox-Gastaut Syndrome is characterized by multiple seizure types, mental retardation and slow spike-wave EEG discharges. Seizures begin at ages 1-7; up to 25% of patients initially presented with West Syndrome. Tonic, atonic, atypical absence, and tonic-clonic seizures are common, while myoclonic seizures
are less common. The onset of the Lennox-Gastaut syndrome may be gradual or abrupt, but is typically associated with some developmental regression.

The prognosis for patients with the Lennox-Gastaut syndrome is poor. Multiple seizure types gradually give way to a single predominant pattern by the second decade, while mental impairment and social limitations are permanent. Recurrent bouts of status epilepticus are common, and standard AEDs often produce unsatisfactory seizure control. Onset of the Lennox-Gastaut syndrome before age 2 years has a particularly unfavorable outcome. Corticosteroid therapy may provide short term seizure control and the ketogenic diet has been successful in selected patients. Sodium valproate and lamotrigine are favored by many clinicians, and preliminary studies of topiramate suggest a beneficial role. Felbamate is also beneficial but may have a greater potential for serious adverse events.

3. Myoclonic epilepsies of infancy and early childhood are a heterogeneous group of disorders characterized by differing clinical manifestations of epileptic myoclonus, often associated with generalized or partial seizures, neurodevelopmental delay and generalized EEG abnormalities. The variety of electroclinical presentations has led to a complex and confusing classification system. All patients with myoclonic epilepsy, especially those with developmental delay or regression, should undergo careful evaluation for underlying causes including cerebral dysplasia, tuberous sclerosis, neuronal ceroid lipofuscinosis, and Angelman syndrome.

B. Febrile Convulsions

Febrile convulsions are the most common seizures in early life, generally occurring between 6 months and 5 years, and have an excellent long-term prognosis. Simple febrile seizures last less than 15 minutes and lack focality. Complex febrile seizures are longer in duration, may have focal manifestations, or recur within 24 hours. The EEG is nonspecific and rarely adds useful prognostic information. In later life, some patients exhibit specific epileptiform patterns indicating a genetic or structural basis for epilepsy. (Slide 51)

The diagnosis and management of febrile seizures rests largely with the general practitioner or pediatrician. Prophylactic AEDs should be avoided, although oral diazepam can be given when fevers are identified in susceptible children. Multiple or prolonged attacks can be aborted by administration of rectal diazepam.

Approximately one third of patients with one febrile seizure will have a second or (less commonly) third; recurrences are more common in younger patients. Between 1.5% and 4.6% of children with febrile seizures later develop afebrile seizures, i.e., epilepsy. The higher percentage applies to those with complex
febrile seizures (as defined above), and the epilepsy risk may be even greater in those with neurodevelopmental abnormalities.

**C. Idiopathic Partial Epilepsy Syndromes**

Two clinical syndromes, benign partial epilepsy with centrotemporal spikes and childhood epilepsy with occipital paroxysms, present distinctive seizure and EEG patterns during the first decade in neurologically normal children. (Slide 52)

1. Benign partial epilepsy with centrotemporal spikes (BECTS) is the most common epilepsy syndrome in childhood. Partial seizures typically occur within hours of falling asleep and are characterized by sensorimotor symptoms affecting the face, oropharynx, and occasionally the limbs. Up to 25% of patients develop secondarily generalized seizures. Centrottemporal spikes, more common during sleep, are the electrographic hallmark of the syndrome and indicate focal seizure origin from perioroladic cortex.

   At times, children without a seizure history have centrotemporal spikes typical of BECTS on an EEG obtained to evaluate a different complaint; in this situation it should be regarded as an incidental finding. Most symptomatic children with BECTS respond promptly to treatment with first-line AED therapy. The disorder remits by the middle of the second decade.

2. Benign childhood epilepsy with occipital paroxysms usually begins at ages 4–12 years and accounts for approximately 20% of idiopathic childhood epilepsies. Older patients generally manifest distinct visual phenomena including simple or complex visual hallucinations, visual distortions, hemianopsia and amaurosis. Misdiagnosis as migraine is common (and migraine may co-exist). In younger patients, seizures are less frequent and often nocturnal, but can present more dramatically with prolonged unresponsiveness and convulsions. Both variants may have repetitive occipital discharges on the EEG during eyelid closure.

   Long-term prognosis for both the early-onset and later-onset variants is good, with remission being the rule by the end of the second decade. However, patients with the later-onset variety may continue to experience partial seizures in adulthood. There is a recognized association of idiopathic occipital epilepsy, celiac disease and occipital calcifications in some patients. Response to first-line AEDs is usually good.
D. Idiopathic Generalized Epilepsy Syndromes

1. **Childhood absence epilepsy** typically begins at ages 4-8 years with frequent absence seizures, which may not initially be recognized; tonic-clonic seizures occur in approximately 40%, often beginning near puberty. Development is typically normal, and EEG is characterized by 3 Hz spike-wave complexes activated by hyperventilation. Both absence and tonic-clonic seizures usually respond well to treatment. Absence seizures usually remit by adolescence, but infrequent tonic-clonic seizures may occur in adulthood. (Slide 53)

2. **Juvenile myoclonic epilepsy** is characterized by onset of generalized tonic-clonic seizures, especially after awakening, beginning in adolescence. While some patients have myoclonus resulting in dropping things, this may go unnoticed in many. Diagnosis may not be made until, often under the stress of sleep deprivation or alcohol withdrawal, a tonic-clonic seizure occurs. EEG typically shows generalized spike-wave or polyspike-wave complexes, usually faster than 4 Hz. A minority of patients also have absence seizures, and some have photosensitive seizures, which may be diagnosed on strobe light stimulation during routine EEGs.

   Because both myoclonic and tonic-clonic, as well as absence, seizures respond to valproate, this is generally considered the drug of choice in juvenile myoclonic epilepsy. Preliminary studies with lamotrigine and topiramate show promise as alternative AEDs. Although seizure control is usually excellent, drug therapy must typically be continued indefinitely, since less than 20% of patients seem to outgrow their condition.
IX. Managing Pediatric Epilepsy

A. AEDs—Pediatric Considerations

Because efficacy data in childhood are limited, AED selection for childhood seizures relies on comparative efficacy studies in adults. Fortunately, the efficacy of most agents in children parallels the adult experience. However, adverse effects and toxicity are often the major determinant of drug selection. It is not unusual, for example, for parents to request drug withdrawal due to adverse events, even at the cost of seizure exacerbation.

In the infant and young child, interactions of AEDs with milk and infant formulas are a potential problem. Administration of AEDs while feeding should be avoided in this population. Maturation factors and variability in absorption and metabolism mandate careful attention to serum drug concentration monitoring. Specific problems with adverse effects may also require metabolic monitoring. (Slide 54)

B. Psychosocial Management

Social and neurobehavioral deterioration are strongly associated with epilepsy onset in childhood. The long-term prognosis of refractory epilepsy is poor and often precludes normal adult functioning. If schooling is compromised, fewer than 5% of patients followed into adulthood function normally. For this reason, it is essential that allied health care practitioners such as neuropsychologists, special educators, and social workers help manage the child with epilepsy.

C. Epilepsy Surgery

Children suffering from refractory epilepsy are being increasingly referred for surgery. This trend has resulted from advances in appreciating the poor long-term outlook of these children, identifying neuropathologic substrates of the condition, selecting appropriate patients, and localizing the epileptic focus. A small minority of children with refractory seizures have spontaneous remission, but seizure freedom may not occur for many years, and predicting when remission will occur is virtually impossible. Earlier seizure alleviation contributes to a greater reduction in psychosocial morbidity and improved quality of life.
A major problem for primary care physicians and neurologists is recognizing transient events that resemble seizures (nonepileptic seizures). (Slide 55)

**TABLE 6. SOME EVENTS IMITATING EPILEPTIC SEIZURE**

<table>
<thead>
<tr>
<th>Physiologic Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Syncope (Arrhythmia)</td>
</tr>
<tr>
<td>Non-Cardiac Syncope (Vasovagal, Dysautonomic)</td>
</tr>
<tr>
<td>Metabolic (Hypoglycemia)</td>
</tr>
<tr>
<td>Migrainous (Especially Confusional Migraine)</td>
</tr>
<tr>
<td>Sleep Disorders (Narcolepsy)</td>
</tr>
<tr>
<td>Movement Disorders (Paroxysmal Dyskinesia)</td>
</tr>
<tr>
<td>Transient Ischemic Attacks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychological Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychogenic Seizures</td>
</tr>
<tr>
<td>Malingering</td>
</tr>
<tr>
<td>Panic Attacks</td>
</tr>
<tr>
<td>Intermittent Explosive Disorder</td>
</tr>
<tr>
<td>Breath-holding Spells</td>
</tr>
</tbody>
</table>
A. Physiologic

Transient ischemic attacks, migraine, sleep disorders, movement disorders, and metabolic disturbances can produce episodes of altered mentation or movement. History, physical examination during or after attacks, and appropriate laboratory and radiologic studies can usually distinguish these from epileptic seizures.

B. Psychogenic

Psychogenic seizures are a common symptom of conversion or somatization disorder and should be recognized as a disabling psychiatric illness requiring treatment. One must maintain a high degree of suspicion when seizures are refractory to therapy or when atypical features are present. Because physicians generally rely on patient and witness accounts rather than direct observation of seizures, the chances for misdiagnosis are high. Diagnosis is best established by recording typical attacks with video-EEG, although limitations of this technique must be kept in mind, particularly susceptibility to movement and other artifacts, and potential false negatives during simple partial seizures and some frontal lobe seizures (Table 7).

Psychogenic seizures are noted in 10-45% of patients evaluated at epilepsy centers. They can occur at any age after early childhood and are somewhat more common in women. Recognition allows avoidance of the intoxicating AED doses which are often used because seizures are refractory. A detailed assessment of psychosocial stresses and underlying psychopathology is essential. In many cases, the underlying stressor can be identified (e.g., history of physical or sexual abuse, marital discord). A significant proportion (10-40%) of patients with psychogenic NES also have epilepsy, an extremely challenging situation for both diagnosis and therapy. (Slide 56)
In many cases, the mechanism underlying psychogenic seizures is never identified, as patients may be resistant to psychologic or psychiatric intervention. Although the diagnosis is difficult for both physician and patient to confront, learning the diagnosis and, usually, following through with treatment controls NES in approximately 50% of patients. (Slide 57)

Psychogenic NES must be distinguished from malingering, or consciously feigning epileptic seizures.

C. Syncope

Syncope of vasovagal or cardiogenic origin can mimic epileptic attacks, especially when tonic extension of the trunk and limbs or several clonic jerks are observed, and lead incorrectly to the diagnosis of a seizure. Brief tonic posturing or clonic movements are common with syncope. Rarely, when the person is particularly susceptible or the ischemia is prolonged, a convulsion can result—convulsive syncope, which is a primary cardiovascular not cerebral disorder, and should not be treated as an epileptic seizure. Loss of consciousness exclusively in the standing or sitting position; painful stimuli or a very hot environment as provocative factors; and a prodrome of warmth, nausea, diaphoresis, and a gradual fading of binocular vision suggest syncope rather than seizures. A rapid return to normal mentation is also more characteristic of syncope than of seizures. (Slide 58)
### TABLE 7. ICTAL FEATURES SUGGESTING NONEPILEPTIC PSYCHOGENIC SEIZURES

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Caveats/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradual onset of ictus</td>
<td>Epileptic seizures begin suddenly, but are often preceded by auras</td>
</tr>
<tr>
<td>Prolonged duration</td>
<td>Epileptic seizures usually last &lt; 4 min, but any seizure type can be prolonged; distinguish between ictal and postictal states</td>
</tr>
<tr>
<td>Thrashing, struggling, crying, pelvic thrusting, side-to-side rolling, wild movements</td>
<td>Bizarre complex automatisms can occur with frontal lobe CPS</td>
</tr>
<tr>
<td>Intermittent arrhythmic, out-of-phase jerking</td>
<td>GTCS jerking is rhythmic and usually in-phase</td>
</tr>
<tr>
<td>Clonic activity that abruptly ends</td>
<td>At the end of GTCS, the interval between jerks becomes progressively longer</td>
</tr>
<tr>
<td>Motor activity stops and starts</td>
<td>Extremely rare in isolated seizures; distinguish from a series of seizures</td>
</tr>
<tr>
<td>Ability to talk while “unresponsive”</td>
<td>Automatic speech can occur with right temporal CPS</td>
</tr>
<tr>
<td>Preserved consciousness with bilateral tonic or clonic movements and speech</td>
<td>Supplementary motor area seizures may have bilateral convulsive movements</td>
</tr>
<tr>
<td>Convulsive movements of extremities without facial involvement</td>
<td>Facial involvement in GTCS can be subtle</td>
</tr>
<tr>
<td>Gradual offset of seizure</td>
<td>Epileptic seizure activity usually ends abruptly, but can merge into postictal state</td>
</tr>
<tr>
<td>Features fluctuate from one seizure to the next</td>
<td>Epileptic seizures are usually stereotypic</td>
</tr>
<tr>
<td>Lack of postictal confusion</td>
<td>Often absent after frontal lobe, and less often, temporal lobe, CPS</td>
</tr>
<tr>
<td>Postictal crying or shouting obscenities</td>
<td>Aggressive verbal and physical behavior can occur after epileptic seizures if patients are restrained</td>
</tr>
<tr>
<td>Suggestibility (ability to talk someone into or out of the seizure)</td>
<td>Stress of suggestive testing very rarely triggers an epileptic seizure</td>
</tr>
<tr>
<td>No injuries after many recurrent seizures</td>
<td>Injuries may also occur with NES, particularly in patients with a history of self-injury</td>
</tr>
<tr>
<td>Tongue biting at the tip</td>
<td>Tongue biting in epileptic seizures typically is on the side of the tongue</td>
</tr>
</tbody>
</table>

*CPS - complex partial seizure; GTCS - generalized tonic-clonic seizure*
XI. Pregnancy and Epilepsy

A. Medical Management

Although seizure control during pregnancy historically has been reported to worsen in a large proportion of women, in most cases this can be prevented by careful attention to drug dosing and levels, because much of the seizure increase is associated with lower drug levels as a result of increased metabolic rate and volume of distribution. The latter is mitigated somewhat, for highly bound drugs, by decreases in serum proteins resulting in a higher free fraction (which can be assessed by measuring free as well as total levels), but most women require increasing doses of AEDs as pregnancy progresses. A minority of women will have improved seizure control during pregnancy, but for most there will be no significant change. There is an increased risk of seizures at the time of delivery, resulting from sleep deprivation, gastrointestinal factors, and physical exhaustion; use of parenteral AEDs, including benzodiazepines, can be considered at this time. (Slide 59)

A major concern of women of childbearing age is the teratogenic potential of AEDs. Whereas the incidence of major birth defects (those requiring medical or surgical intervention) in the normal population is approximately 2-3%, approximately twice as many, or 4-7%, of the offspring of women on AED monotherapy have recognizable major birth defects, with another 5-10% having minor cosmetic anomalies such as shortened distal digits. Some fraction of these may arise from genetic abnormalities carried by the mother, some from the injury imposed by seizures during the pregnancy, and some from the effects of AEDs. While physicians can do little about the former, there is an obvious tension between the two latter risk factors, optimal control of maternal seizures (particularly early in pregnancy) vs. teratogenicity of AEDs. (Slides 60-62)

A wide variety of birth defects are associated with the use of virtually all AEDs (data are limited on the newer drugs), and there is considerable overlap between the fetal syndromes seen in the offspring of mothers treated with phenytoin, phenobarbital, carbamazepine, and valproate. One feature in particular, however, the occurrence of neural tube defects, has been clearly associated with the maternal use of valproate and more recently carbamazepine. Since there is evidence that folic acid supplementation can decrease the risk of these defects, many neurologists provide supplemental folate to all women of childbearing age under treatment for epilepsy.
XII. Driving and Epilepsy

Epilepsy is unique in the variety of legal problems that it creates. Among these, none engenders as much debate and controversy as driving. All states regulate driving by persons with epilepsy. The appropriate seizure-free interval before driving is permitted may be prescribed or suggested by each state board, but often the privilege of driving is based on a physician statement concerning the particular patient. Most states rely on applicants to disclose their medical condition relevant to driving. Some states (currently six) mandate physician reporting.

Medical statements are scrutinized by a medical review board which typically includes neurologists. The board either permits driving or specifies the period of restriction before driving may be legally resumed. Prescribed seizure-free periods for driving vary from three months to two years.

Driving by people with epilepsy poses a small but identifiable risk to public safety, whereas individual risks to patients may be greater. It is a difficult task to devise an effective method of monitoring driving safety among people with epilepsy that is not discriminatory and at the same time protects both the patient and his or her surroundings. (Slide 63)
References


Hauser WA, Hesdorffer DC. *Epilepsy: frequency, causes and consequences*. New York: Demos, 1990.


Seizure Recognition and First Aid

An outline follows for recognition and first aid for generalized tonic-clonic and complex partial seizures, the two most common seizure types in adults. For more information go to www.efa.org/answerplace/recognition/chart.htm

Generalized Tonic-Clonic Seizure

Appearance: Sudden cry, fall, rigidity, followed by muscle jerks, shallow breathing or apnea, possible urinary incontinence, typically lasts 1-2 minutes with post-seizure somnolence, lethargy, confusion, and/or agitation.

What to do: Turn person on his side with head inclined towards ground to keep airway clear and protect from nearby hazards. Transfer to a hospital is often unnecessary if there is a history of seizures. Further evaluation is needed if person is pregnant, injured, or diabetic. If multiple seizures occur or a seizure lasts longer than 5 minutes, treatment for status epilepticus should ensue. (Slide 64)

What not to do: Do not put rigid objects in the person’s mouth or hold the tongue. Do not use artificial respiration unless breathing is absent after jerking subsides. Do not restrain patient after seizure unless needed to prevent imminent injury (e.g., confused patient running into the street); restraint can provoke aggressive response.

Complex Partial Seizures

Appearance: Usually starts with blank stare, chewing, then random activity. The person appears unaware of surroundings and unresponsive to commands. Seizure usually lasts 1-2 minutes, often with post-seizure confusion and memory loss for the event.

What to do: Speak calmly and guide gently away from obvious hazards. If outside the hospital, stay with the person until he or she is completely aware of environment and offer to help him or her get home. Medical evaluation is needed for a new onset seizure, if the person is pregnant or injured, or if the seizure (not post-ictal) state lasts longer than 10 minutes.

What not to do: Do not hold or restrain unless there is a dangerous situation such as traffic. Do not shout or expect verbal instruction to be obeyed during or immediately following the seizure.
AAN Guidelines: Counseling Women Who Plan Pregnancy

Current practice should be influenced mainly by the following guidelines, which were arrived at by a consensus panel of the American Academy of Neurology:

1. The risk of major malformations, minor anomalies, and dysmorphic features is twofold to threefold higher in infants of mothers with epilepsy who receive treatment with antiepileptic drugs (AEDs) compared with the risk in infants of mothers without epilepsy.

2. A possibility exists that some of the risk is caused by a genetic predisposition for birth defects inherent in certain families. Both parents' family histories should be reviewed for birth defects.

3. Possibilities for prenatal diagnosis of major malformations should be discussed. If valproate or carbamazepine is the necessary AED, the likelihood of amniocentesis and ultrasound examinations during pregnancy should be discussed. Ultrasound examination for a variety of major malformations can be done during the 18th to 22nd weeks.

4. Effects of tonic-clonic seizures on the fetus during pregnancy are not well established. However, tonic-clonic convulsions might be deleterious to the fetus, injure the mother, and lead to miscarriage.

5. The diet prior to conception should contain adequate amounts of folate.

6. If the patient is seizure free for at least 2 years, i.e., free from absence, complex partial, or tonic-clonic attacks, withdrawal of AED should be considered.

7. If AED treatment is necessary, a switch to monotherapy should be made if possible.

8. The lowest AED dose and plasma level that protects against tonic-clonic, myoclonic, absence or complex partial seizures should be given. Closed-circuit television electroencephalographic monitoring should be used if necessary.
Appendix C

Nursing Student Case Studies

Managing Epilepsy Successfully: Insights from Clinical Experience with AED Therapy

Link to www.webclinics.org Log in as AED and use password NURSE

Seizure Assessment Algorithm for Nurses (Slide 65)
Appendix D

Epilepsy Reference Guide for Nurses and Epilepsy Reference Guide for Persons with Epilepsy

Journals (Slide 66)

**Clinical Nursing Practice in Epilepsy**

**Epilepsia** (the Journal of the International League Against Epilepsy).

**Epilepsy Currents** (Bimonthly Journal for American Epilepsy Society. Also on www.aesnet.org.)

**Epilepsy USA** Magazine, published by the Epilepsy Foundation. Also available on www.epilepsyfoundation.org.

The **Journal of Neuroscience Nursing** (the Journal of the American Association of Neuroscience Nurses). There is a yearly index in the December issue by author and by topic (epilepsy) for easy reference.

**Seizure** (European Journal of Epilepsy)

Books (Slides 67-68)


**Clinical Epilepsy**, Duncan, JS, Shorvon, SD, Fish, DR, Churchill Livingstone, 1995.

**Core Curriculum for Neuroscience Nursing**, third ed., American Association of Neuroscience Nursing.


**The Epilepsy Diet Treatment An introduction to the Ketogenic Diet**, Freeman JM, Kelly MT, Freeman JB. Demos, 1994.


**Students with Seizures A manual for school nurses**, Santilli N, Dodson WE, Walton AV. Health Scan Publications, 1991. (*there is a section in this book that lists references for specific groups.*)
**Networking** (Slide 69)


**American Epilepsy Society**, 342 North Main Street, West Hartford, CT 06117-2507, (860) 586-7505, www.aesnet.org. A membership society of professionals interested in epilepsy. Within the Society are special interest groups including a nurses group. Contact the Society for more information.


**Epilepsy Foundation**, eCommunities. Chat rooms for four different groups: Women and Epilepsy; Parents Helping Parents; The Teen Chat Room; and Living Well with Seizures. Located at www.epilepsyfoundation.org

**Videos**

The **Epilepsy Foundation Catalog** contains many videos that can be used for education for nurses, families and schools (800) EFA-1000 or www.epilepsyfoundation.org. (Spanish videos also available)

**Web Sites** (Slide 70)

**American Association of Neuroscience Nurses**  
http://www.aann.org

**American Epilepsy Society**  
http://www.aesnet.org

**Epilepsy Foundation (National Office)**  
http://www.epilepsyfoundation.org  
or  
http://wwwefa.org/education.firstaid.html

**Nursing Care Implications**  
http://www.nurseweek.com/ce/191-sb1.html

**Nursing CEUs for Neurological Nursing**  
http://www.nurseccen.com/nur.htm

**Other**

**AED Pregnancy Registry**, a registry for pregnant women receiving antiepileptic drugs, address: Genetics and Teratology unit, 149 CNY-MGH East, Room 5022A, Charlestown, MA 02129-2000, (888)233-2334.

Comprehensive Clinical Management of the Epilepsies, a publication of the Epilepsy Foundation, 4351 Garden City Drive, Landover, MD 20785-2267, (800) EFA-1000.

Centers for Disease Control Epilepsy Program, working to increase awareness of epilepsy and seizures as a public health problem, address: Division of Adult and Community Health, 4770 Buford Highway, MS K-45, Chamblee, GA 30341, (770) 488-5502, email at pap4@cdc.gov for Patricia H. Price, DO, FACPM.

The Epilepsy Foundation Catalog contains many items that can be used for education for nurses, families and schools. Products include books, manuals, pamphlets and videos. Spanish books, pamphlets and videos are available. Contact (800) EFA-1000 or www.epilepsyfoundation.org or The Epilepsy Foundation, 4351 Garden City Drive, Landover, MD, 20785, and/or your local EF Affiliate. Pamphlets include:

“Epilepsy Breaking Down the Walls of Misunderstanding”
“Epilepsy Recognition and First Aid”
“Medication for Epilepsy”
“Questions and Answers About Epilepsy”
“Recognizing the Signs of Childhood Seizures”
“Seizure Man, First Aid for Seizures”

Issues and Answers, A Guide for Parents of Teens and Young Adults with Epilepsy, published by the Epilepsy Foundation. (800) EFA-1000 or www.epilepsyfoundation.org.

National Center for Learning Disabilities, not-for-profit organization dedicated to improving the lives of those affected by learning disabilities, address: 81 Park Ave. South, Suite 1401, New York, NY 10016, (888) 575-7373.

National Information Center for Children and Youth With Disabilities, information clearinghouse, address: P.O. Box 1492, Washington DC 20013, (800) 695-0285.

Parents Helping Parents, a parent-directed family resource center for children with any kind of special need, address: 3041 Olcott Street, Santa Clara, CA 95054, (408) 727-5775.

Non-Epileptic Seizures, a guide for patients and families, address: Department of Neurology, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, (216) 444-2200.


Seizure Recognition and First Aid, curriculum produced by the Epilepsy Foundation, includes a trainer’s guide, overhead transparencies, videos, slides and curriculum handouts. A standardized tool for training school personnel.

Seizure Assessment Algorithm, American Association of Neuroscience Nurses, (800) 477-AANN, http://www.AANN.org. (Slide 65)
Epilepsy Reference Guide for Persons with Epilepsy

Journals/Magazines

*Epilepsy USA* Magazine, published by the Epilepsy Foundation. Also available on www.epilepsyfoundation.org.

*Exceptional Parent* magazine, published by Psy-Ed Corp, published monthly, special editions related to epilepsy. Also available on www.edparent.com

Books


*Brainstorms Series*, Schachter, S, available through the Epilepsy Foundation Catalog.

*Dotty the Dalmatian Has Epilepsy*, The Dr. Wellbook Collection, Tim Peters and Company, 1996.


*Issues and Answers, A Guide for Parents of Teens and Young Adults with Epilepsy*, published by the Epilepsy Foundation. (800) EFA-1000 or www.epilepsyfoundation.org.


*Me and My World Storybook*, available through the Epilepsy Foundation Catalog.


*Students with Seizures: A manual for school nurses*, Santilli N, Dodson WE, Walton AV. Health Scan Publications, 1991. (*there is a section in this book that lists references for specific groups.)*

Videos

The *Epilepsy Foundation Catalog* contains many videos for persons with epilepsy and their family and friends; also for teachers and schools. Spanish language videos are available. (800) EFA-1000 or www.epilepsyfoundation.org.
**WEB SITES**

**American Epilepsy Society**  
http://www.aesnet.org

**Epilepsy Foundation (National Office)**  
http://www.epilepsyfoundation.org  
or  
http://www.efa.org/education.firstaid.html

**OTHER**

The *Epilepsy Foundation Catalog* contains many items that can be used for education for nurses, families and schools. Products include books, manuals, pamphlets and videos. Spanish books, pamphlets and videos are available. Contact (800) EFA-1000 or www.epilepsyfoundation.org.


**Non-Epileptic Seizures**, a guide for patients and families, address: Department of Neurology, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, (216) 444-2200.

Appendix E

Case Studies

Case 1: 5-Year-Old Female with Episodes of “Blanking Out”

A 5-year-old female is brought to your office by her parents because of episodic “blanking out” which began approximately one month ago. They describe episodes in which she abruptly stops all activity for about 10 seconds, followed by a rapid return to full consciousness. During most of these episodes her eyes are open and she remains motionless, although they have noticed some occasional “fumbling” hand movements. She does not respond to her name being called. When the episode ends she usually resumes whatever activity she was engaged in previously, and appears unaware that anything has happened. Her parents have counted as many as 30 such episodes a day. They have not identified any provoking factors and there is no particular time of day in which these episodes are more frequent. She tells you that she is unaware of the episodes described by her parents. She has not had any convulsive episodes. (Slides 2-6)

Her perinatal and developmental histories are unremarkable. Other than typical, uncomplicated childhood illnesses she has been healthy. She takes no medication and has no known allergies. She has no siblings. Her father was told that he had “staring spells” as a child and took medication for about three years. He denies problems since then. He has a cousin who had febrile seizures in childhood.

The general physical and neurological examination is normal. After several minutes of hyperventilation in the office, she stops hyperventilating. She remains motionless with her eyes open and does not respond to verbal stimuli. After about 10 seconds she abruptly regains consciousness and begins hyperventilating again. Her parents describe this as typical of the events she is having at home. During an EEG, frequent generalized, 3 Hz spike and slow wave discharge are recorded, similar to the one shown in the figure. (Slide 7)

Discussion questions. (Slide 8)
**Case 2: “Nervous Disorder”**

*Note:* This case is meant to generate discussion and encourage reading about the many aspects of epilepsy occurring in a highly functioning young woman. It is not meant to endorse any particular treatment course. There may be differing answers to some of the questions due to differing opinions and even to different geographic locations! Therefore, in addition to providing teaching points, the questions serve to elucidate some of the controversies in the field of epilepsy as well. (Slides 9-11)

The patient is a 25 year-old right-handed marketing executive for a major credit card company, who began noticing episodes of losing track of conversations and having difficulty with finding words. These episodes lasted 2-3 minutes. At times, the spells seemed to be brought on by a particular memory from her past, but she couldn’t recall the memory exactly. No one at her job noticed anything abnormal, but notably, when the patient felt the strange memory distortion coming on, she would often go into the company lounge and sit by herself until the feeling passed. She usually returned to her job after 15 minutes.

The patient had no significant past medical history, and took no medicines except for the birth control pill. She was in psychotherapy for feelings of depression and anxiety, but was not taking medications for mood or anxiety disorder. She told her therapist about the strange episodes. The therapist noted that the patient had been going through a lot of stress at her job recently, had just broken-up with her boyfriend and had some insomnia. The therapist then sent her to a psychiatrist for evaluation the treatment of depression and/or anxiety.

**What is your differential diagnosis at this point?**

The patient made an appointment with the psychiatrist and on the first visit, described to the doctor the episodic periods of confusion and memory distortion. The psychiatrist noted that the patient had no previous history of major depression or suicide attempt and was currently mildly anxious, but had no need for anxiolytic medication. A careful medical history revealed that she had one febrile seizure at age three; no family members had epilepsy. The psychiatrist prescribed a benzodiazepine sleeping pill to be used as needed, and scheduled her for an electroencephalogram (EEG). (Slide 12 & 13)

Prior to the EEG, the patient was required to travel from her job on the East Coast to the West Coast, crossing three time zones. After arriving, she met with her colleagues and went out to a business-related reception, where she consumed several drinks. She stayed out until 1 a.m. (Pacific time) and then went to bed, exhausted. She set the alarm for an early morning meeting.
The next thing she remembers is waking up on the floor near the bathroom of her hotel room. She had a severe headache and noted some blood in her mouth, along with a very sore tongue. She called the hotel physician and was taken to the local emergency room. (Slide 14)

**What is your differential diagnosis now?**

How would you classify the events, both the episodes of memory disturbance and the nocturnal convulsion? (Slide 15)

**How would you evaluate this patient in the emergency room?**

In the emergency room, she was seen by the doctors, examined and told she likely had a seizure during her sleep. A computerized tomographic scan of the head was normal, showing no evidence of bleeding or abnormal masses in the brain. Her laboratory tests including a complete blood count, blood chemistries including glucose and toxicology screen were normal. She was given fosphenytoin 1000 mg intravenously and observed. She was then sent from the emergency room with a prescription for phenytoin 300 mg per day and told to follow-up with her local physician. (Slide 16 & 17)

The patient left the ER feeling dizzy and slightly nauseated, and very sore in the muscles of her neck and back. She cancelled the rest of her trip and returned home.

**What would the continued evaluation and treatment consist of?**

When the patient returned home, she called the psychiatrist and related what had happened. She was advised to continue the daily maintenance phenytoin dose and was given the name of a neurologist. She felt slightly tired, but she wasn’t sure if it was from the seizure she was told that she had, or if it was from the new medication, phenytoin. She made an appointment with the neurologist and continued working every day. She had no further episodes.

The neurologist took a complete neurologic and medical history. It was revealed that the patient had an uncomplicated febrile seizure as a toddler, but no other seizures, including nocturnally, as far as she knew. There was no family history of epilepsy in her immediate family members. She was the product of a normal, uncomplicated, full-term pregnancy and normal vaginal delivery. She has no history of head trauma with loss of consciousness and there is no history of brain infection such as meningitis. Medical history is otherwise benign and she has no medication allergies. She had regular menstrual periods since age 13 and has
never been pregnant, although she stated she wants to have children in the future. Oral contraceptive pills have been effective and well tolerated for her. General and neurologic examination was normal. (Slide 18)

The patient underwent an EEG that showed right anterior temporal spike and wave discharges interictally. An MRI of the brain was normal. Due to her persistent complaints of feeling sedated, the neurologist was considering changing her medication to another antiseizure medication. With the patient included in the discussion, it was decided to change phenytoin to oxcarbazepine, at a dose starting at 50 mg twice a day and increasing by 50 mg/day every two weeks to a target dose of 300 mg/day of lamotrigine. Side effects were explained to the patient. She was also started on folic acid 1 mg per day and was advised to take a multivitamin daily. What are the most reasonable choices of antiseizure treatment for this patient? (Slide 19 & 20)

Was an appropriate choice made? (Slide 21)

What considerations must be made since she is a woman of child-bearing potential?

Are there considerations regarding the oral contraceptive pill? (Slide 22)

What is the reason for the extra folic acid and multivitamin?

What advice should be given regarding lifestyle (sleep habits, alcohol intake) and driving?

The patient changed medications without problems and had no further seizures. She continued to see her therapist, but not the psychiatrist. Her insomnia worsened slightly and she reported discrete periods of feeling very anxious. Her therapist again referred her back to the psychiatrist and called the neurologist to talk over the new symptoms.

What is your differential diagnosis of the new symptoms?

References:

Case 3: 70 Year Old Man with His First Seizure

A 70 year old man presents with a single seizure. His wife was awakened at 5:30 this morning. Although she has never seen a seizure before, she thinks that is what she saw. She describes the following “After I woke up, I noticed that his head was turned to the left and his left arm was sticking straight out. He was making an odd gurgling noise and his mouth was moving a little. Then he started to jerk all over and I reached for the phone to call 911. When I looked back at him, the jerking didn’t seem quite as bad, but he wouldn’t talk to me and didn’t seem to look at me, even though his eyes were open. The rescue squad seemed to take forever to get to the house, but it was probably only 10 minutes. When they got there, he would moan when someone called his name and it looked like he was able to focus on people. The EMT did a quick exam and he was able to cooperate and follow orders. They told me that he was weaker in the left hand than the right. By the time they had him ready to move to the hospital, he was nearly back to his normal self and had no signs of weakness.” (Slides 23-25)

On arrival in the emergency room approximately 15 minutes later, he was oriented to person, place and time, although he had no memory of the seizure. His neurological examination was normal, except for mild peripheral neuropathy. Past medical history is notable for non-insulin dependent diabetes for the past 15 years. He has no history of seizures. The patient has no known allergies, has never smoked and does not drink alcohol.

Current medications: Glyburide 5mg/day (Slide 26)

Vital signs: BP 200/130, HR 75 (regular), RR 14, temp 100.1°F

Laboratory studies: (Slide 27 & 28)

Blood chemistry:
- Sodium: 141 mEq/L
- Potassium: 4.2 mEq/L
- Chloride: 99 mEq/L
- Bicarbonate: 27 mEq/L
BUN 8 mg/dL
Cr 0.7 mg/dL
Glucose 60 mg/dL
Urine Analysis 15 WBC/HPF
Nitrite: Positive
ABG pH: 7.3, PC02: 36, PO2: 86; O2 saturation: 93%

CBC
Hematocrit 44%
Hemoglobin 15.4 g/dL
White count 12,000 with 80% neutrophils and 6% bands
Platelet Count 180

CT scan: shown (normal) (Slide 29)
EEG: shown (temporal slowing bilaterally) (Slide 30)

Questions for discussion

1) What work-up is needed after a single seizure? (Slide 31)
2) What are the causes of seizures, including what conditions lower the seizure threshold?
3) Would you treat this patient or not? If you would treat, which drug would you choose and why?
4) What are the predictors of seizure recurrence?

Case 4: A 62 year old man with continuous seizures

A 62-year-old male without a previous history of seizures presents to the Emergency Room with repeated tonic-clonic seizures. The patient presented to the ER following one generalized tonic-clonic seizure. However, while you left to check the computer for his lab results, the patient has begun to seize again. Initial assessment after the first seizure revealed poorly reactive pupils, no papilledema or retinal hemorrhages and a supple neck. Oculocephalic reflex is intact. Respirations are rapid at 22/min and regular, heart rate is 105 with a temperature of 101. (Slides 31-33)

• What should the initial management be? (Slide 34)
• What initial investigations should be performed in this setting?
• What is the appropriate management with continued seizures if initial therapy does not terminate the seizures?

You opt to obtain laboratory studies. (Slides 35-37) The following results are obtained:

CBC
WBC- 13.1
HGB 11
Plt 200,000

Na- 132
K- 4.5
Ca- 9.0
Glucose- 90
Creatinine- 1.0
Mg 1.0

CSF color- clear
Cell count tube # 1 – 500 RBC/ 35 WBC- 100% Neutrophils
tube # 3 - 100 RBC/ 11 WBC
Protein 65
Glucose 60

Urinalysis- (+) ketones
  0 WBC
  0 bacteria

Tox screen: negative for alcohol
  positive for benzodiazepines

**You obtain an MRI of the brain with the following images** (Slides 38-39)

• Which of the above studies helps to explain the current seizures? (Slide 40)
• Would you ask for other studies?
• What are the CSF findings during repeated convulsions?
• You try an initial dose of antiseizure medications but it does not work, what is an acceptable protocol for status epilepticus management? What medications are useful at the onset of status and which are better suited to later stages of management?
Questions for Discussion

1. Define Status Epilepticus. (Slide 41)
2. Describe the systemic manifestations of status epilepticus.
3. What causes status epilepticus?
4. What is the role of EEG in status epilepticus management?

Case 5: 51 Year Old female present to the clinic complaining of frequent seizures

Seizure History: Her birth was unremarkable except that she was born with syndactyly requiring surgical correction. Early developmental milestones were met at appropriate ages. She had her first convulsive episode at age 1 in the setting of a febrile illness. (Slides 42-43)

How would you evaluate and treat a patient with a febrile seizure? What clinical features are important in guiding your evaluation? (Slide 44)

She began to develop a new type of episode in the third grade. The attacks consisted of her seeing a pink elephant that was sitting on various objects and waving to her (of note, the patient has subsequently found a ceramic model of an elephant that was the same as the elephant that she saw during her seizures). (Slide 45)

How are her symptoms different from most patients with schizophrenia? (Slide 46)

She was not diagnosed with seizures until the age of 15. Initially, the seizures were controlled with medicine. After a few years, however, the attacks occurred despite treatment with anticonvulsants. (Slide 47)

When she was 20-years-old, the seizures changed in character to the current pattern. She no longer sees an elephant. The seizures begin with an aura of “a chilling sensation starting at the lower back with ascension to the upper back over the course of 10-20 seconds.” (Slide 48) Observers then note a behav-
When are seizures “medically refractory”? When should you consider an inpatient video/EEG evaluation? What might you learn from such an evaluation that would change your treatment strategy? (Slide 53)

Past Medical History: 1) Migraine headaches (with the last one occurring in 1996); 2) status-post hysterectomy with removal of one ovary in 1976-1978; 3) history of syndactyly at birth with surgical corrections; 4) partial thyroidectomy in 1968 during pregnancy. (Slide 54)

Social History: She currently lives with her mother. She works as a sales clerk. She completed twelve years of school and finished one semester of college. She has not driven a car after being reported to the DMV by her doctor in 1977. (Slide 55)

She tells you that she still has her driver’s license. What are your legal and ethical obligations as a physician? (Slide 56)

Family History: She has a cousin with a history of ”grand mal” seizures who died at age 12.

Habits: She does not use of alcohol, tobacco, or illicit drugs.

Medications: Carbamazepine 200/200/100/200 mg a day, Lamotrigine 50/50/25 mg a day, Conjugated estrogens 1.25 mg PO qd, Thyroxine 100 mcg PO qd, and Sumatriptan PRN.

Neurologic Examination: Normal. (Slides 57 & 58)
Referral to an Epilepsy Center

- She hated having seizures in public and she “felt like a prisoner in my own home”
- Upon hearing of seizure surgery, she requested a referral for evaluation

Pre-surgical Evaluation: Video/EEG monitoring (Slide 59)

- During 5 days she had 3 CPS
- All began with her aura followed by lip smacking and a post-ictal aphasia (Slide 60)
- During the attack her right hand was held in a fist
- EEG onsets consisted of a rapid build up of rhythmic theta frequency activity over the left temporal region (Arrows) (Slide 61)

Pre-surgical Evaluation: MRI reveals an atrophic L. hippocampus (Slide 62) (arrows)

Pre-surgical Evaluation: Neuropsychological Testing (Slide 63)

- Wada (Intracarotid amytal) test
  - Language on Left side only
  - No memory difference with left and right injections
- Performance and Verbal IQ normal

Pre-surgical Evaluation: Conclusions (Slide 64)

- She has complex partial seizures refractory to anticonvulsant treatment
- Clinical and EEG features are compatible with seizure origin from the left, language-dominant temporal lobe
- MRI suggests mesial temporal sclerosis is the underlying pathology
- She has an excellent chance for a seizure-free outcome with a left anterior temporal lobe resection
Surgery (Slide 65)

- Surgery under local anesthesia
- Language map determined by electrical stimulation
- Language areas (blue arrow) and epileptogenic tissue (white arrow) labeled (Slide 66)

Surgery

- Anterior temporal lobe resected (arrow) (Slide 67)
- Amygdala and hippocampus also resected

**Follow-up** (Slide 68)

- Immediately following surgery she had mild dysnomia
- At three months post-op, cognitive testing confirmed no change from pre-op
- She has had no seizures for two years. She declines a trial off of anticonvulsants for fear of recurrent seizures. She drives to her appointment in a new car.
- She writes, “I’m now having a life I never knew was possible”