

## CHAPTER 11

### Seizures and Epilepsy

#### DEFINITION AND INCIDENCE

Hughlings Jackson defined epilepsy as a group of disorders characterized by excessive and paroxysmal neural discharges causing sudden alteration in neurologic function. The terms “epilepsy” and “seizure” refers to similar clinical conditions; however, epilepsy refers to *recurrent* seizures. It implies the presence of cerebral dysrhythmia (paroxysmal discharges of cerebral neurons indicating an underlying condition characterized by abnormal cortical excitability) for which there may be underlying genetic basis or underlying structural abnormality. Epilepsy implies recurrent seizures unprovoked by toxic, febrile, or metabolic conditions. Recurrent seizures can be symptomatic of underlying microscopic or macroscopic brain lesion; but they can occur in absence of identifiable pathologic or biochemical abnormality (idiopathic). Seizures are classified according to clinical manifestations of episodes and EEG pattern.

Incidence of seizures is 6.5 people out of 1000; this affects almost 1.5 million persons in this country. One of every 10 or 20 patients will have one seizure during his or her lifetime, and one out of 200 develop epilepsy. Diagnosis of epilepsy should be established accurately on clinical and EEG features because of adverse impact on the patient of an incorrect diagnosis, for example, stigma of being diagnosed as “epileptic,” need to use potentially toxic antiepileptic medications, and restrictions imposed on patient’s lifestyle by the diagnosis of epilepsy. Despite importance of high degree of accuracy, 10% to 25% of patients subsequently evaluated for medically intractable seizures actually have nonepileptic events (psychogenic seizures).

#### CLINICAL HISTORY

The keystone to diagnosis and classification is accurate description of clinical event. It is most important that observers (friends, family, and co-workers) be questioned because patient may be amnesic and unable to provide complete description or assess episode frequency. Clinical features of seizures are analyzed by individual stages. Try to characterize these as carefully and completely as possible for each seizure. Remember patient may have more than one seizure type.

#### Prodrome

This can last for several hours. There can be subtle changes in mood, behavior, or thinking, characterized by increased anxiety, depression, or inability to concentrate or think clearly. Close observers can be cognizant of this change and able to predict subsequent seizure occurrence. There are no changes in EEG pattern during this stage; therefore, prodrome is not the beginning of the seizure. If prodromal pattern is stereotyped, occurs early, and lasts long

enough, it is sometimes possible for patients to abort the attack with extra doses of medications, but medication does not take effect rapidly enough to be effective when taken in this manner only.

## Aura

The aura is the *initial* portion of the seizure: EEG pattern changes, signaling the localized seizure origin. The aura usually lasts several seconds to minutes. Aura occurs in *partial* seizures of simple partial type with elementary symptomatology (jacksonian motor march, spreading paresthesias) or complex partial seizures (foul odor, rising feeling in chest or stomach, bitter taste in the mouth, though disorders). The aura frequently helps localize the cortical region origin of seizure discharge. In primary generalized seizures, patients experience *no* aura.

## Ictus

Ictus refers to the seizure episode. Ictus begins abruptly; the patient can be normal then suddenly unconscious or unaware of surroundings and unable to respond appropriately seconds later. Individual attacks may last 15 to 30 seconds in absence seizures, 2 to 5 minutes in major motor seizures, and 1 to 5 minutes in simple or complex partial seizures. EEG is invariably abnormal if recorded during the ictus; however, rarely in certain partial complex seizures, surface EEG is normal, but an abnormal pattern is usually seen if sphenoidal, nasopharyngeal, or depth electrodes are used (Figure 11-1). Normal EEG is strong evidence that “seizure” is *nonepileptic*, for example syncope or psychogenic seizure. The patient is amnesic for ictus in generalized (major motor, absence) and partial complex seizures but is not amnesic in simple partial seizures.

## Postictal Stage

This refers to events immediately after the seizure. Following absence seizures patients can be perfectly alert and resume speech or work at the point it was discontinued, whereas following major motor or partial complex seizures patient can be dazed, confused, or disoriented. Family members may report that on certain mornings the patient awakens and appears “not to be quite right”; this suggests that nocturnal seizure has occurred, and patient has early morning postictal state. During postictal period patient should be examined carefully for Todd’s post-ictal neurologic deficit (hemiparesis, aphasia, anesthesia, reflex asymmetry, Babinski sign, visual field defect); this usually resolves within hours and almost always within 24 hours. This can be the diagnostic signature to lesion localization. In postictus, EEG can show diffuse or focal slow wave activity with suppression of normal background activity and then slowly normalize. Elevation of serum prolactin content can develop immediately following generalized tonic-clonic and partial complex seizure (within 30-60 minutes), rapidly normalizing in interictus. This prolactin elevation differentiates epileptic seizures from psychogenic nonepileptic seizures. Following major motor seizures, creatine kinase may be elevated due to intense muscle contraction.

## Interictal Period

Between attacks patient appears entirely normal, especially if seizures are infrequent. Other patients have persistent focal deficit because of presence of underlying structural brain lesion.

## SEIZURE HISTORY

In patients with seizures, the following information must be ascertained:

- Family history of seizures, episodes of sudden unexplained death, neurologic, or neurocutaneous diseases.
- Birth history, especially relating to perinatal hypoxia.
- Prior episodes of head trauma or CNS infection.
- Use of medication or drugs including alcohol, antihistamines, antipsychotics, antidepressants, and illicit drugs, especially phencyclidine and cocaine. These drugs and others can precipitate seizures.
- Precipitating factors for seizures, including fever, sleep deprivation, menstruation, hyperventilation, emotional stress, and exposure to flashing lights (photic stress) as occurs with video games.

Description of seizure should include detailed account of the patient during each stage.

The types of questions that should be asked are listed in Box 11-1.

A neurologic examination can be performed in interictal or postictal phase. In interictal stage, attention is directed toward defining mental change (memory loss, behavioral change, dementia), focal neurologic deficit, and intracranial hypertension. Listen over the patient's head with a stethoscope for bruit caused by vascular malformation, and inspect skin for evidence of neurocutaneous disorders (café au lait spots, neurofibroma, facial hemangioma, depigmented spots). Examination in postictal period should be made for Todd's neurological deficit. Look for meningeal signs suggesting meningitis or subarachnoid hemorrhage.

## CLINICAL SEIZURE DISORDERS (OUTLINED IN BOX 11-2)

### Generalized Seizures

#### *Tonic-Clonic Seizures (Primary Generalized, Major Motor, and Grand Mal)*

Primary generalized seizures begin without aura. Initially there is sudden loss of consciousness. If standing, patient falls to ground like wooden board in hypertonic (rigid) position; patient can be injured by falling. An initial tonic position is assumed: trunk and neck are hyperextended, shoulders and arms are extended, and feet are plantar flexed. Epileptic cry occurs as air is expelled forcibly through abducted vocal cords. Patient can become cyanotic, but apnea and respiratory arrest are infrequent unless seizure is prolonged or status epilepticus occurs. Tongue can be macerated; urinary or fecal incontinence can occur. The tonic phase is interrupted by clonic phase, during which there are symmetrical and rhythmical jerking movements of head, body, and extremities. Initially, these occur at 2 cps; they become irregular and intermittent and then stop. The clonic jerking never stops *abruptly* in epileptic seizure, as this abrupt cessation of clonic jerking is characteristic of psychogenic seizures. Seizures usually

last 2 to 5 minutes, but it is not uncommon for observers to overestimate seizure duration because of anxiety engendered by the attack. If seizures occur at night (nocturnal) and the patient is alone, the only evidence that seizure occurred may be that patient awakens on the floor having violently been thrown off the bed by the motor activity, has bloodied or macerated tongue, or has urinated in bed.

Postictally, patient is confused and drowsy; this can last several minutes to 24 hours. Because of intense muscle contractions during the seizure, myalgias can persist for several hours after the seizure and serum creatine kinase may be elevated. Autonomic phenomena include pupillary dilatation, salivation, diaphoresis, tachycardia, and hypertension. Respirations are rapid and shallow as result of lactic acidosis caused by intense muscle activity. Patients complain of headaches caused by vasodilation and muscle contractions resulting from seizure activity.

During tonic phase, EEG demonstrates generalized symmetrical spike discharges; this changes to spikes interspersed with slow waves in clonic stage. Because of intense muscle activity, EEG can be obscured by muscle potential artifact. Postictally there is generalized slowing, and low-voltage pattern and background activity is suppressed. A normal EEG during the episode would be inconsistent with epileptic seizures; however, 25% of seizure patients have a normal interictal EEG. Patients with frequent seizures are more likely to have abnormal EEG than patients with infrequent seizures. The more times that interictal EEG is performed, the more likely that EEG abnormality is detected because of increased EEG "sampling time." The "routine" EEG obtained during an awake state should be supplemented by EEG obtained during hyperventilation (2 to 3 minutes), during natural or drug-induced sleep, and following photic stimulation. Newer techniques including video monitoring (observing simultaneous EEG and patient activity during a "seizure") and ambulatory EEG monitoring (similar to cardiographic Holter monitoring) are useful in *selected* patients suspected of having seizures but in whom there is diagnostic uncertainty. In patients with clinically witnessed generalizing tonic-clonic seizures but in whom focal onset may not be observed, EEG is crucial for detecting electrical focality of the seizure. The presence of focal spike and slow wave discharges suggests underlying pathological lesion, but focal spike discharge alone can occur without underlying lesions detected by CT/MRI.

Because diagnosis of seizure disorder is established clinically, role of EEG in suggesting diagnosis of "epileptiform activity" without any clinical evidence to support this impression should be discouraged. Because 5% to 15% of normal population (without seizures) have nonspecific abnormal EEG patterns and even some nonepileptic patients have EEG spike patterns, over reliance on EEG for establishing epilepsy diagnosis should be discouraged. For example, history of fainting spells occurring in patients with nonspecific EEG abnormality should not be used to make the diagnosis of epilepsy.

If patient is evaluated *immediately* following initial seizure, studies including complete blood count, urinalysis, blood sugar, calcium and phosphorus, serum electrolytes (including bicarbonate and magnesium), liver and renal function profile, toxicology screen, and urine porphyrins should be performed. If these are negative, lumbar puncture should be done to exclude subarachnoid hemorrhage or meningitis. Skull roentgenography is important to detect intracranial calcification as seen in certain congenital diseases (tuberous sclerosis, Sturge-Weber syndrome), infections (toxoplasmosis), neoplasms (meningioma, astrocytoma, oligodendroglioma), or vascular malformations. With high-resolution CT, intracranial calcification is readily detected. CT/MRI is indicated for patients with partial seizures and for

patients with generalized seizures and for patients with generalized seizures who have EEG evidence of focal discharge or focal postictal neurologic deficit. MRI is indicated for patients with partial seizures with negative CT as certain cortical abnormalities (cortical heterotopia, hippocampal sclerosis) are better visualized with MRI. CT/MRI is not necessary in patients with *primary generalized* epilepsy because of very low likelihood of an underlying structural abnormality being present. CT is much less sensitive than MRI in detecting focal lesions in patients with epilepsy. MRI may detect microscopic lesions (e.g., gliosis) and congenital lesions (e.g., cortical heterotopias), not seen with CT. MRI is therefore the procedure of choice to assess patients with epilepsy except in the acute situation when a hemorrhagic or infectious-inflammatory lesion is suspected.

Certain patients diagnosed *initially* as having primary generalized tonic-clonic seizures have no clinical or EEG findings to indicate focal onset; however, focal features can develop at a later time. This indicates need for periodic reassessment of seizure patients, especially if seizures remain frequent. Specific indications for reassessment for epilepsy patients include the following: change in type of seizure pattern, increase in seizure frequency despite compliance with drug therapy and high anticonvulsant blood levels, and development of neurologic deterioration of generalized (dementia, memory loss) or focal type not explained by medication effect.

The onset of primary generalized tonic-clonic seizures is before age 25. There is increased familial incidence especially if seizures occurred in childhood; this familial tendency decreases in older patients. It has been speculated that the genetic pattern for primary generalized tonic-clonic seizures is autosomal dominant with incomplete penetrance.

Once diagnosis of primary generalized tonic-clonic seizure has been established and diagnostic studies have not detected pathological or metabolic abnormality, decide whether to treat initial seizure and make choice of the appropriate medication. Utilization of antiepileptic drugs (AED) is initiated when it is believed the risk of treatment is less than medical and psychosocial risk of further seizures. Treatment does not guarantee that seizures will not recur; it reduces the probability and risk of recurrence. Most physicians assume that the initial seizure is the harbinger of epilepsy attacks and requires prophylactic therapy; however, 5% of general population has single nonfebrile and nonprovoked seizure. If patient has seizure recurrence, this usually occurs within 1 to 3 years of initial seizure. Because certain patients do not have recurrence, risk of treatment must be weighed against “watchful waiting” approach (danger of patient injury from the next seizure or possibility that status epilepticus will be next seizure). The decision to withhold treatment to determine if seizure is an isolated episode or is recurrent carries risk because there is suggestive evidence that early control is associated with low recurrence rate. Prophylactic therapy for a single seizure is warranted for the following situations: the initial seizure was long in duration with prolonged postictal Todd’s paralysis, interictal EEG shows specific epileptiform activity, second seizure would interfere with the patient’s life (financial, vocational, social, psychological), and prior history of neurologic injury that is the probable cause of the seizure (e.g., head trauma, encephalitis). Drug treatment is not usually initiated if there is an obvious precipitating factor (e.g., emotional stress, alcohol or drugs, sleep deprivation) unless seizure is of the partial (simple or complex) type. If driving privileges, the patient vocation or independence are threatened, the decision should be to initiate therapy immediately. The rules concerning driving are determined by the laws of the individual state, not the physician beliefs.

Certain general principles of prophylactic anticonvulsant management should be

followed:

- Each drug has relative specificity for clinical and EEG seizure patterns (Table 11-1). In general terms, drugs that are effective against generalized tonic-clonic seizures exacerbate absence seizures (with exception of valproic acid).
- If patient has several seizure types, including generalized tonic-clonic seizures, initial treatment is directed toward this seizure, which represents greatest risk to the patient. After major motor seizures are well controlled, drugs can be initiated to treat other seizure types if these persist.
- Treatment should be initiated with single drug (monotherapy) at low dose and gradually increased. Increase dosage of single agent until seizures are controlled or side effects of medication occur. Adjust dose administration schedule to accommodate patient's lifestyle but in accordance with drug half-life. With monotherapy, it is possible to avoid multiple drug interaction problems. Multiple drugs can interfere with drug metabolism, and this increases need for frequent anticonvulsant blood levels. If adverse effects occur when patient is treated with two drugs, it is not possible to know precisely which drug caused adverse effect. Goal of treatment is to render patient seizure free without causing drug toxicity. Attainment of blood level that is in the correct "therapeutic range" is important; however, therapeutic blood levels represent a range of values at which normal individual patients achieve seizure control and at which, if exceeded, most patients become toxic. The effect for the individual patient can be quite different from the "average normal patient." If the individual patient continues to have frequent seizures with high blood levels but no clinical signs of toxicity, increase anticonvulsant dosage until control is achieved or *signs* of toxicity occur. If control is not achieved with one drug and the patient shows signs of toxicity, switch to second drug rather than initiate polypharmacy (using more than one medication). Two thirds of epileptic patients achieve seizure control with one medication; the addition of second medication achieves increased seizure control in only 10% additional patients, and toxicity develops in 90% of those using two or more drugs. Potential for drug toxicity and adverse interactions between multiple antiepileptic drugs are two reasons to avoid polypharmacy. When changing drug regimen, only modify one drug at one time so that if adverse effects occur it can easily be attributed to most recent change. When changing drugs never *abruptly* discontinue an AED because this can precipitate drug-withdrawal seizures.
- Patient noncompliance is major reason for poor seizure control. This is defined as failure of patient to take medication in manner prescribed by the physician. Ideally, frequency of drug administration should be based on pharmacokinetics (e.g., absorption time, drug half-life), but frequently patients alter drug schedule to fit their lifestyles and to attempt to minimize drug toxicity (e.g., sedation of phenobarbital, disequilibrium of phenytoin). Patients are more likely to take morning and evening doses and to omit the midday dose while at work or school. Because anticonvulsants affect CNS function, they can adversely influence alertness, attention, thinking, concentration, and memory. Compliance with anticonvulsant treatment is best ensured by educating patients about seizures, goals of seizure control, the effects of medication, and their responsibility for monitoring the effects of treatment. It is futile to take medication only when the patient feels a

seizure is about to occur as is attempted by some patients. All too often, the physician hears about the seizure patient who completes prescription but never returns for follow-up evaluation until the seizure recurs. This is especially dangerous because blood levels of anticonvulsant medication fall rapidly and status epilepticus can develop as a result of this rapid fall. This occurs because the patient did not understand chronic and recurrent nature of epileptic disorder.

- Anticonvulsant blood level determinations are sometimes done “routinely” but are of real value in only certain circumstances. If seizure control is poor, blood levels are indicated. If they are low, possible explanations include noncompliance, poor absorption, drug interactions, abnormal plasma protein binding, rapid drug metabolism, or inactive outdated drug preparations. Noncompliance is the most common cause of low drug blood levels. Before increasing dosage or changing medications, evaluate patient under controlled circumstances (physician is certain that patient has taken drug). If patient has adequate seizure control but low blood levels, it is not necessary to increase medication dose. Anticonvulsant blood levels are frequently necessary if patients are taking medications for other conditions (diabetes, hypertension, infections) or if patients receive multiple anticonvulsants.

*Treatment of Generalized Tonic-Clonic Seizures.* In adults, the initial drugs of choice include phenytoin, valproic acid, or carbamazepine; phenobarbital is less frequently used. Phenobarbital is safe, cheap and effective anticonvulsant but it is sometimes poorly tolerated because of sedative effect and cognitive impairment. Unfortunately, many patients cannot function competently when taking phenobarbital. Therapy is initiated with dose of 0.5 mg/kg using bedtime dose; this can be gradually increased to maximal dose of 2.0 mg/kg daily. Because there is marked variation in individual phenobarbital tolerance, toxic level is difficult to predict. This drug can induce its own metabolism; therefore, stable dose of phenobarbital can give consistent blood levels for 4 weeks, then blood level can drop rapidly as result of increased hepatic metabolism. Because of half-life of phenobarbital, it is acceptable to give the entire dose at bedtime; the alternative approach is to administer phenobarbital twice daily, with two thirds of total dose at bedtime if patient awakens too tired in the morning on once-a-day dose schedule.

Phenytoin (Dilantin) is the most widely used AED. It does not cause sedation at usual therapeutic doses. Because absorption is slow and its half-life ranges from 12 to 24 hours, divided doses (twice daily) are usually used, although in some patients it can be administered only daily and adequate seizure control is obtained. The usual starting dosage is 300 mg daily (5 mg/kg, 4 to 7 range). When therapy is initiated at this level, therapeutic blood levels are attained in 7 to 10 days. Rapid attainment of therapeutic blood levels (“dilantinization”) within 2 days is achieved by loading dose (i.e., initial dose of 1 g, followed by 800 mg and 600 mg on second and third days followed by maintenance dose of 300 or 400 mgm daily) Phenytoin is metabolized by hepatic enzymes and shows nonlinear saturation kinetics. This may require using 30 mgm tablets to titrate dose and avoid toxic effects. The therapeutic range of phenytoin is 10 to 20 µg/ml; horizontal nystagmus is usually present at this level, and its demonstration on neurologic examination is a rough estimate of “normal” therapeutic blood level. At blood levels higher than 20µg/ml vertical nystagmus and ataxia develop; at levels greater than 30µg/ml encephalopathy can develop. Phenytoin has narrow therapeutic range; seizures can be a toxic manifestation of high blood levels or a consequence of low blood level. Phenytoin causes gingival hyperplasia. Gum disease is prevented by careful oral hygiene including frequent dental check-ups. Because

phenytoin can cause hirsutism and gingival hyperplasia, it is not well accepted in young patients, especially females. Valproic acid and carbamazepine have more side effects than phenobarbital and phenytoin but are also excellent anticonvulsants (Table 11-1). For primary generalized seizures, valproic acid is frequently the drug of choice.

*Treatment of Active Single Generalized Tonic-Clonic Seizure.* During active seizure, protect patient from injury, then administer medication to stop the seizure if it has not stopped spontaneously. Almost all seizures stop spontaneously after several minutes; and single seizure does not cause permanent CNS damage. To protect the patient, place the patient's head on soft pillow to prevent head injury. A soft, padded tongue blade is inserted in the mouth to prevent tongue biting, but care must be taken not to force the tongue blade into the mouth against clenched teeth. A metallic spoon should never be used because of the risk of breaking teeth that can be aspirated. Respiration can become labored and irregular, and there can be short apneic periods, but usually no respiratory support is necessary. No attempt should be made to restrain patients because this effort can cause orthopedic injuries. Immediately obtain blood studies and toxicology; then administer glucose and thiamine. If intravenous line is in place, seizure can usually be aborted clinically and electrically by administering 5 mg of diazepam (Valium) or 1 to 2 mg of lorazepam (Ativan). These drugs can be repeated if seizures do not stop after initial dose. Lorazepam is more effective than diazepam as it has longer half-life, and less respiratory and cardiac toxicity. The seizure usually stops spontaneously within 2 to 5 minutes even without medication; therefore, it is unnecessary to try to establish an intravenous line in an acutely seizing patient. If patient is known epileptic under treatment, administering an additional dose of medication is frequently sufficient treatment, although probably not necessary, and the patient should be observed until fully conscious. Do not attempt to administer oral medication if patient is not fully awake. Although patient is quiet in postictal state, intravenous route should be established because it is possible that another seizure will occur and intravenous would be necessary.

### *Absence Seizures (Petit Mal)*

Absence seizures occur without prodrome or aura. There is sudden loss of awareness during which patient appears dazed and unresponsive. In simple absence seizures, there is no observed change in body tone and no myoclonic or stereotyped semipurposeful (automatic) movements. If patients are carefully monitored by videotape recordings, clonic eye blinking, mild myoclonic jerks of extremities, slight hypertonia of neck or trunk, slight hypotonia with head drooping, or semipurposeful automatisms can be detected. When these occur, this is defined as complex absence seizures. During absence attack, calling or shaking the patient does not interfere with trancelike state. If patient is talking, speech abruptly stops in midsentence. If patient is standing, posture is maintained, but loss of awareness can lead to injury if patient is riding bicycle or driving a car. Attacks last 10 to 45 seconds or sometimes even longer. Awareness abruptly returns, and patient continues activities performed before the "spell." Postictally, patient is only aware of "blank period." Initially these patients are sometimes thought to be daydreamers or to have behavior problems in school or at work before correct diagnosis of absence seizures is established.

Attacks can occur so infrequently that they are not detected, or as often as several hundred times daily and interfere with patient's daily living and school activities. Absence seizures are provoked by hyperventilation and worsened by anxiety and exercise. These seizures

begin in childhood, decrease in frequency in adolescence, and occasionally persist into adulthood, but usually cease and are replaced by another seizure type. Fifty percent of patients with absence attacks subsequently develop generalized tonic-clonic seizures, and this usually occurs in the early teenage period with maximal vulnerability for girls during menarche. During absence attack, EEG shows abrupt change from normal background to a 2- to 3 cps spike and wave pattern. The patient does not have clinical episode every time this EEG pattern occurs unless electrical dysrhythmia persists for longer than 5 to 10 seconds. In patients with absence attacks, an underlying lesion is rarely present; therefore, CT/MRI is not usually performed. EEG studies of patients with absence seizures and their noneffected (no clinical seizures) family members show that these siblings have 3 cps spike and wave pattern but may have no clinical seizures.

Valproic acid (Depakene) or divalproex sodium (Depakote) is the most appropriate drug for absence seizure treatment. Depakote is absorbed in duodenum and not the stomach; this reduces nausea. Liver toxicity, pancreatitis and thrombocytopenia are potential toxic effects; careful laboratory monitoring for these conditions is necessary. This is usually a problem only in patients in which valproic acid is used with other anticonvulsants. Valproate is highly plasma protein bound, but unbound component increases at higher plasma concentrations as protein binding sites saturate. Because sodium valproate has a broad spectrum for seizure control, including major motor type, it is the treatment of choice in absence seizures. Ethosuximide (Zarontin) is used for absence attacks if valproate cannot be used.

## **Partial Seizures**

Partial seizures are those in which initial clinical disturbance signifies focal unilateral activation of specific anatomical or functional cerebral cortical region. Partial seizures are classified as to whether consciousness is normal (simple) or altered (complex). Partial seizures can spread locally (Jacksonian march) and then terminate, or evolve into generalized motor seizure. Partial seizures are characterized by having an initial aura.

### *Simple Partial Seizures*

Simple partial seizures originate from localized (focal) cortical region to result in motor, somatosensory, autonomic, or psychic symptoms. One type begins with clonic rhythmical flexor movements of the thumb that stop or spread to contiguous muscle groups such as the wrist, arm, and shoulder, then involve the face and later the leg with initial involvement of hips, knees, ankles, and lastly toes (jacksonian march). In rare instances motor activity remains confined to one group of muscles; this can persist for hours or even years without stopping or spreading (epilepsia partialis continua). If abnormal electrical discharge originates in the frontal region, seizure begins with adersive (contralateral) deviation of head, shoulder, and eyes.

Partial somatosensory or special sensory seizures are less common. In one type, the patient describes numbness, tingling, or pins-and-needle sensations. Less frequently, there are feelings of heat, burning, electricity, or vibration. In these cases, abnormal discharge originates in postcentral primary somatosensory cortex. If localized abnormality is in the inferior somatosensory cortex, sensations can be bilateral and involve abnormal visceral sensations in the abdomen and chest. Symptoms of partial special sensory seizures include flashing white lights, kaleidoscope of colors, or sensation of darkness moving across the visual field (occipital cortex)

or appreciation of sound with buzzing, clicking, or roaring (temporal auditory cortex). Simple partial seizures with neurobehavioral symptoms include language (aphasic) disturbance, memory aberrations, ranging from vivid recall of past experience (*déjà vu*) to faulty recall (*jamais vu*), and illusions with distortion of size such that objects appear inappropriately large (*macropsia*) or small (*micropsia*), affective response (fear or anger), or cognitive effects (forced thinking).

During ictus of simple partial seizure, the EEG usually shows localized spike discharges. In the interictal phase the EEG can show localized spike or slow wave discharge, but *rarely* EEG can be normal in both ictal and interictal phase. This is because the lesion causing abnormal electrical discharge is located in cortical depths and does not project to the cortical surface. In patients with simple partial seizures complete neuroimaging studies – including EEG, CT, MRI, and possibly CSF examination – should be performed because suspicion of underlying focal lesion is high. MRI is more sensitive than CT in evaluating patients with partial seizures. Diagnostic studies usually demonstrate causal lesions in adult patients, whereas in certain adolescent patients simple partial seizures are benign without an identifiable underlying lesion. Certain metabolic conditions including diabetic nonketotic hyperosmolar coma cause partial seizures in absence of identifiable focal pathologic lesion. Even if diagnostic studies are negative, periodic reassessment is essential because certain lesions are not detected on initial evaluation, but may be detected when reassessment is done. Medical treatment of partial seizures can be difficult. No well-controlled clinical studies for this seizure type have demonstrated superiority of one anticonvulsant, but phenytoin or carbamazepine is usually the initial treatment. Several new anti-epileptic drugs have been introduced which are add-on therapy.

### *Complex Partial Seizures (Temporal Lobe or Psychomotor Seizures)*

Complex partial seizures are associated with altered awareness and responsiveness and frequently with stereotyped motor activity (automatisms). The aura can consist of varied behavioral and autonomic sensations, including visceral abdominal sensations (pain, flatulence, nausea, vomiting, and rising or fluttering abdominal sensations), bitter taste in mouth, olfactory hallucinations consisting of unpleasant odors, affective changes with free-floating fear or anger, and structured (auditory or visual) but not command hallucinations.

During the ictal period, mental and behavioral responsiveness is altered. The patient suddenly appears dazed, confused, or agitated or can act “crazy.” When physician speaks to a patient during partial complex seizure, patient can turn toward the sound and mumble incoherently and insensibly. There is no change in body tone; however, stereotyped semipurposeful movements – including picking and repetitive washing or rubbing hands – are observed. During episodes, the patient can become agitated and aggressive if restrained. It is unusual for patients to carry out sequential or planned activities during the seizure or the post-ictal phase. Patients can become incontinent. The seizure usually lasts several minutes and ends gradually, emerging into postictal state, whereas in other cases a complex partial seizure can spread into generalized tonic-clonic seizure.

Ictal EEG findings are variable. Characteristically there are spike discharges that originate from one temporal region and secondarily spread to contralateral hemisphere, or independent spike discharges can originate from both temporal lobes. Postictally there is usually diffuse slowing. In 10% to 30% of cases, the surface electrode EEG shows no ictal pattern change. Interictal EEG frequently shows spike, spike and wave, or rhythmical slow pattern in temporal region but can show no abnormality. If localized discharge originates from mesial

temporal (uncus) region, routine scalp electrodes may show no abnormality and nasopharyngeal, sphenoidal, or special temporal electrodes can be necessary. Complex partial seizures probably do not have a genetic basis. They can begin in childhood or adulthood. The pathological substrate for the complex partial seizures is mesial temporal sclerosis; believed to be related to perinatal hypoxic brain injury. This is especially true when the seizures begin before age 20. In patients with later onset complex partial seizures, there is a high incidence of temporal lobe vascular malformations, hamartomas, gliomas, meningiomas, atrophic regions secondary to head trauma or brain infections. CT/MRI can detect these pathological conditions. Again, MRI is most sensitive.

Carbamazepine is the drug of choice in controlling complex partial seizures. It induces enzyme activation for its metabolism (autoinduction). With increased autoinduction, there is shortened half-life. Begin with low starting dose and slowly increase dose. Administration of dose needs to be 3 or 4 times daily as half-life shortens. Newer extended release formulations allow twice-daily schedules. Phenytoin is the second drug of choice; phenobarbital and primidone are less effective. Newly approved drugs (felbamate, gabapentin, lomotrigine, topamax, zonegran, oxcarbazepine, tiagabine, levetiracetam) can make partial complex seizures less difficult management problem. Gabapentin has renal excretion and has no significant other drug interactions. On the other hand, lamotrigine is effective for partial complex seizures, but has significant interactions with the anticonvulsant drugs and 10 to 15% of patients develop skin rash. Topiramate cause significant cognitive impairment -- half-life is shortened by enzyme inducing anticonvulsant medication. Felbanate may cause dangerous side effects including aplastic anemia and hepatic toxicity. If these seizures are refractory to medical therapy, surgical resection of the anterior portion of temporal lobe, corpus callosal sectioning vagal nerve stimulation can be necessary for seizure control.

### *Partial Seizures Evolving to Generalized Tonic-Clonic Seizures*

Patients with complex or simple partial seizures can progress to generalized motor seizures. In some instances, initial seizure portion is not witnessed and attack can be diagnosed as generalized motor seizure. EEG is especially valuable in defining presence of localized electrical discharge. If localized origin is detected, diagnostic evaluation for underlying cause is mandatory. Treatment should be initiated with phenytoin, phenobarbital, or carbamazepine.

## **SEIZURES UNIQUE TO CHILDHOOD**

### **Neonatal Seizures**

Neonatal seizures can be difficult to recognize clinically because of their fragmentary nature. They do not have well-defined stereotyped pattern of other seizure types. Neonatal seizures can simulate normal jitteriness of newborn. Seizures can consist of tonic deviation of head and neck, oral-buccal movements, opisthotonic posturing, or multifocal myoclonic movements. Episodes of apnea without other motor findings are usually not caused by seizures. In equivocal cases diagnosis is established by abnormal EEG findings. It can be difficult to differentiate jitteriness, benign neonatal sleep activity, or myoclonus from neonatal seizures. There are multiple causes for neonatal seizures. The majority are due to perinatal complications

(asphyxia, intracranial hemorrhage, cerebral contusion caused by obstetrical trauma), sepsis, congenital malformations, metabolic disturbances (hypoglycemia, hypocalcemia, hypomagnesemia, biotinidase deficiency, pyridoxine dependency), or drug withdrawal (related to maternal drug addiction).

The prognosis of neonatal seizures depends on the cause. Certain conditions such as benign idiopathic neonatal seizures that occur most commonly on the fifth day of life have a good prognosis; benign familial seizures that occur on the second or third day have favorable outcomes. Pyridoxine deficiency should be suspected if the seizures do not respond to antiepileptic medication. Treatment consists of identifying an underlying cause and controlling seizures with phenobarbital or phenytoin.

## **Infantile Spasms**

Infantile spasms are seizures beginning in children between 3 and 12 months of age. The child may have shown previous neurologic signs or may have been previously normal. Infantile spasms consist of sudden brief flexor spasms of head, neck, trunk, and extremities that cause the child to double up or “jack-knife.” Each individual spasm lasts for only seconds; however, they can occur in clusters. The EEG pattern is “hypsarrhythmia” characterized by diffuse, irregular, high-voltage slow waves with interspersed spikes. The West syndrome includes a triad of infantile spasms, mental retardation, and “hypsarrhythmia” EEG pattern.

The prognosis is better if the child was neurologically normal before the attack, if no underlying cause is defined, and if attacks can be rapidly controlled with medication. One fifth of patients with infantile spasms have normal intellectual and behavioral development. CT/MRI should be done because neurocutaneous conditions (tuberous sclerosis) and congenital brain malformations are associated with infantile spasms. These seizures do not respond well to conventional anticonvulsants including treatment with valproic acid and clonazepam. The most effective treatment is felbatol; however very careful monitoring of CBC is required.

## **Lennox-Gastaut Syndrome**

Some patients develop seizure disorder characterized by multiple clinical patterns including sudden attacks of altered responsiveness that develop and terminate gradually, sudden akinetic “drop attacks” with the loss of postural tone that cause the patient to fall to the ground, and generalized myoclonus. Attacks usually begin between 2 and 4 years of age. Almost all patients are mentally retarded. EEG shows symmetrical spike and wave pattern usually with frequency of 1.5 to 2.5 cps; this is activated by sleep stage rather than by hyperventilation (as is characteristic of classic absence seizures). Therapy for this disorder has been improved by valproic acid or felbamate.

## **Juvenile Myoclonic Epilepsy**

This is genetically based disorder in which the abnormal gene locus is located in the short arm of chromosome 6. It is classified as generalized epilepsy. The disorder usually begins in adolescence. Symptoms include myoclonic jerks involving shoulders and arms; these characteristically occur on awakening. Initially, myoclonic jerks are not recognized as an epilepsy disorder; they can be considered manifestations of anxiety, nervousness, or “tic” disorder. These patients then develop generalized major motor seizures; however, some patients can also have absence seizures. Precipitating events for seizures include alcohol, fatigue, and

sleep deprivation. EEG shows 3.5 to 6 symmetrical polyspike and slow wave discharge. During myoclonic episodes EEG can show 6 to 16 polyspikes; this can precede EEG spike and slow wave pattern. Valproic acid is the treatment of choice for this seizure type. This disorder responds well to medication treatment; however, lifelong therapy is needed even with good seizure control.

## **Benign Epilepsy Syndromes**

Benign partial epilepsy with central midtemporal sharp waves (rolandic epilepsy) begins in childhood. Seizures are secondary generalized and usually occur nocturnally. Focal facial twitching and paresthesias and a focal clonic jerking of extremities occur during the day. AED are utilized if seizures are frequent, but this is rare as most patients have infrequent seizures.

## **Febrile Seizures**

Febrile seizures consist of brief episodes of generalized major motor seizures occurring as child initially develops febrile response. The child usually has only brief postictal depression and no focal neurologic deficit, and interictal EEG (obtained 1 week after the seizure) is normal. The initial seizure usually develops between 6 months and 4 years of age. Three to 5% of children develop seizures as part of febrile illness. In any child who experiences initial seizure and is febrile, the possibility of CNS infection must be excluded by lumbar puncture and CSF analysis. Two thirds of these patients develop nonfebrile seizures. Some children also develop nonfebrile seizures. Prognostic factors for development of nonfebrile recurrent seizures in these patients include the following:

- Prolonged attack lasting 20 to 30 minutes
- Focal origin of seizures
- Abnormal EEG at least 1 week after the seizure
- No family history of febrile seizures
- Abnormal neurologic development of the child before or after the initial seizure

Fifty to 70% of patients with febrile seizures have positive family history for this disorder, and the genetic pattern seems to be autosomal dominant. Efficacy of prophylactic treatment of febrile seizures with phenobarbital is controversial. Chronic phenobarbital prophylactic treatment reduces recurrence risk if compliance is maintained. There is no evidence that this decreases subsequent nonfebrile illness is not effective because the period of maximum vulnerability occurs as the temperature rises. Because phenobarbital is associated with sedation and behavioral disturbances in children, the major issue is whether febrile seizures represent a greater potential risk than chronic drug therapy. Rectal preparation of diazepam (Diastat) is effective if the seizure is prolonged.

## **DIFFERENTIAL DIAGNOSTIC PROBLEMS**

### **Fit (Seizure) Versus Faint (Syncope)**

During syncopal aura, patient can experience lightheadedness, visual blurring, and dizziness. This is followed by loss of consciousness; the patient falls limply. Certain syncopal patients experience random sporadic myoclonic jerks. In rare syncopal cases, the patient becomes unconscious and assumes a decerebrate (tonic) position followed by random irregular

clonic jerks. EEG show diffuse symmetrical slow wave pattern. Following syncopal episodes, the patient is dazed for several minutes. Certain seizure features – confusion, focal neurologic deficit – are not seen with syncope. It is important to differentiate convulsive syncope from generalized motor seizure because treating syncope with lorazepam or diazepam can lead to cardiorespiratory arrest.

## **Epileptic Versus Psychogenic (Nonepileptic) Seizure**

Emotional factors can precipitate epileptic seizures that can occur during sleep and while the patient is alone and unobserved. Nonepileptic psychogenic seizures invariably occur in the presence of observers, especially in the setting of emotionally charged situations. The term psychogenic seizures is preferred to “pseudo-seizures” or “hysterical” seizures. Psychogenic seizures indicate that there is no underlying neurochemical or neurophysiological abnormality; therefore, EEG is normal during the episode. There is frequently a history of prior physical or sexual abuse in these patients. In nonepileptic psychogenic seizures onset usually occurs gradually. The aura of nonepileptic seizure can consist of a choking sensation, chest pain, shortness of breath, and palpitations. The patient falls to the ground with writhing, struggling movements and side-to-side head movements. Motor components are not rhythmical in-phase tonic-clonic upper and lower extremity movements but appear as out-of-phase extremity motor activity accompanied by prominent pelvic thrusting and neck movements. There is usually no body rigidity (tonic phase) or abnormal eye movements. During nonepileptic psychogenic seizures patients can bite their lips and injure other people; tongue maceration and incontinence do not occur. There is no epileptic cry, but the patient may talk semicoherently. If restraint is attempted, patients become more violent. Consciousness does not appear to be lost, and the patient may respond to verbal or noxious stimulus. The attack can be aborted by verbal suggestion of the physician. After the psychogenic episode, the patient is not postictally confused, and there is usually no amnesia, although certain patients cannot accurately report episode details. The patient comes out of the attack *abruptly* without the twilight confusional state that is characteristic of epileptic seizures. Also, clonic jerks stop abruptly rather than gradually slowing; cyanosis, incontinence, and tongue biting are absent, and neurologic signs (abnormal pupillary reactivity, amnesia, Babinski signs) are not seen post-episode. During and immediately after attacks, the EEG shows no significant change in psychogenic nonepileptic seizures; this is clearly different from epileptic seizures. In diagnosing psychogenic seizures, simultaneous video monitoring and EEG recording has been beneficial. The highest incidence of psychogenic seizures occurs in patients who *also* have true epilepsy. If patient is evaluated for “episodes” and is observed to have psychogenic true seizures, this should not decrease the index of suspicion of true epilepsy because of the high association between epileptic and psychogenic seizures. It is important to recognize psychogenic nonepileptic seizures *not* caused by abnormal cerebral electrical activity as these do not respond to anticonvulsant medication. These patients are therefore exposed to medication risks without any potential benefit. Provocative testing to induce an “attack” such as using normal saline and the suggestion that this “medication” will induce an attack is helpful; however, ethical considerations of tricking the patient should be considered. Psychogenic seizures represent learned behavior; therefore, appropriate treatment should involve teaching patients more satisfactory psychological coping skills. Psychiatric evaluation is mandatory to identify psychological stressor for psychogenic seizure (prior physical

or sexual abuse).

## **Partial Complex Seizures and Periodic Psychoses**

Patients with partial complex seizures become confused and carry out semipurposeful stereotyped repetitive activities. The aura can include hallucinations that are visual or auditory, but do not command the patient to action. The patient is amnesic but does not perform purposeful or organized activity. Patients with absence or partial complex status epilepticus may mimic psychoses. EEG should show abnormalities in seizures, but not psychoses. Following a seizure, postictal psychiatric disturbances including psychoses may occur. These psychiatric disturbances usually resolve rapidly. Because symptoms are self-limited, antipsychotic medication is rarely necessary. Interictally, patients with partial complex seizures can have psychiatric disturbances including schizophreniform disorders characterized by well-circumscribed psychosis with hallucinations of hyperreligious nature, panic, or anxiety states.

## **Episodic Confusional States**

Episodic confusional states can be transient or prolonged. If occurring suddenly, they can represent partial complex or absence status epilepticus; EEG would be expected to show continuous abnormal electrical activity if they represent seizure activity. If the confusional episode is caused by drug intoxication, blood and urine toxicology and the EEG would be important to differentiate confusional state not associated with epileptic EEG process, for example, metabolic encephalopathy, from epileptiform process. Transient global amnesia can cause acute confusion with marked impairment of recent memory. These patients can be found wandering and be lost, but they are aware of their identity and address. This condition usually resolves completely in several hours. EEG is usually normal and does not show epileptic activity.

## **Simple Partial Seizures or Vascular Episodes (Migraine and Transient Ischemic Attacks)**

Simple partial seizures can spread in orderly progression during several seconds or minutes, whereas the focal neurologic (scintillating scotoma, fortification spectra, homonymous hemianopsia, hemiparesis, hemianesthesia, aphasia) phenomena of migraine spread more slowly (10 to 30 minutes). With migraine the onset of neurologic disturbances are usually *followed* by contralateral headache. Syncope can accompany migraine, but altered awareness does not usually occur in patients with migraine. In TIAs focal neurologic deficit or impairment develops suddenly with maximal deficit at the onset of attacks. Progression does not occur. There are “negative” and not “positive” symptoms. There is no altered consciousness, and headache is uncommon.

# **COMPREHENSIVE MANAGEMENT PROBLEMS**

## **Status Epilepticus**

Status epilepticus includes situations in which clinical and EEG expression of seizures occur with continued frequency, and the patient does not recover consciousness fully between

attacks. Also, a continuous seizure which lasts more than 5 minutes is defined as status epilepticus as most single seizures last less than 2 to 3 minutes; the longer the seizure the more difficult to stop. There are two major types of status-major motor convulsive and non-convulsive behavior episodes. Continuous tonic-clonic motor attacks from which patient does not completely recover consciousness between individual attacks represents a medical emergency because of potential risk of permanent neuronal damage resulting from hypoxia, rhabdomyolysis, hyperthermia, autonomic dysfunction, hypoglycemia, lactic acidosis, cardiac arrhythmias, and respiratory depression. The most common cause of status epilepticus is abrupt anticonvulsant medication withdrawal; other causes include brain lesions such as intracerebral hemorrhage, brain neoplasm, and hypoxic-ischemic and traumatic brain injury. The prognosis depends on the nature and extent of the pathologic process and not upon duration of seizures. Of medical patients in unexplained coma, consider non-convulsive status, especially if there is head or eye deviation, or slight twitching of an extremity or eyelid blinking to confirm this diagnosis. EEG is necessary if patient stops seizing but does not awaken. Without EEG, it is not possible to determine if depressed consciousness is post-ictal depression or nonconvulsive status. Mortality of major motor status is 25%; this is lower if status epilepticus is due to abrupt anticonvulsant medication withdrawal.

Initial management of status epilepticus includes ventilatory support with insertion of oral airway; this is followed by placement of an endotracheal tube. The patient should be positioned on one side to prevent aspiration. An intravenous pathway is established using large-gauge tubing, and blood is immediately analyzed for glucose, electrolytes (including calcium), liver, and renal function studies. Electrocardiographic monitoring is warranted especially if potentially cardiotoxic medications are used and it is important to avoid systemic arterial hypotension. Consider elective intubation especially if medication used to treat status depress respiration. Insert a Foley urinary catheter for urine output monitoring. It is extremely helpful (but frequently not feasible) to monitor drug treatment with portable EEG. Initial treatment should include 50 grams of glucose and 200 mg of thiamine administered intravenously after the blood is sampled for laboratory testing.

There are several major anticonvulsant treatment regimens, but no controlled study indicates superiority of one drug. AED must be administered intravenously although if patient is seizing an IV line cannot be immediately established; therefore initially use rectal diazepam (2 mg/kg) or intramuscular lorazepam, fosphenytoin or phenobarbital. Once intravenous line is established, utilize diazepam at 5 to 10 mg per minute; this is repeated every 10 to 20 minutes to maximum of 50 to 70 mg. This dosage usually stops seizures within several minutes; however, seizure will recur within 10 to 20 unless a longer-acting anticonvulsant is supplemented (e.g., phenytoin, phenobarbital). Diazepam can cause hypotension, sedation, and respiratory and cardiac depression. Lorazepam (0.1 mg/kg) can be substituted because it has less respiratory depression, no cardiac toxicity, and longer duration of action (4 to 24 hours). The initial dose should be 2 mg per minute; this can be followed by 1 mg every 2 minutes. Phenobarbital is administered in dose of 250 mg over 5 minute intervals. If seizure control is not achieved, this dose is repeated every 10 minutes to total dose of 20 mg per kg or EEG show burst suppressive. Disadvantages of phenobarbital include respiratory depression and excessive sedation. There is synergistic toxicity between diazepam and phenobarbital that can cause cardiovascular toxicity. Phenytoin is administered in doses of 20 mg/kg at a rate not exceeding 50 mg/min. This drug affects cardiac conduction system, and electrocardiographic monitoring is necessary; it also causes hypotension and blood pressure monitoring is necessary. Phenytoin is

poorly soluble; it must be given by direct intravenous injection containing normal saline and not mixed with other intravenous fluids. It is alkaline and irritating to veins; direct injection causes pain and has the potential to cause phlebitis. The solvent has recently been changed, and there is now less risk of hypotension and cardiac arrhythmias. Fosphenytoin is a prodrug (phosphate ester prodrug of phenytoin) which is less alkaline and irritating and can be administered at more rapid rates. It is converted to phenytoin by phosphatases. Depacon is the intravenous form of valproate and can be used at dose of 10 mgm/kg at rate of less than 200 mgm/minute. It is possible to load a patient within 10 minutes. Paraldehyde is supplied in ampules that each contains 5 ml. Five ampules are mixed with a solution containing 500 ml of dextrose and water or saline. Because of lipid properties, paraldehyde is poorly soluble and droplets are seen in the mixture. It is rapidly administered until seizures stop. This medication causes no acute cardiac toxicity, but unusual effects include metabolic acidosis and pulmonary hemorrhages. At the present time, its major disadvantage is that it is difficult to obtain because of limited availability.

If these AED are not effective, utilize midazolam (Versed) at initial dose of 0.2 mgm/kg and follow with infusion of .1 mgm/kg/hour or propofol (Diprivan) at dose of 2.0 mgm/kg and follow with infusion of 2 mgm/kg/hour. For continued refractory seizure use pentobarbital at dose of 12 mg/kg administered at initial dose of 1 to 2 mg/kg per hour. The goal is to obtain complete seizure control and burst-suppression pattern on the EEG. Continue pentobarbital for 24 hours and then decrease dosage after 24 hours. Thiopental (1 gram diluted in 500 ml of normal saline as a microdrip infused at 2 mg per minute until seizures stop and then maintain at 0.5 ml/min for 4 hours) may be used for barbiturate coma, but this has more cardiovascular toxicity than pentobarbital. If necessary, inhalational anesthetic medications (halothane, ketamine) may be utilized. In status epilepticus, patients may stop having active seizures but not awaken. Possibilities include continuous brain seizure activity or sedation from medication. It is therefore necessary to utilize EEG monitoring to determine the most likely mechanism (continuous spikes indicates seizures with need for additional medication or diffuse EEG slowing due to post-ictal or medication effect with risk of additional medication as brain has stopped seizing). Also, in refractory status epilepticus consider psychogenic seizures, and this is diagnosed by EEG findings.

Other forms of status occur but are not life threatening; however, the possibility of their progressing to generalized major motor status exists. For absence or partial complex status, the patient is in prolonged dazed or unresponsive state. Diagnosis is established by EEG recording. Absence status epilepticus is initially treated with 5 mg of intravenous diazepam or lorazepam; if this is not successful, the dose should be repeated. Partial complex seizure responds to intravenous diazepam, phenytoin, depacon, or phenobarbital. Simple partial seizure usually responds to lorazepam and diazepam.

## **Nonconvulsive Status Epilepticus**

Onset is relatively sudden with altered level and content of consciousness. These patients may be alert and show behavioral or other psychiatric symptoms. When behavioral abnormalities, change in affect or hallucinations, predominate, psychiatric diagnosis is considered. Motor and tone disturbances are not prominent in nonconvulsive status; however, ocular deviation and intermittent jerking may occur. Ten percent of patients in coma of undetermined etiology have behavioral electrical nonconvulsive status. Once diagnosis is considered EEG is necessary and shows 2.0 cps spike-wave discharge. Utilizing diazepam and

lorazepam, the mental state and EEG normalizes. Consider this diagnosis in all patients with sudden unexplained change in mental state or behavior.

## Criteria to Discontinue AED

Adequate seizure control can be achieved in majority of patients: generalized major motor, 70% to 80%; absence, 80% to 90%; complex partial, 50% to 60%; simple partial, less than 50%. There are different definitions of “control”; the number of seizures acceptable to the employed patient who needs to drive to work is less than that acceptable to institutionalized mentally retarded patient. If goal of therapy is to eliminate all seizures, patient may be forced to use higher dose of single drug or multiple drugs with associated potential risk of drug toxicity.

If patient is seizure free, decision to discontinue medication is sometimes reached because patient compliance decreases when patients become asymptomatic. It should be emphasized to patients that although seizure free there is risk that seizures can recur without medication. In this case, inconvenience and harm of long-term drug toxicity must be weighed against potential consequences of seizure recurrence. If patient is seizure free for 24 months and interictal EEG has normalized, there is still the possibility of seizure recurrence without medication in 25% to 33% of patients. If seizures recur after medication is discontinued appropriately, they sometimes become more difficult to control. Although this is a general impression, its validity is a highly debated issue. If medication treatment is to be stopped, withdrawal must be gradual and usually requires 2 to 4 months depending on type and dosage of anticonvulsant medication and prior duration of therapy. Those criteria suggesting highest probability that seizures will not recur without medication include the following: infrequent seizures before complete control achieved, normal EEG, rapid initial control of seizure, normal neurologic examinations, and normal CT/MRI. Adult patients with simple or complex partial seizures have high recurrence risks. Recurrence is least likely in petit mal seizures when patient is seizure free for 12 to 24 months and EEG has normalized. Patients with absence seizures are at significant risk of developing generalized motor seizures; this most frequently occurs at onset of puberty. Because this represents the period of greatest seizure development vulnerability, cessation of medication for absence attacks should not usually be attempted until the patient is older.

## SPECIAL SITUATIONS

### Pregnancy

If a patient has longstanding, well-controlled seizure disorder, the risk of precipitating seizures by altering the drug regimen is probably greater than the teratogenic effect of phenytoin, carbamazepine, or phenobarbital; however, many mothers would risk having a seizure in an effort to have healthy child. *All* anticonvulsant drugs cross the placenta, and all have been associated with increased risk of congenital malformations. Most common are orofacial clefts and cardiac abnormalities. Neural tube defects have been reported with valproic acid. There is some evidence that multivitamins containing folate can reduce risk of major malformations. In high-risk patients, alpha-fetoprotein levels should be obtained as well as ultrasound findings at 16 to 18 weeks of pregnancy. If ultrasound findings are inconclusive for spina bifida or cardiac or limb defects, amniocentesis should be performed. It is best if the patient and physician work prospectively regarding pregnancy rather than react to finding out the epileptic patient is

pregnant and then having to make decisions hastily. Be aware that oral contraceptive medications are less effective in epileptic patients taking enzyme inducing anticonvulsant medication.

One third of pregnant women will have increase in seizure frequency during pregnancy, probably because antiepileptic drug levels frequently fluctuate as result of changes in protein drug binding and metabolism. During pregnancy, if there is a problem with seizure control, utilize free drug blood levels because of the change in plasma protein binding that occurs in pregnancy. Epileptic patients have higher complication risks during pregnancy and delivery; children born of epileptic mothers have more neonatal complications including growth and developmental problems. If the patient develops a seizure during the first trimester, utilize the most effective AED at lowest effective dose for that seizure type. Poor seizure control is associated with greater risk of adverse events than the potential teratogenic effect of antiepileptic medication. Valproic acid and carbamazepine have increased risk of neural tube defects. Multivitamins with folate may reduce risk of malformations in pregnant women utilizing antiepileptic medication. In the second and third trimesters, the major risk is fetal hypoxia during a seizure and respiratory depression and excessive sedation caused by medication (e.g., phenobarbital, primidone). Seizures can develop during pregnancy as manifestations of eclampsia and cortical vein thrombosis. During labor, short acting benzodiazepines are probably the safest and most effective treatment for seizures. Eclampsia with convulsions is initially treated with magnesium sulfate. If this is not effective or causes respiratory depression or weakness, utilize lorazepam or phenytoin.

## **Drug-Withdrawal Seizures**

In our drug-oriented culture, drug abuse has become a significant problem. As part of the initial evaluation of a first seizure in any young person, toxicology should be performed. If seizure is related to drug use, it is probably not necessary to treat with anticonvulsant medication. There is an exception to this general rule: if drug-precipitated seizure occurs in a patient with a genetic predisposition for epilepsy, treatment would be indicated. The only way to determine this would be to see if subsequent seizures occurred in the drug-free state and then begin antiepileptic medication. In addition, a patient with predisposition for seizures may not develop recurrent seizures if the patient stops using illicit drugs, and prophylactic anticonvulsants may not be needed.

Drug withdrawal seizures are most frequently related to alcohol. These seizures usually occur during or after an episode of heavy alcoholic use and consist of single or multiple short bursts of generalized motor seizures. These attacks are rarely focal and focal seizures should be evaluated for underlying focal lesions. Acutely it may be necessary to treat with anticonvulsants if seizures are multiple because 5% of patients develop status epilepticus. Treat with lorazepam or diazepam and not phenytoin. Patient with alcohol-withdrawal seizures should not be treated with chronic anticonvulsant medication because if they begin alcoholic binge they stop their anticonvulsant medication abruptly and thereby increase risk of drug-withdrawal seizures.

## **Posttraumatic Seizures**

Following traumatic brain injury seizures may develop. The risk is dependent upon severity of injury. Patients with depressed skull fracture, brain contusion or hemorrhage,

persistent neurological dysfunction, or loss of consciousness in excess of 24 hours have high risk. Seizures that develop within one week of trauma are due to presence of brain necrosis or hemorrhage; whereas, those that develop after one week post-trauma may have gliosis as mechanism of seizure. Following severe head injury, prophylactic use of phenytoin is controversial. Some physicians will treat for 2 weeks and then taper if no seizures develop. Impact seizures that occur immediately at the time of trauma do not usually recur. Patients who suffer mild traumatic brain injury (brief loss of awareness, no neurological deficit, normal CT and MRI) do not have increased risk of seizures.

## **Psychiatric Aspects of Epilepsy**

Patients with a well-controlled seizure disorder do not have any characteristic personality or behavioral disturbances. There is no reason why these patients should not lead normal lives with certain simple and practical precautions. In patients with poorly controlled disorders, psychiatric symptomatology can result from social factors that these patients experience, or from social factors that these patients experience or from the results of epileptic cortical-hyperexcitability spreading to involve the limbic and septal systems, although these hypotheses are hard to prove. Intelligence in some patients with idiopathic epilepsy is within lower end of intelligence scale, and some require chronic institutionalization. If intelligence is adequate, epileptics should attend regular school unless seizure frequency or sedation from medication makes this impossible. If seizures become frequent, there may be evidence of mental deterioration that is not seen in patients with infrequent seizures.

In patients with partial complex seizures, certain interictal behavioral features have been reported including hypergraphia, hypersexuality, hyperreligiosity, and circumstantiality. In addition, well-circumscribed delusional psychosis with a religious preoccupation is seen in these patients. The relationship of clinical seizures and psychosis is not clear, but some observers have indicated that psychosis becomes more severe when the seizures are well controlled. A tendency toward aggressive but not organized violent or hypersexual behavior is seen in patients with partial complex seizures especially if seizures are poorly controlled.

## **Social Aspects of Epilepsy**

Patients with epilepsy are at risk for bodily injury and should avoid unprotected activities such as climbing, working near electrical machinery, and driving an automobile until control is established. The patients should avoid unprotected water or cycling activities because many epileptic deaths are related to water activities. Despite the potential risk of injury during a seizure, epileptics should attempt to lead a well-regulated but active life. There are no restrictions regarding food; alcohol must be avoided, and patients should not be deprived of sleep.

Patients with epilepsy should adhere to certain restrictions in operating motor vehicles. The law varies for different states, but usually licenses can be obtained when patients have been seizure free for several months to 2 years. Patients may be required to have a statement verifying the medical condition. It should be noted that patients with epilepsy cannot usually buy automobile insurance through conventional channels and must apply through the Assigned Risk Plan, in which there is pooling of high-risk policies shared equally by all companies. Similar problems are encountered with medical, life, and disability insurance. Because of unjustified and

unwarranted prejudice against patients with epilepsy, patients frequently conceal this condition when applying for employment.

### **Causes of Death in Epileptic Patients**

Epileptic patients can suffer sudden, unexplained death. If an epileptic has an attack while driving an automobile, the patient can suffer bodily injury or injure others. During a seizure, severe laryngospasm or blockage of the epiglottis by the tongue can cause asphyxia and death. Many deaths are related to water, and epileptic patients can have an attack and drown in a bathtub or in several inches of water. Death may also result from “autonomic storm.”

### **SUMMARY**

The term “seizure” is used to describe a paroxysmal clinical episode usually characterized by an alteration in consciousness and abnormal muscle tone. “Epilepsy” refers to recurrent seizures caused by abnormal cerebral cortical electrical hyperexcitability as manifested by abnormal electrical discharges detected with an EEG. Epilepsy can be generalized as a result of an underlying genetic basis that causes a cerebral dysthymia or be a focal component caused by an underlying structural brain lesion. The diagnosis of epilepsy is established by clinical and EEG criteria and appropriate treatment should be initiated with antiepileptic medication. Common causes of failure to control epilepsy are patient noncompliance and incorrect diagnosis, for example, pseudoseizure and syncope. It is crucial to control seizures as quickly as possible to prevent brain injury caused by recurrent seizures especially if status epilepticus occurs, but it is also important to use a carefully titrated dosage of antiepileptic medication to minimize systemic and CNS side effects of these medications.

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**BOX 11-1**

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1. Was there any change in patient's personality, mood, or behavior before the seizure?
  2. What were the circumstances in which the seizure occurred?
  3. Was there an abrupt beginning to the episode, and how did the attack terminate including the postictal phase?
  4. Were there premonitory symptoms? (Lightheadedness, visual blurring, weakness, dizziness indicate syncope.)
  5. How did patients appear during the seizure?
    - a. Was there loss of awareness or responsiveness, or did patient completely lose consciousness?
    - b. Did patient lose postural control? Any evidence of patient injury?
    - c. What type of motor (rhythmical symmetrical tonic-clonic, diffuse myoclonic jerking, stereotyped repetitive semipurposeful) activity occurred?
    - d. Did tongue biting or maceration occur?
    - e. Did urinary or fecal incontinence occur?
  6. What characterized the patient in the postictal stage?
    - a. Lethargy, disorientation, or focal neurologic deficit? How long in duration?
    - b. Autonomic disturbance? Hyperventilation and tachycardia can be seen following seizures; hypotension, bradycardia, and other cardiac arrhythmias are more common with syncope.
    - c. Other symptoms, including headache and myalgias?
  7. When do attacks occur?
    - a. Pattern: single or bursts?
    - b. Duration of each attack?
    - c. Time of occurrence: diurnal or nocturnal?
    - d. Relationship to other precipitating factors?
  8. Are attacks stereotyped or are there multiple clinical seizure patterns?
  9. Are seizures controlled with medication?
  10. Does patient comply with medication?
  11. Is there medication toxicity?
-

## BOX 11-2 Classification of Seizures

### **Generalized Seizures**

Tonic-clonic seizures

Absence seizures

Simple

Complex or atypical (with myoclonic jerks, change in postural tone, automatisms)

Myoclonic seizures

Infantile spasms

Tonic seizures

Atonic seizures

### **Partial Seizures**

Simple partial (consciousness preserved)

Motor symptoms

Somatosensory symptoms

Special sensory (visual, auditory) symptoms

Autonomic features

Psychic symptoms

Complex partial (consciousness impaired)

Cognitive

Affective

### **Secondarily Generalized Seizures**

Simple partial evolving to generalized seizure

Complex partial evolving to generalized seizure

Simple partial evolving to complex partial, then to generalized seizure

Simple partial evolving to complex partial, then to generalized seizures

**TABLE 11-1. Oral Administered Anticonvulsant Medications**

<i>Drug</i>	<i>Frequency of Administration</i>	<i>Seizure Type</i>	<i>Toxicity</i>
Phenobarbital	Single	Grand mal, partial	Sedation, nystagmus, skin reaction, paradoxical hyperkinesias (common in children)
Phenytoin (Dilantin)	Single or twice daily	Grand mal, partial	Gingival hyperplasia vertigo, ataxia, EEG slowing, encephalopathy, neuropathy, skin reaction, pseudo-lymphoma, systemic lupus, hepatitis, neutropenia, aplastic anemia; hirsutism osteomalacia
Primidone (Mysoline)	Divided	Partial, grand mal	Sedation, nystagmus, skin reaction
Carbamazepine (Tegretol)	Divided	Partial	Sedation, nystagmus, dizziness, ataxia, slurred speech, liver dysfunction, bone marrow suppression, skin reaction
Ethosuximide (Zarontin)	Divided	Absence	Nausea, vomiting, sedation, dizziness, pancytopenia, skin reaction
Valproic acid (Depakene, Depakote)	Divided	Lennox-Gastaut, partial, absence, grand mal	Nausea, vomiting, liver dysfunction, tremor, amenorrhea, skin reaction; pancreatitis, thrombocytopenia
Clonazepam (Clonipin)	Divided	Absence, Lennox-Gastaut	Sedation, dizziness, skin reaction, hyperactivity
Diazepam (Valium)	Divided	Absence	Sedation, ataxia, skin reaction

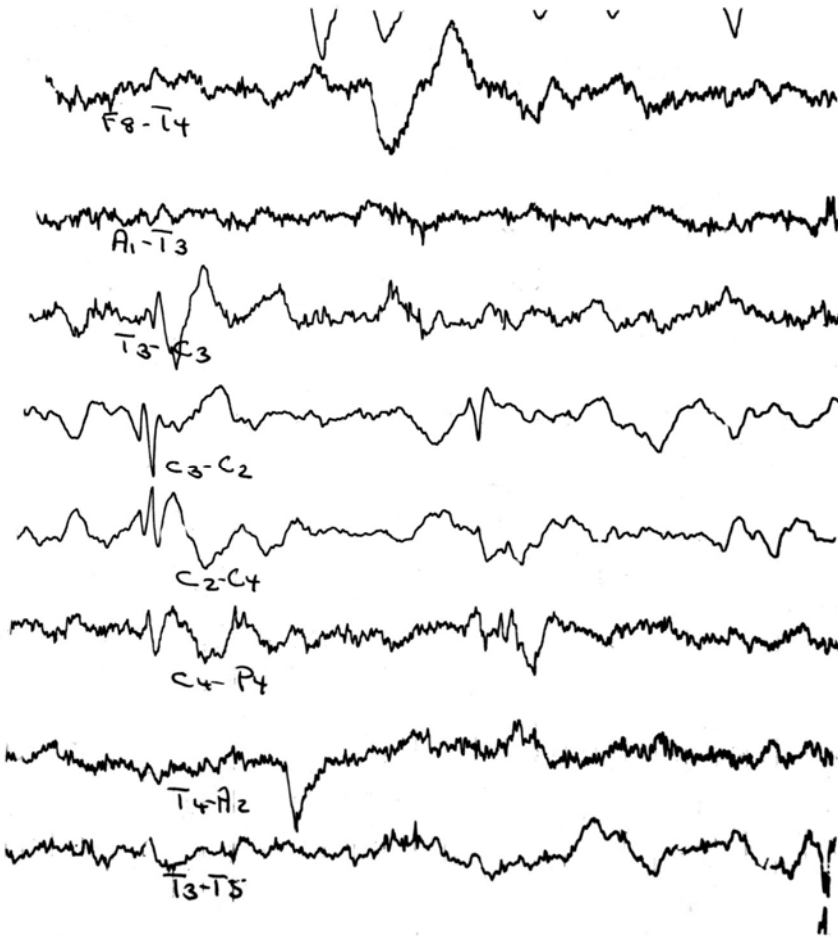
TABLE 11-1. Anticonvulsant Medications – cont'd

<i>Drug</i>	<i>Frequency of Administration</i>	<i>Seizure Type</i>	<i>Toxicity</i>
Felbamate (Felbatol)	Divided	Lennox-Gastaut, infantile spasm	Insomnia, fatigue, headache, weight loss; bone marrow suppression, gastro-intestinal
Gabapentin (Neurontin)	Divided	partial	Somnolence, fatigue, ataxia, dizziness
Lamotrigine (Lamictal)	Divided	partial	Fatigue, diplopia, dizziness, skin rash
Topiramate (Topamax)	Divided	partial	Renal stones, cognitive slowing, weight loss
Tiagabine (Gabitril)	Divided	partial	Weight gain, anxiety, depression
Levetiracetam (Keppra)	Divided	partial	Fatigue, anxiety, depression, reduced sweating, skin rash, kidney stones
Zonisamide (Zonegran)	Divided	partial	Weight loss; dizziness; skin rash
Oxcarbazepine (Trileptal)	Divided	partial	Hyponatremia, dizziness, hematological effects uncommon

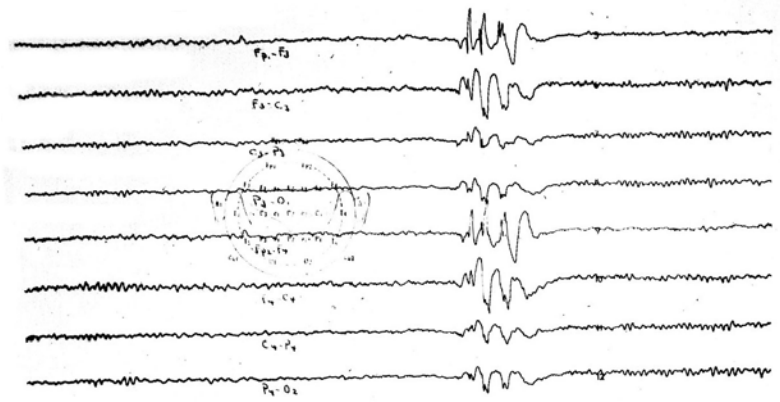
## FIGURES



**FIGURE 11-1, A** Symmetrical 3-cps spike and wave pattern in a child with absence seizures.



**FIGURE 11-1, B** Several bursts of spikes followed by slow wave in the interictal period of a patient with generalized seizures.



**FIGURE 11-1, C** Normal background rhythm followed by drowsiness (suppression of normal background) followed by a burst of spike and wave in a patient with generalized seizures.