

Seizures and Epilepsy Syndromes

Faculty

Kelley M. Anderson, MSN, ARNP, CCRN, received her undergraduate education at the University of Virginia. She completed her Master's degree at the University of Texas, Austin and her post-master's family nurse practitioner education at the University of Florida. While at the University of Florida, she worked with epileptic patients in the outpatient and acute care settings. She provided care with conventional modalities and assisted in the management of patients under investigative research medications and protocols. Her nursing background includes critical care, administration and faculty positions. Ms. Anderson is currently employed at the Chatham County Health Department, Savannah, Georgia, as a Family Nurse Practitioner.

Philip Matin, MD, received his Bachelor of Science degree in physics from Penn State University and was a Radiological Health Fellow at the Oak Ridge National Laboratory. He received an MS in physics at Vanderbilt University followed by his MD from Stanford University. After residency and fellowship in internal medicine and nuclear medicine at Santa Clara Valley Medical Center and Stanford, he was Clinical Assistant Professor, Associate and then Clinical Professor at the University of California School of Medicine, Davis. Dr. Matin was also an adjunct Professor of Pharmacy at the University of the Pacific. He is certified by the American Board of Nuclear Medicine. He is a past chairman of the Department of Medicine and the Department of Medical Education at Sutter Medical Center, Roseville, California. Dr. Matin has authored and edited several textbooks, textbook chapters, medical journals and scientific articles.

Faculty Disclosure

Contributing faculty, Kelley M. Anderson, MSN, ARNP, CCRN, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Philip Matin, MD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner

Chris Keegan, CST, MS

Division Planner Disclosure

The division planner has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for all surgical assistants and technologists who have contact with patients with seizure disorders.

Accreditation

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Course Objective

The purpose of this course is to expand the understanding of seizure disorders for surgical assistants and technologists in order to facilitate more effective treatment and care.

Learning Objectives

Upon completion of this course, you should be able to:

1. Differentiate between a seizure and epilepsy.
2. Recall the incidence of epilepsy.
3. Identify the major etiologies of epilepsy.
4. Describe the phases of a seizure and exacerbating factors.
5. Define the major seizure classifications.
6. Differentiate specific seizure types and list specific examples.
7. Discuss the significance of history taking and differential diagnosis in identifying epilepsy.
8. Identify diagnostic studies useful in the care of patients with epilepsy.
9. Detail the management of epilepsy in specific populations.

10. Discuss advantages and disadvantages for the most commonly prescribed pharmacologic agents.
11. Describe nonpharmacologic treatments for epilepsy.
12. Identify the most common complications occurring during or after a seizure.
13. Explain the emergent treatments for status epilepticus.
14. List measures that should be instituted to ensure patient safety.
15. Discuss the prevention of epilepsy, including specific patient education needs for non-English proficient patients.



Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

It is common in many medical settings to encounter individuals with epilepsy or to be in contact with their families. The purpose of this course is to expand the understanding of seizure disorders for physicians, nurses, and other healthcare professionals in order to facilitate earlier diagnoses and more effective treatment. This course will provide basic information about epilepsy and its management and note sources of additional patient education resources for patients with seizure disorders. Important features of the care of the patient with epilepsy will be presented. This will include an overview of the incidence and etiology of epilepsy, treatment modalities, prevention and self-care management. The impact of epilepsy on the individual, family and the community will also be discussed. Finally, special epilepsy concerns, including psychosocial issues, will be reviewed.

OVERVIEW OF SEIZURES AND SEIZURE DISORDERS

Seizures are common neurological disorders that occur across the entire spectrum of age, gender, race and socioeconomic background. As a result, professionals in most healthcare professions will have contact with or care for individuals who experience seizure events. Understanding seizure treatment and management will assist all healthcare professionals to provide the most appropriate care for this patient population.

DEFINITIONS

In the mid-1800s, Hughlings Jackson described a seizure as an abnormal electrical discharge of the brain [12]. Today, this description continues to typify our conceptualization of the definition of seizures. A seizure is an episode of excessive and disorganized electrical activity involving the neurons within the cerebral cortex. This activity can interrupt the ongoing mental and behavioral activities of the individual. In general, a seizure is a transient alteration in cognizance and/or control over physical processes. The alterations in brain

activity occur suddenly. These disturbances may cause changes in awareness, bodily movements, sensations and/or emotions.

A seizure can be a symptom of central nervous system (CNS) irritability due to a nonneurological disorder or medical illness. There are many examples of these extra-cranial disorders, including metabolic disturbances such as diabetes mellitus; substance abuse; dehydration and water intoxication; liver, kidney, cardiac or pulmonary disease; hypertension; septicemia; fever; and trauma. If a seizure ceases when the systemic or metabolic condition is corrected, it may be considered a symptom of the underlying disorder. In these cases, the patient is not considered to have epilepsy.

The word epilepsy is derived from the Greek word *epilambanein*, meaning to attack or seize. Epilepsy is a chronic neurological disorder characterized by recurrent, paroxysmal seizure activity. An isolated seizure does not indicate epilepsy. Approximately 10% of Americans will experience a seizure in their lifetime. [1]. The majority of these seizures, however, are attributable to a specific cause, such as those mentioned above. Epilepsy, in contrast, is a recurrent illness, and the patient must have at least two seizures before a diagnosis of epilepsy is considered. It is a paroxysmal neurological disorder consisting of recurrent episodes of alterations in level of consciousness, convulsive movements or other motor activity, sensory phenomena, behavioral abnormalities, and mental impairment. Unfortunately, the word "epilepsy" is often inappropriately used as a generic term to describe disorders in which patients experience seizures.

In this course, the generally accepted classifications of the term "seizure," referring to a specific neurological event, will be used. The event can be classified as a primary or secondary seizure depending upon the etiology.

Epilepsy refers to the syndrome that is characterized by multiple incidences of seizures for a patient. Epilepsy syndromes are classified according to the types of seizures experienced, and are divided broadly into generalized and partial. The seizure types are then further categorized into specific

diagnostic groups, such as absence seizure, partial simple seizure, etc. The terms generalized and partial are also applied to the epilepsy syndromes. In addition, there are specific epilepsy syndromes, some with similar names such as classic absence epilepsy and Rolandic epilepsy. These are usually classified by symptoms and etiology.

INCIDENCE

According to the Centers for Disease Control and Prevention, epilepsy is one of the most commonly diagnosed neurological disorders [1]. Approximately 1% of the United States population, or 2.7 million people, have epilepsy. More than 200,000 new cases are reported each year. Prevalence tends to increase with age; 570,000 patients with epilepsy are older than 65 years of age. The financial toll is estimated to be \$12.5 billion in direct medical costs and indirect costs [35]. Indirect costs include the corresponding reduction in employment earnings from unemployment and underemployment.

The incidence of this disorder is highest in patients younger than 2 years of age and rises again after 65 years of age. More than 20% of cases are discovered before a child is 5 years of age [35]. In infants, birth injuries and congenital defects are the primary causes of epilepsy. Birth injuries, genetic factors, infections and trauma are major contributing factors in children and adolescents from 2 to 20 years of age. For individuals between 20 and 30 years of age, brain tumors and other structural lesions are the foremost contributing causes. In those older than 50 years of age, cerebral vascular accidents (CVAs) and metastatic tumors are significant causes of seizure activity.

FINANCIAL IMPACT

The financial issues associated with the care of patients with epilepsy are far reaching. Considerations include reduced income due to the loss of work and increased long-term medical expenses.

Medical costs include office visits, medications and diagnostic studies. In a study sponsored by the Epilepsy Foundation with support from Aventis Pharmaceuticals, the average direct medical cost per person with epilepsy was more than \$6,400 over a six-year period. Patients with more severe and intractable epilepsy averaged direct medical costs near \$10,000 for the same time period. In the United States, the annual financial burden of epilepsy is approximately \$12.5 billion. These estimated costs were based on the cost of direct medical care and on the indirect cost of lost wages through unemployment or underemployment [4].

One challenge for persons with epilepsy is to find employment. Men and women with intractable epilepsy were expected to have a 35% and 25% reduction in lifetime earnings, respectively [4]. In individuals with controlled epilepsy, approximately one-fifth are less likely to work. In order to work, some patients are forced to accept positions that do not fully utilize their knowledge, skills and abilities. Although the person with epilepsy may be a good employee and complete assigned tasks, overcoming negative attitudes may be the more daunting challenge.

The patient may require referrals to a social worker or state agency for financial support or assistance with living arrangements. These agencies may assist with job training, vocational rehabilitation, counseling, transportation or housing. Some patients may qualify for financial support through a disability program. In 1999, the Work Incentives Improvement Act was established. This law allows individuals with epilepsy and other disabilities to obtain employment and maintain Medicare benefits for 4½ years. Additional assistance may be obtained for patients through the Health Department, Epilepsy Foundation or a pharmaceutical company's indigent program.

TYPES OF SEIZURES

PRIMARY AND SECONDARY SEIZURES

There are many possible etiologies that can lead to the development of seizures or the specific diagnosis of epilepsy. As noted, the prevalent forms of seizures are grouped into two categories, primary and secondary. The onset of seizures that are suspected to be primary epilepsy is usually experienced prior to 25 years of age. For these patients, more than 60% will never have a known etiology for the disorder [14].

Primary Seizures

There is some suggestion that primary epilepsy is of genetic origin. There is a genetic predisposition for controlling neural inhibition, excitatory neurotransmitters, and neuronal networks involved in the spread of a seizure. Everyone inherits some degree of susceptibility for the development of seizures. There is no consistent pathological identification; however, theories suggest an alteration due to synaptic structures or deranged chemical neurotransmitters. Between 1996 and 2006, researchers identified more than two dozen genes associated with epilepsy [36]. The genetic link may also affect an individual's predisposition to epilepsy or lower the threshold for seizure activity. These individual differences may account for diverse neurological manifestations after a head injury, fever or similar insult.

Secondary Seizures

There are multiple possible causes of secondary seizures. Events that occur in the prenatal period can contribute to the predisposition for seizure activity in newborns. Infection or systemic illnesses during pregnancy can adversely affect the developing fetus. The fetus is susceptible to central nervous system (CNS) injury during gestation, and the pregnant woman is increasingly in danger of seizures during this time. Throughout her pregnancy, the pregnant woman is susceptible to the development of eclampsia with hypertension and seizure activity. During the perinatal period, the fetus is susceptible to hypoxic and traumatic insults.

Adverse situations that occur during the prenatal and perinatal period are believed to be predisposing factors for hippocampal sclerosis in the medial temporal lobe, increasing susceptibility to seizures [12].

Congenital abnormalities, birth injuries, infections, genetic alterations, and hyperpyrexia can result in seizures in the susceptible individual. Throughout infancy and childhood, particular situations predispose a child to the development of seizure activity. A frequent etiology of seizure activity is a head injury. Head trauma occurs for a variety of reasons, including motor vehicle accidents, sports-related injuries or gunshot wounds. A blow to the head resulting in seizures may occur from physical abuse, a fall or accident in the home or may be work related. More severe injuries, such as trauma with a depressed skull fracture or hematoma, present a greater risk of developing epilepsy [4]. During the first year after the traumatic head injury, the injured individual has a significantly greater probability than the general population to suffer a seizure.

Seizures may also be a symptom of other neurological disorders and may lead to the diagnosis of a separate disease process. Cerebral vascular disease and arteriosclerotic disease, which deprive the brain of oxygen, are antecedent to the development of seizures. Arteriovenous malformations, intracranial tumors and brain abscesses are other central nervous system lesions that may provoke seizures. Central nervous system infections, such as meningitis, encephalitis, mumps, measles and diphtheria, may result in seizure activity. Another predisposing factor to the development of seizures is a history of surgical procedures or manipulations of brain tissue. Other neurological diseases, such as Alzheimer's disease, alter brain structure, and seizures may result from these changes.

An uncommon neurological disease, tuberous sclerosis (TS), is a genetic disorder that results in the formation of benign tumors in vital organs. The tumors may appear in multiple locations, including the brain, heart and kidneys. The incidence of TS is approximately 1 in 10,000 in the United States.

Seizures are a common symptom of this disorder and affect more than 80% of TS patients [23]. Seizure types vary and may present as infantile spasms, tonic-clonic, atonic, tonic, myoclonic, atypical absence, complex partial and other partial seizures.

Another common etiology for the development of secondary seizure activity is metabolic change. Alterations in electrolytes and glucose can enhance the predisposition for seizure activity. Prevalent metabolic changes include hypoglycemia, hyperglycemia, hyponatremia, hypernatremia and hypocalcemia. Absolute values from the clinical laboratory are not always predictive of seizure activity because rapid metabolic shifts can predispose neurological tissue to electrical instability. Other metabolic changes include those associated with organ dysfunction, including uremic and hepatic encephalopathy. Hypertensive encephalopathy can result in convulsions. In these cases, the blood pressure is generally greater than 250/150 mm Hg.

Toxic agents are another secondary etiology for the development of seizure events. Toxins, such as lead and other materials, are implicated in the development of seizure activity. Prescription medications, including antibiotics, psychotropic agents, antiarrhythmic agents, anesthetics, barbiturates and benzodiazepines, are known causes of seizures in susceptible patients [6]. Radiographic contrast agents are another occasional causative factor. Drugs of abuse, such as alcohol, cocaine, amphetamines, barbiturates and benzodiazepines, are known causative agents for the development of seizures, especially when associated with overdose and withdrawal. More than 5,000 individuals each year endure a seizure due to alcoholism [4].

One evening in Japan in 1997, 685 people simultaneously developed epileptic seizures. Most were children watching a televised cartoon with a background of rapidly changing blue and red. Although this situation was unprecedented, rapidly changing color patterns can cause nerve cells to be stimulated more quickly, resulting in seizure activity.

This form of epilepsy is referred to as photosensitive epilepsy. Tobimatsu and colleagues, who reported this incident, proposed a new form of epilepsy termed chromatic sensitive epilepsy [19].

Age and Etiology

The age at which a patient first develops the seizure is often an indication of the etiology, if an identifiable etiology can be elicited. Neonates and infants often experience seizures due to perinatal injuries, hypoxia, metabolic changes and congenital defects. Children can experience seizures due to hyperpyrexia, central nervous system infections or idiopathic reasons. During adolescence, the primary cause of seizures is head trauma [14]. In adulthood, a brain mass is a common etiology. As noted, cardiovascular diseases are the most common causes in individuals older than 50 years of age.

In summary, for the majority of patients there is no known etiology for epilepsy. Primary epilepsy is often genetic or idiopathic. Common secondary causes include head trauma, brain tumor, stroke, poisoning, infection and maternal injury. Clearly, the etiologies of epilepsy are very diverse.

BASIC PATHOPHYSIOLOGY OF SEIZURES

The mechanism of cerebral function during seizures is very complicated and is still the object of study by many investigators. The brain has even been studied *in vitro* to help elucidate the nature of epileptic activity [42]. This section will provide a very basic and brief description of the physiologic process during a seizure.

It is well understood that the brain transmits information and controls movement by electrical and chemical processes. Neurons located in the cerebral cortex intercommunicate to allow the integration of higher mental function as well as the required coordination for normal motor activity. Any event that significantly disrupts the normal propagation of this activity can result in a seizure.

The neuronal membranes and synapses are permeable and can be influenced and/or activated by many factors, including glucose and electrolyte levels, ischemia, trauma, and temperature. Some cells, such as neurons in the temporal lobe, are more easily excitable than others. When there is significant cerebral malfunction, the affected neurons can become an epileptogenic focus and begin to discharge rapidly. The involved cells may start firing with an increased frequency and with increasing amplitude. If this process continues without inhibition, the nearby neurons can become recruited and the process can begin to spread. The excitation can involve the local area or spread to the entire cerebral cortex. The thalamus, basal ganglia and the brain stem can be affected. If the brainstem is involved, there can be total loss of consciousness.

There are inhibitory neurons present that can act, in conjunction with exhaustion of the excitatory neurons, to end the seizure. The activity of the inhibitory neurons may be enhanced by some of the antiepileptic medications. When the seizure, or ictal, activity ends there may still be inhibition of the central nervous system leading to depression, impairment of consciousness and somnolence.

As mentioned, seizure activity can originate in an area of the brain that contains an abnormality, such as gliosis or scar tissue. These regions of altered tissue can interfere with normal neuronal activity in a way that predisposes them to initiate seizures and become an epileptogenic focus. These foci of seizure activity can be located in any of several locations in the brain.

Animal studies have shown that with repetitive seizure activity, the likelihood of additional seizures becomes greater. To patients, this means that early and appropriate intervention is necessary to obtain the best seizure control [11; 42].

PHASES OF A SEIZURE

The four generally recognized phases of a seizure are the prodrome, aura, ictal, and postictal stages. Not all patients experience, nor do all seizures include, every phase. The prodromal phase can last several days preceding a seizure. The prodrome is generally characterized as malaise or emotional changes. An aura occurs immediately prior to a seizure, usually lasting a few seconds. Patients often describe an aura as a warning. An aura may be autonomic or involve the auditory, olfactory, sensory, or visual senses. The description of an aura can vary and may include weakness, an epigastric sensation, a sense of fear, visual hallucinations, aphasia, headache, feelings of being hot or cold or sensing unpleasant odors. If a patient experiences auras, the auras are usually fairly consistent in that individual. However, auras can vary in the same patient and the use of antiepileptic drugs (AEDs) may alter or obscure the aura.

The ictal phase is the duration of the actual seizure activity. The patient experiences a paroxysmal, uncontrolled, abnormal, excessive discharge of electrical activity in the brain. There are also corresponding electroencephalogram (EEG) changes. The clinical manifestations will coincide with the type of seizure activity that the patient is experiencing.

The postictal period is the interval after the seizure episode. The patient may experience some change in consciousness or behavior. Some patients experience Todd's paralysis, a numbness or weakness of an affected extremity or the side of the face. After a tonic-clonic seizure, the postictal phenomena may be more severe. The patient may experience amnesia, confusion, fatigue and/or coma. Often, neuronal discharges remain abnormal and the EEG may indicate some slowing.

Exacerbating Factors

There are several known situations that may cause an increase in seizure activity in susceptible individuals. Sleep deprivation, mental and physical stress, acute illness, excessive fatigue, flashing lights and hyperventilation are among the most common exacerbating factors. The use or abuse of stimulants or alcohol is also linked to the increase in seizure activity in sensitive individuals.

MAJOR CLASSIFICATIONS OF SEIZURES

The classification of a patient's seizure is meaningful for a number of reasons. Classification provides a common terminology and understanding, directs effective treatment, influences appropriate management and guides patient education.

Seizures are broadly classified according to the location of origin. Generalized seizures begin in both cerebral hemispheres and occur throughout the brain tissue at onset. When a generalized seizure begins, there is synchronous involvement of the entire brain with diffuse electroencephalogram (EEG) abnormalities. During all generalized seizures, the patient experiences a sudden loss or lapse of consciousness at the onset of the seizure. According to the Epilepsy Foundation of America, "by definition, generalized seizures are not preceded by an aura or focal motor manifestation" [14]. Approximately 20% of seizures are classified as generalized at onset and are therefore the less common type. Generalized seizures can result in a loss of consciousness, convulsions, falls or muscle spasms. Some generalized seizures may encompass all of these events, while others may involve only one symptom.

Partial, or focal, seizures are the more common classification and originate in a circumscribed area or areas of the brain. Partial seizures occur in 75% to 80% of patients with epilepsy. Partial seizures are further subclassified according to symptoms and brain involvement. The three major subclassifications are simple partial, complex partial and partial seizures secondarily generalized. During

a simple partial seizure, the patient does not experience a loss of consciousness, but will experience motor, sensory or emotional phenomena. If patients experience impaired consciousness, a complex symptom, the seizure is considered to be a complex partial seizure. A partial onset seizure may occur at the area of initiation and terminate, or it can spread through more cerebral tissue. If the seizure continues to spread throughout the brain tissue, the seizure is classified as a partial onset seizure with secondary generalization, or partial seizure secondarily generalized. These secondarily generalized seizures may be tonic-clonic, tonic or clonic [14]. Many patients will experience more than one partial seizure type. A patient may describe simple partial seizures as "small" and complex partial seizures as "larger."

To summarize, the major classifications of seizures are not based upon severity or loss of consciousness, but are determined by the location of the initiation of the seizure. Although it is possible to have both generalized and partial seizures, the combination is extremely rare. By far, the greatest numbers of patients experience either partial onset or generalized onset seizures.

GENERALIZED SEIZURES

The generalized seizures include the absence, tonic-clonic, tonic, clonic, myoclonic and atonic types. Each of these seizures occurs with a predictable pattern accompanied by distinctive differences based on the individual patient.

Absence Seizures

The absence seizure has been long known as a *petit mal* seizure. Absence seizures are rare in adulthood and usually begin in children between 4 and 12 years of age [14]. This seizure is characterized by a brief period of altered consciousness, often described as a staring spell. The duration of the seizure is generally 5 to 30 seconds. The absence seizure may occur up to 100 times per day, or only rarely. The child is often described as having a blank stare that interrupts motor and mental activity, which begins and ends suddenly. The patient will have no loss of postural tone, but may experience a mild increase or decrease in muscular tone. Occasionally, the

child will exhibit minimal myoclonic movements around the eyelids or mouth. The patient may have automatisms associated with the seizure, including chewing or rapid blinking. During the seizure there is a loss of awareness. There is usually no postictal period and the individual can continue activities with full awareness after the seizure has subsided.

The EEG pattern is unique and is probably related to an etiology that is different than other seizure types. The typical ictal EEG shows a characteristic three per second generalized spike and wave discharge. The absence events can often be elicited with hyperventilation.

Most children will outgrow absence seizures and have no sequelae. There are some who also have associated tonic-clonic seizures and individuals who experience absence seizures in childhood are more susceptible to developing tonic-clonic or partial seizures in adulthood.

Tonic-Clonic Seizures

A tonic-clonic seizure has historically been referred to as a *grand mal* seizure. Tonic-clonic seizures account for only 10% of all seizures. However, when most individuals envision a typical seizure, the events of a tonic-clonic seizure are considered the classic occurrence. At the onset of the seizure, the patient will often vocalize a sudden cry. The cry is caused by the abrupt contraction of the diaphragm and chest muscles with the subsequent expulsion of air through the respiratory tract. This is quickly followed by the tonic phase. It can be observed as a fall with a stiff or rigid posture. The eyes often roll back; the jaw is clenched and the muscles are contracted. The patient may bite his or her tongue or cheek during this stage. The tonic phase will last approximately 30 to 60 seconds. Clonic movements will follow this phase with repetitive flexion movements of the body, including the arms, neck and hips. The movements are rhythmic, synchronous and jerky. The clonic movements usually continue for several minutes, but less than 5 minutes. The patient may produce excessive saliva, exhibit shallow breathing or develop cyanosis. The clonic movements will progressively slow, then

stop. The patient will then become flaccid and exhausted. Anal and urinary sphincters may relax, with resulting incontinence. The patient may remain unconscious for several minutes. As consciousness returns, the patient often experiences fatigue, loss of memory, headache and confusion. This postictal period can last from several minutes to hours.

Tonic-clonic seizures can occur in an unpredictable pattern and vary in frequency. A patient may experience a pure tonic seizure without clonic findings or a pure clonic seizure without the associated tonic events. These events are less common and are generally associated with other seizure types.

Myoclonic Seizures

A myoclonic seizure causes a quick muscular jerky movement. This movement may affect a specific part of the body, such as the face, trunk or extremities, or it may involve the entire body. A myoclonic seizure results in the involuntary, momentary, total loss of major muscle movement or muscle tone. These movements can be as simple as a jerky contraction or a head that droops, or as overwhelming as the entire body collapsing. Consciousness is briefly impaired. The jerky movements can be quite violent and cause the individual to fall or hit objects. Myoclonic seizures can occur as single events or be repeated in a rapid fashion.

Atonic Seizures

An atonic seizure or “drop attack” is evidenced by a seizure in which a patient suddenly collapses and falls with the legs unable to support the body. These seizures generally begin in childhood, between 2 and 5 years of age. The patient is unconscious during the event. The patient, if seated in a chair, may slump and fall to the floor. After a short period of approximately 10 to 60 seconds, the patient will regain consciousness. The postictal period is short and patients can generally continue with their activities. Less typically, the patient may experience a sudden loss of tone in the muscles of the jaw, neck or extremity.

PARTIAL SEIZURES

Partial, or focal, seizures occur when there is a localized brain disturbance. The majority of patients with epilepsy experience partial seizures. Partial seizures vary in terms of manifestations and severity and can result in changes in motor, sensory and emotional functions with no impairment of consciousness. Complex partial seizures involve an alteration in consciousness, which translates to an inability to react normally to external stimuli, either because of changes in awareness or an altered response. Secondarily generalized seizures are simple partial or complex partial seizures that propagate throughout the cerebral hemispheres.

Simple Partial Seizures

Simple partial seizures can be broken down into categories depending upon the observed symptoms. They include motor, sensory, autonomic and psychic seizures.

A partial motor seizure occurs from a focus in the region of the brain's motor cortex. Motor activity occurs in the corresponding part of the body innervated by the motor neurons that are affected. The hands and fingers have a large cortical representation; consequently, seizures are frequently noticed in these areas. The duration of these seizures is usually 1 to 2 minutes, although the patient may require additional time to completely recover after the event. The patient will present with twitching, jerking movements in an extremity, the face, the eyes or another area of the body. The patient remains fully conscious and aware of the seizure, but has no control of the event. These seizures usually remain localized, but the involuntary movement may spread centrally and involve an entire limb, one side of the body or the entire body. A Jacksonian march seizure involves the recruitment of additional muscles along the same side of the body in a progressive, step-wise fashion. The seizure may progress to involve other parts of the brain and affect other parts of the body. In these instances, it can become a complex partial or secondarily generalized seizure. After the seizure, the patient may experience temporary paralysis in the area involved for several minutes to several hours.

A partial sensory seizure is usually not observable by others, but may involve any of the senses. Transient sensory symptoms are experienced and may involve alterations in vision, hearing, taste, touch and smell. As with motor seizures, there is no loss of consciousness. These sensory seizures may occur in the parietal, occipital or posterior temporal lobes. The patient may describe paresthesias or numbness, tingling, bright flashing lights in vision fields, nausea, odd smells, buzzing sounds, voices, epigastric sensations or difficulty speaking.

Autonomic symptoms can include changes in heart or respiratory rate, increased sweating, *cutis anserina* (goose flesh), or unpleasant sensations in the viscera or head. Other patients may experience pilo-erection, pupillary changes, nausea and flushing.

In addition to sensory and motor phenomena, the seizures may involve psychological and other neurological changes. The psychic seizure may involve emotions, such as a feeling of fear, sadness, anger or joy. Some patients actually describe a pleasant sensation or a feeling of *déjà vu* during the simple partial seizure episode. The simple partial seizure may constitute the aura phase of other seizure types, such as the complex partial seizure.

Complex Partial Seizures

Another category of partial seizures includes those with complex symptoms, often called psychomotor seizures or complex partial seizures. The partial seizure is considered to be complex if there is the corresponding symptom of an impaired awareness or loss of consciousness. These seizures usually arise in the anterior temporal lobe, although they may occur in the frontal lobe. The most common radiologic and pathologic finding associated with the tendency to develop complex partial seizures is hippocampal sclerosis of the medial temporal lobe [12]. The duration of complex partial seizures is usually between 30 seconds and 2 minutes, although occasionally they may last longer. Some patients will experience an aura at the beginning of the complex partial seizure, especially those with a temporal lobe focus.

The patient with complex partial seizures often experiences and describes a variety of unusual sensations. These sensations may be memory flashbacks; feelings of *déjà vu*, a feeling of familiarity in a strange environment; *jamais vu*, a feeling of strangeness in a familiar environment; depersonalization from their surroundings; out of body experience; or distortions of visual or auditory sensations. The patient may have unprovoked emotions such as rage, terror, elation or sadness. The patient is often confused and unfocused during the event.

Typically, the first indication of a complex partial seizure is a blank stare. The patient will be unaware of his or her surroundings and will be unresponsive. The patient may exhibit automatisms, purposeless and repetitive activities, such as lip smacking, chewing, picking at objects, aimless walking, removing clothing or patting him or herself. If restrained, the patient may resist and struggle. The patient may repeat the same phrase several times or cry out. Usually, the patient's actions are disorganized and random, although occasionally a patient may continue with a repetitive activity throughout the seizure in an unfocused manner. The patient is not able to respond appropriately during the seizure, even though he or she may be able to speak. The patient is unaware of dangers such as traffic, fire or heights. After the event, patients are amnesic and have no memory of what occurred during the seizure. They are usually fatigued and, if more than one episode occurs, may sleep for a while. It is common for patients to have a typical, or "stereotyped," seizure in which the events of the seizure occur in the same order and are of the same type.

The events of a complex partial seizure have been described as follows:

The patient suddenly stopped talking and stared at the ground. Her head moved slowly to the side and she began rubbing the table with one hand, as if she was smoothing down a piece of paper. Her movements were slow and appeared deliberate. I asked the patient to remember "purple elephant." I asked the patient to lift

one foot off of the floor, but there was no response. The event lasted 90 seconds. The patient moved back to her previous position in the chair with her head in a neutral position and her hand in her lap. She looked at me, with a groggy expression, and stated repeatedly, "I'm ok." The patient was slow to respond and lethargic for several minutes. After she was alert, she could not recall the event or the phrase "purple elephant." The patient complained of a headache and fatigue. After a period of rest, she was able to resume her usual activities.

Secondarily Generalized Seizures

Partial seizures, whether they are simple or complex, have the potential to evolve. A simple partial seizure may begin in a specific region of the brain and affect a corresponding body part. The electrical activity in the brain may then spread and involve other tissues, resulting in a change or loss of consciousness, and causing a complex partial seizure. A complex partial seizure may progress to involve the entire cerebral network and the patient will experience a generalized seizure. A seizure that begins in a focal area and later involves the entire brain tissue is termed a secondarily generalized seizure. The progression is quite rapid, and the partial portion may be almost unnoticed. This necessitates a thorough history and evaluation to provide a proper diagnosis.

In many instances, patients will experience an aura followed by tonic and clonic movements and a period of unconsciousness. The entire episode typically lasts a few minutes and is followed by a period of somnolence. This type of seizure may occur during sleep, making the differentiation from a true generalized seizure more difficult.

Unclassified Seizures

Some seizures are not classified because they do not fit current definitions. Many seizures that occur during the first year of life are difficult to classify completely. The seizures may not be included in the previous descriptions, or additional data may be necessary to confirm a characteristic seizure type.

THE EPILEPTIC SYNDROMES

There is a difference between the classification of seizure types and epileptic syndromes. Some patients with epilepsy experience one type of seizure; others experience several different seizure events. Different syndromes account for the varying patient histories, etiology of seizures, seizure type, clinical presentation, EEG readings and neuroimaging findings. The International League Against Epilepsy (ILAE) has established an International Classification of Epilepsies and Epileptic Syndromes. Common epileptic syndromes include febrile epilepsy, childhood absence epilepsy, juvenile myoclonic epilepsy (JME), primary idiopathic generalized epilepsy, and localization-related epilepsy with complex partial seizures [24]. In total, the ILAE has identified more than 50 epileptic syndromes.

For example, the JME syndrome has specific associated diagnostic criteria. Patients with JME experience a series of myoclonic seizures, usually in the mornings. JME patients also experience tonic-clonic or absence seizures. Patients often have a family history of seizures and their onset is typically in childhood to early adulthood. Precipitating factors include sleep deprivation, emotional stress and alcohol consumption. According to Dreifuss and Henriksen, these patients have a 70% to 80% response to valproate as monotherapy [2].

DIAGNOSING SEIZURE DISORDERS

PATIENT HISTORY

The patient's history and the witness' detailed account of the seizure are very critical elements in treating any patient with epilepsy. An accurate and detailed seizure description is only achieved by asking open and pertinent questions. A seizure diary, kept by the patient and/or his or her family, can provide very useful information.

The patient should be questioned regarding any significant medical history.

- Has the patient ever experienced head trauma, loss of consciousness, central nervous system infection or febrile seizure?
- Is there any history of accident, injury or hospitalization?
- Is there any significant childhood illness or history, such as a perinatal insult or altered developmental history?

The patient should also be questioned regarding any significant family history of epilepsy. In addition:

- Determine if the patient has ever had a prolonged seizure in the past that would be considered severe or suggest status epilepticus.
- Ask which medications were used in the past and which drugs are currently prescribed.
- Find out if there are any known allergies.
- Ascertain the response to past medications and compliance with the prescribed regimen.
- Recognize that important aspects of the patient's medical treatment will involve the past surgical history, psychiatric history, previous diagnostic testing and social history.
- Investigate social history, including the patient's educational achievement, employment and living arrangements.
- Obtain information regarding the use of tobacco, caffeine, alcohol, illicit drugs and other substances.
- Inquire about the patient's sleep patterns, methods of transportation and leisure activities.

Determining the patient's knowledge of the seizure is an important aspect of the history.

- Can the patient and/or family describe the seizure episode?
- Are there any aggravating or precipitating factors, such as flashing lights or sleep deprivation, which correspond to the event?

- What occurs during each seizure phase, the preictal, ictal and postictal periods?
- How does the patient first gain knowledge that a seizure has occurred or is going to occur?
- The earliest emotional or sensory symptoms experienced by the patient can often convey very accurate localizing information.

The patient and family should be questioned about the duration of the seizure, timing the active event in seconds.

- Is there any change in consciousness?
- Is the patient able to react, recall or respond in a meaningful way?
- Can the patient follow commands, such as clapping hands, or remember something unusual, such as “green cat”?
- Can the patient answer a question during the seizure?
- What forms of motor activity occur?
- How does the patient tolerate the seizure?
- Are there any associated symptoms, such as incontinence, respiratory changes or injuries?
- How does the patient feel during the postictal period?

Any witness can provide substantial information regarding a seizure episode. The witness can describe the patient’s level of consciousness and behavior. Furthermore, the witness can detail events related to the patient’s muscle tone, injuries, state of confusion, residual paralysis and alertness. Fortunately, another individual often accompanies the patient with epilepsy due to imposed driving restrictions.

The patient’s and/or family member’s report of seizure activity is significant in caring for the person with epilepsy. These reports are often the primary mechanism to assess seizure intensity, duration and frequency. This information often determines medication choices, dosage adjustments and follow-up recommendations.

Patients and family members often inaccurately label the type of seizure experienced. Healthcare personnel should interpret a patient’s description of the seizure in order to determine seizure type. A patient may state that he has “*grand mals*” when his seizures are actually tonic-clonic, complex partial seizures or complex partial seizures that secondarily generalize. Or, a patient may simplify the categorizations to little and big, meaning partial motor and complex partial, respectively. Often, the patients have referred to their seizures with their individual terminology for years and renaming them for the patient is not helpful. A notation can be placed in the chart clarifying the patient’s descriptions to assist all care providers to depict the seizures in a consistent and accurate manner.

Dalrymple and Appleby conducted a study to determine seizure reporting to general practitioners and linked the findings to anonymous questionnaires that were completed two weeks after patients visited their doctors. The findings revealed that patients reported significantly more seizures on the questionnaire than were reported during the office visits. The authors contend that patients conceal seizure reporting because of the effect on various lifestyle patterns, including driving, employment and leisure activity [2].

Patients and families must be encouraged to provide accurate and honest answers. A supportive environment should be provided to allow for candid and truthful discussions in order to provide the most applicable and beneficial care.

PHYSICAL EXAMINATION

A comprehensive physical examination helps to determine the patient’s health status, contributing factors or secondary causes of epilepsy. The assessment should focus upon genetic diseases, neoplasm, infections, poisonings and autoimmune diseases, including systemic lupus erythematosus. Characteristics of organ dysfunction, including hepatic, cardiac, pulmonary and renal alterations, must also be evaluated.

Neurological Examination

A comprehensive neurological evaluation is essential for any individual who has experienced a seizure or has a diagnosis of epilepsy. Seizures may be the result of a distinct neurological disorder, or the disorder may be epilepsy itself.

The patient's mental status is evaluated throughout the examination. Mental status evaluation includes an assessment of orientation, level of alertness, affect and memory. Speech is evaluated for articulation, fluency, comprehension and repetition. The patient's cognitive function is assessed for attention, memory, information, calculation and abstract thinking.

The patient's neck should be evaluated for suppleness and carotid artery bruits. Cranial nerves I-XII are individually assessed and evaluated. This assessment includes an examination of the eyes, including vision, eye movements, extraocular movements, pupil equality and reaction to light and accommodation, fundi and visual fields. The cranial nerve examination includes an assessment of smell, jaw clenching, facial symmetry, facial sensation, taste, hearing, speech, tongue and uvula position, gag reflex, and trapezius/sternomastoid movement.

An evaluation of the motor system is performed to determine muscular function. Strength is appraised in upper and lower extremities on a five-point scale. Muscles are assessed for tone and bulk. Involuntary movements, such as tremor, clonus and fasciculations are noted. Ask the patient to perform rapid alternating movements, pointing movements, pronator drift and the Romberg test, as well as other tests to assess coordination. The patient's gait should also be assessed, including posture, base and tandem walking. Sensations are tested in all extremities and include the ability to sense pinprick, body part position, light touch, temperature and vibration.

Reflexes are evaluated and deep tendon reflexes are examined in all extremities, including the biceps, triceps, quadriceps, hamstrings, and the muscles affecting the knees and ankles. Additional reflexes are assessed, including those of the abdomen, feet and genital area.

In the acute care setting, additional neurological testing is appropriate. A detailed assessment will include the Glasgow Coma Scale and measures of level of consciousness (LOC) in association with stimuli.

Epilepsy is unlike many diseases in which the physical manifestations are the key to the diagnosis and treatment. In fact, the physical exam is often normal and unremarkable when the patient is not experiencing a seizure. Physical findings that are observed may be consistent with epilepsy or with a secondary medical or neurological disorder. Some of the important clinical findings include alterations in consciousness, sensation, motor abilities and reflexes. If seizures are due to an underlying disorder, these conditions are often discovered during the physical examination.

DIFFERENTIAL DIAGNOSIS

The diagnosis of epilepsy is based on several factors, with history as one of the most significant. A clinical history of seizures with concurrent EEG changes can usually establish the diagnosis of epilepsy. Signs or symptoms that may be most useful in the differentiation of epileptic seizures from other conditions include abrupt onset; altered or lost awareness (if not a simple partial seizure); brief duration; rapid recovery; and recurrent stereotypic episodes [14]. However, there are numerous disorders that mimic epilepsy. These disorders must be differentiated because they can be serious, life-threatening conditions that require intervention and treatment. Some conditions that must be ruled out in the differential diagnosis include: syncope, hyperventilation syndrome, transient ischemic attack (TIA), migraine and cataplexy [12].

Syncope can occur due to arrhythmia, cardiac disease, vasovagal response and orthostatic hypotension. Syncope can present with jerking movements and incontinence, which may confuse the diagnosis. Differentiating characteristics in syncope include light-headedness, weakness, hypotension and nausea. In a simple "vasovagal faint," the person usually recovers immediately after becoming recumbent.

Hyperventilation is often diagnosed in young adults. The patient may exhibit carpal-pedal spasms or muscle cramping similar to epileptic twitches. The patient, however, will usually complain of shortness of breath with light-headedness. These patients will also exhibit alterations in breathing that are dissimilar to those noted during an epileptic seizure.

Transient ischemic attacks usually present with paralysis, visual changes, aphasia and sensory alterations. The patient is conscious during a TIA, although confusion can occur.

A migraine can occur with an aura, although the aura associated with migraine is generally of a longer duration than a focal seizure. Cataplexy occurs in patients diagnosed with narcolepsy. The sudden changes in movement and muscle tone noted during cataplexy could mimic seizures; however the other clinical symptoms, including daytime sleep attacks, challenge this diagnosis.

There are other disorders that imitate the clinical picture of a seizure disorder. Metabolic and toxic disorders can occur in a number of settings. These situations include alcoholic blackouts, ingestion of hallucinogens or anticholinergics, sleep disorders, cardiovascular events, porphyria, movement disorders and psychiatric disorders. Some individuals will have a variety of independent, yet overlapping diagnoses. There may be a pathophysiological and clinical correlation of migraine, epilepsy and cerebral vascular disease in the same individual. One diagnosis does not automatically rule out other considerations in the same patient.

Psychogenic Pseudoseizures

Psychogenic pseudoseizures can be difficult to diagnose accurately, and often require simultaneous EEG and video monitoring. The patient often relates a history of sexual abuse, post-traumatic stress disorder or other psychological trauma. The seizures may appear very similar to an epileptic seizure, but careful history and seizure descriptions are crucial to an accurate diagnosis. Frontal lobe epilepsy is often confused with pseudoepileptic seizures. Pseudoepileptic attacks have no physiologic CNS abnormalities. Injuries are uncommon

with pseudoseizures. When eliciting the seizure description from the patient or witness, every detail can be important.

The following is an example of a patient with non-epileptic pseudoseizures:

Patient E is a man who experiences pseudoseizures after serving in the Vietnam War. A witness described the patient's pseudoseizure: "He began by crying, then becoming very withdrawn and quiet. He slowly leaned against the wall and slumped gradually to the floor onto his back. His eyes rolled around and his mouth was moving as if he was speaking without any words. Movements began in his left shoulder then proceeded down his arm, then throughout his entire body. His arms and legs flayed around, as if he were running away from something." Further questioning about the movements of the extremities revealed that the patient's arms moved independently of each other, in a smooth, nonrhythmic fashion. His legs had a kicking and running movement to them. Although this description does not automatically discount an epileptic seizure, there are some details that are not consistent with a common epileptic seizure. One of the most obvious inconsistencies is that the event does not follow a neuroanatomic pattern. Movements during a pseudoseizure may have personal symbolic significance to the patient.



EVIDENCE-BASED
PRACTICE
RECOMMENDATION

According to the American Academy of Neurology, elevated serum prolactin (PRL), when measured in appropriate clinical setting at 10 to 20 minutes after a suspected event, should be considered a useful adjunct to differentiate generalized tonic-clonic seizures or complex partial seizures from psychogenic nonepileptic seizures among adults and older children.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=8103.)

Last accessed May 17, 2007.)

Strength of Recommendation: Class I (Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a reference ["gold"] standard for case definition, where a test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. All patients undergoing the diagnostic test have the presence or absence of the disease determined.)

DIAGNOSTIC STUDIES

There are several diagnostic procedures that aid in the evaluation and management of individuals with suspected seizures or epilepsy. There are procedures available to evaluate brain wave activity, visualize brain structure and explore the blood flow and function of specific regions of the brain. Each test is meaningful and helpful when applied in appropriate and unique situations. However, EEG and magnetic resonance imaging (MRI) are the primary tests utilized.

Electroencephalogram (EEG)

The EEG measures the very small electrical signals that are constantly produced throughout the nerve cells of the brain. The brain waves are labeled by their pattern and frequency and described as alpha, beta, delta and theta rhythms. They normally occur between the range of 2 to 12 cycles per second. The EEG guides the identification and location of seizures and may establish the diagnosis of epilepsy. Unfortunately, it cannot always confirm the diagnosis. Seizures usually occur randomly, and the test may be completed during a time when no seizure activity is present. A small percentage of patients are diagnosed with epilepsy with no EEG changes, while other patients may have EEG abnormalities without epilepsy. Still, the EEG remains one of the most critical tools to assist with the diagnosis and understanding of epilepsy.

The most frequently ordered test is a random, routine or interictal EEG. This is performed when the patient is not having a seizure. As noted, a patient with epilepsy can have abnormal electrical activity in the absence of a seizure. These interictal epileptiform abnormalities may include a spike, which is a burst of electrical activity that is different from the normal EEG pattern. Spikes can occur in a focal area or in multiple foci throughout the brain. The interictal EEG is a beneficial test because a patient can schedule it at a time that is convenient. Unfortunately, although this is the most agreeable test for all individuals involved, seizures may not be present and a definitive diagnosis cannot always be obtained. However, approximately 60% of patients with epilepsy will have interictal EEG changes consistent with epilepsy [14].

Some EEG patterns are associated with specific types of seizures. A bilateral 3 Hz spike-wave discharge on the EEG is a classic pattern for a patient with absence seizures, especially during hyperventilation [6]. Patients with generalized idiopathic epilepsy often have a positive response to photic stimulation.

Often, an ictal EEG is required in order to provide the most accurate diagnosis and the most beneficial treatment. If the timing happens to be coincidental, a seizure may be captured during a random EEG. Unfortunately, this cannot be predicted and does not generally occur. Various methods are used to capture a seizure event, such as through a sleep-deprived EEG, a 24-hour monitor or inpatient monitoring. A sleep-deprived EEG requires the patient to remain awake during the usual hours of sleep, prior to the test. Sleep deprivation may result in a higher probability of capturing seizures on the EEG, especially for patients who are susceptible to seizures due to lack of sleep or for those patients who experience nocturnal seizures.

A 24-hour monitor cassette recording can also be utilized, although it does not include video monitoring. Prolonged recording increases the likelihood of capturing a seizure event, especially those that occur infrequently, during sleep, or those that are provoked by situations that are difficult to replicate. The patient is also instructed to provide a diary of the events of the day and to document the time of any seizures that occur.

Inpatient monitoring is another diagnostic option. This includes the simultaneous monitoring of EEG and video recording in an epilepsy center. Usually, the patient's AEDs are reduced or withdrawn. This setting provides the most thorough evaluation to correspond the patient's electrical activity with the clinical features of the seizures. Patients are placed in a safe setting where seizures can occur in the protected environment of experienced and accessible personnel. Although the environment is well controlled with appropriately trained health-care providers, the situation is often frightening for the patients and the family members. This testing is financially expensive and time consuming for

the patient and family. In order to capture seizures that will allow detailed evaluation, the patient may remain hospitalized for 2 days to 2 weeks.

In addition to the standard scalp electrodes, nasopharyngeal and sphenoidal electrodes may be inserted. Sphenoidal electrodes are inserted under the zygoma and above the mandible to assist with monitoring of the temporal lobes. EEG brain mapping can also be completed during a craniotomy procedure.

In the past, EEGs were only recorded on paper. Today, these recordings can be recorded, reviewed and stored digitally. According to the American Academy of Neurology and the American Clinical Neurophysiology Society, digital EEG recordings are a preferred method of brain wave recordings.

Patient education is necessary prior to the procedure. The random EEG takes approximately 30 to 40 minutes after the electrodes are attached. Patients will be instructed to clean their hair prior to reporting for the scheduled test. Clean hair will allow the electrodes to hold readily. Cream rinses and conditioner should be avoided. The head is measured to allow even spacing between each of the electrodes to obtain clear and symmetrical sampling of electrical activity. It should be explained to the patient that the application of the scalp electrodes and the monitoring of brain waves are painless procedures. Typically 23 or more electrodes are attached for the basic EEG. (The patients will ordinarily be required to shampoo their hair several times to remove all of the glue after the procedure.)

If a more extensive procedure is performed, such as the insertion of sphenoidal or other electrodes, some discomfort may be experienced. In these cases, an application of topical anesthetic is often prescribed and combined with oral analgesics.

The EEG is not a flawless diagnostic test and does not provide a definitive diagnosis of seizures or epilepsy, although the simultaneous video/EEG monitoring procedure can provide accurate diagnostic information. However, the EEG remains an essential tool to determine if a patient is having seizures, the type of seizures and the location of the seizures. In all situations, the patient's clinical

status and history must be assessed in conjunction with any diagnosis and care plan.

Magnetic Resonance Imaging (MRI)

Imaging studies are essential to determine the anatomy, function and possible structural abnormalities in the brain. Seizures may arise from specific areas or the general regions of anatomic abnormalities. MRI uses strong magnetic fields and radiofrequency electromagnetic radiation to produce images of body structures without the use of x-rays or other ionizing radiation. MRI is one of the most sensitive imaging tools to assess intracranial abnormalities, including tumors, arteriovenous malformations, infections, ischemia, cysts, atrophy, CVAs and hemorrhage. The hippocampus and medial temporal lobe can be visualized and evaluated with MRI. Assessment of these areas is an essential component of imaging studies, as alterations in this area are often helpful to localize an epileptogenic focus. The observation of mesial temporal sclerosis often correlates with the clinical findings of temporal or complex partial seizures. Surgically treatable lesions, such as low-grade gliomas, cortical dysplasia and cavernous angiomas, may be detectable by MRI but not by other imaging modalities [11; 43]. Intravenous contrast media may be used to increase the sensitivity and specificity of the examination.

Most patients are able to undergo an MRI scan without any difficulties. Exceptions include those patients who are markedly obese, unable to be in a supine position for approximately one hour, cannot tolerate a confined area or who are pregnant. A sedative, such as diazepam, is useful in many cases to mitigate the effects of claustrophobia in patients who are too uncomfortable to enter the apparatus.

To ensure a safe and successful MRI, patients must remove any items or substances that contain metallic (ferromagnetic) components, including jewelry, wallets, car keys, dentures or pins. The patient must also forgo cosmetic use, as some brands contain ferromagnetic ingredients. Patients must not have any implanted devices, such as a vagus nerve stimulator, hearing aid, cerebral aneurysm clip or cardiac pacemaker, that might be

dislodged by the procedure. This also includes susceptible metal objects, including shrapnel or other metal fragments. Titanium implants are not influenced by the procedure, and orthopedic implants that have been in place for long periods of time are also usually allowable.

Computerized Axial Tomography (CAT)

Computerized axial tomography (CAT), also commonly referred to as computed tomography (CT), is useful to obtain visualization of the brain at several depths. As with MRI, thin tomographic slices are obtained. Utilizing x-rays, the densities of intracranial structures can be calculated, resulting in the detection of tumors, arteriovenous malformations, hemorrhages and other intracranial abnormalities. The images produced by the CT scan, in most instances, are not as beneficial as the MRI for patients with seizures. However, the CT scan may be very useful if the patient has a new onset seizure. The test can detect a wide variety of acute abnormalities and is readily available in most medical centers. The procedure is noninvasive, painless and easier than an MRI for some patients to tolerate.

Positron Emission Tomography (PET)

Positron emission tomography (PET) presents an image of the function of the brain by quantifying the amount of glucose, oxygen and other substances used by different regions the brain. The resulting analysis assists in locating areas of seizure activity by noting changes in the brain's metabolism and chemistry. To conduct a PET scan, a very small amount of a short half-life radioactive material is injected intravenously and images are immediately obtained. The patient will often be required to be supine for as long as two hours during the scan. Pregnancy can be a relative contraindication to this test, but the functional information obtained may outweigh the negative effects of the radiation.

Single Photon Emission Computed Tomography (SPECT)

Single photon emission computed tomography (SPECT) is another nuclear medicine diagnostic examination that is gaining importance for patients with seizures. The SPECT scan uses a small amount

of radioactive material to measure cerebral blood flow and assist in locating areas of seizure activity. These scans are particularly helpful if they are completed prior to a seizure and immediately postictally. The study cannot be performed during the ictal phase if it involves significant motion. Comparisons of the scans can assist in determining the position and type of a seizure focus as well as help locate a possible vascular cause of the seizure.

Lumbar Puncture

A lumbar puncture may be performed to help rule out an infectious etiology of a seizure. In addition, measuring the pressure of cerebral spinal fluid is useful in the diagnosis of a possible mass lesion. Laboratory analysis of the cerebral spinal fluid can also often be of benefit.

CLINICAL LABORATORY STUDIES

During an initial evaluation of a patient, a comprehensive laboratory profile should be completed. The laboratory results can assist in determining an etiology for the patient's seizures and aid in treatment decisions. If a causative factor is discovered, treatment will be essential to correct the underlying disorder. Otherwise, the laboratory results are useful in ascertaining which antiepileptic medication will be the most opportune for the patient. Initial laboratory evaluations should include electrolytes, a comprehensive metabolic panel, complete blood count (CBC), erythrocyte sedimentation rate, blood urea nitrogen, creatinine and liver function tests. If the history is suggestive, then toxic screens for drugs, alcohol and toxin levels, such as lead, may be useful.

Patients who are prescribed AEDs will often require additional laboratory testing. Depending on the medication, intermittent testing of liver function, CBC and electrolytes may be required. Monitoring plasma blood levels of AEDs can be a useful tool to assist with the management of medication types and doses. Levels can be used to determine medication compliance, therapeutic failure and adverse reactions. AED blood sampling should be completed at the same time for each patient, usually prior to the first dose of the day. When medication dosages are altered, the new dosage should be maintained

until a steady state is achieved prior to obtaining levels. Generally, 4 to 6 half-lives of the medication should be completed; for phenytoin, this time period is more than 7 days. Blood level evaluations are helpful in patient care, but must always be correlated with the patient's clinical status. Patients may require a level of medication higher or lower than the stated "normal" levels. A therapeutic dose is one that controls the seizures with a minimum number of side effects, regardless of the numerical value of laboratory test results.

EPILEPSY IN SPECIFIC POPULATIONS

EPILEPSY IN CHILDREN

Seizures can begin at any age, but commonly arise before 20 years of age. Children who experience seizures face unique challenges. Some children's seizures may be self-limiting and some experience no disease state, while other children develop devastating forms of epilepsy. These children's needs may vary considerably, but often are related to developmental delays, depression, absence from school and problems with their peers.

Children diagnosed with epilepsy will require regular office visits and evaluations. The administration of AEDs poses unique situations in children. Children grow rapidly and their weight changes, which requires alterations in medication doses. Children also have an increased metabolism and may require higher medication doses than those used in adults. A school-aged child may be able to assist in taking medications on their own with parental or school nurse supervision and aids such as a pillbox. Antiepileptic medications may affect a child's academic performance and achievements. Interfering factors include side effects of medications, unrecognized seizures, alterations in brain function and missed school days. Medications, such as phenobarbital, may make a child sleepy. Adjusting medication doses or timing of the medication may assist in the child's attentiveness and ability to concentrate.

Febrile Seizures

Febrile seizures are the most common seizure type in children, generally occurring between 3 months and 5 years of age. Febrile seizures are tonic-clonic seizures associated with a core temperature greater than 38 degrees Celsius, but with no other recognizable etiology [6]. Febrile seizures are classified as simple or complex. Simple febrile seizures are short and there are no associated focal neurological findings. In an infant less than 6 months of age, a lumbar puncture is indicated to rule out meningitis, as typical signs may be absent. Imaging and laboratory evaluations are completed if trauma or electrolyte disturbances are likely. Parents can minimize febrile convulsions with antipyretics and tepid sponge baths during febrile illnesses. Usually, these children require no further intervention.

Complex febrile seizures are longer than 15 minutes in duration, occur more than once every 24 hours and/or coincide with focal neurological findings. The incidence of developing nonfebrile seizures later in life increases for patients who experience complex febrile seizures in childhood. There is evidence that prolonged febrile seizures can cause medial temporal sclerosis [16]. Antiepileptic drugs may be instituted for children experiencing complex febrile seizures. AED treatment choices include phenobarbital for continuous dosing or diazepam for acute treatment of an event.

West Syndrome

West syndrome is a severe epileptic disorder, usually beginning between 3 months and 2 years of age. The patient displays characteristic infantile spasms, which are sudden jerky movements that often cluster. Although each child may experience spasms in a different manner, the event usually begins suddenly and occurs for a few seconds. A typical spasm results in the patient extending his or her arms outward with the head falling forward and the eyes gazing upward. A child may experience 1 or 2 spasms at a time or 20 may occur in a few seconds. These children have a distinctive EEG pattern, called hypsarrhythmia. The EEG reveals bursts of electrical activity, including high voltage activity, with chaotic recordings.

There are several etiologies for West syndrome. Some causes occur before birth during the early stages of pregnancy and result in abnormal brain development. Other causes occur shortly after birth, and include neonatal encephalopathy. Children may develop this syndrome due to central nervous system infections early in life. Some children develop infantile spasms along with other neurological conditions, such as tuberous sclerosis. For some children, the etiology is unclear.

Although some children experience developmental milestones consistent with their peers, the patient with West syndrome often suffers from mental retardation and developmental delays. In the majority of children with West syndrome, the disease is very difficult to manage. Current medication alternatives include corticosteroids, adrenocorticotropic hormones, benzodiazepines and AEDs. The AED of choice is sodium valproate.

Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome is another severe epileptic disorder in children. These patients have generalized seizures with multiple seizure types, usually between 1 and 5 years of age, but generally before 14 years of age. Ordinarily, one of the seizure types causes the patient to fall. The EEG reveals characteristic slow spike and wave discharges. Most patients suffer from mental retardation, especially if the onset occurs before 3 years of age. Many children will have a history of infantile spasms and multiple disabilities, including cerebral palsy, blindness and hearing impairment.

Juvenile Myoclonic Epilepsy

Juvenile myoclonic epilepsy (JME) is an autosomal inheritance disorder, meaning these children often have a family history of epilepsy. JME is one of the most common benign epileptic syndromes. The onset of this disorder occurs in childhood or early adulthood. The patient experiences myoclonic jerking of the upper extremities shortly after awakening. The patient with JME will also experience generalized tonic-clonic or absence seizures. The seizures may be aggravated by stress or sleep deprivation. More than 70% of patients with JME have a positive response to valproate therapy [3].

EPILEPSY IN THE ELDERLY

Elderly patients with epilepsy may be difficult to manage. One of the primary concerns is that elderly patients are often prescribed multiple concomitant medications, which can predispose the patient to drug interactions and adverse effects. Another concern is that elderly individuals metabolize medications less effectively and often have an increased sensitivity to side effects. These side effects include fatigue, unsteadiness and forgetfulness. Care must be taken to evaluate the patient and to provide therapies consistent with the patient's abilities and situation.

EPILEPSY IN WOMEN

Women may experience epilepsy differently from men due to hormonal changes and the reproductive cycle. There is an unclear relationship between female hormones and neurological functioning. Estrogen can stimulate, and progesterone can inhibit, some neurons that are involved in seizure activity. Women have unique needs in regard to factors related to ovulation, reproduction and menopause that can affect epilepsy. Some women experience changes in seizure activity that coincide with hormonal fluctuations. During puberty, epileptic females may experience a decrease in seizure activity, while others may initially develop an epilepsy disorder at this time. Other women report a change in seizure patterns during ovulation or around the menstrual cycle. Often, patients will report an increase in number or severity of seizures during the premenstrual days and the first few days of the menstrual cycle. This phenomenon is called catamenial epilepsy.

Temporal lobe epilepsy is associated with an increased likelihood of disorders such as polycystic ovarian disease, amenorrhea, early menopause and irregular menses [4]. The hypothalamus and pituitary gland control the regulation of gonadotropin-releasing hormone, luteinizing hormone, follicle-stimulating hormone and prolactin. Thyroid and adrenal corticoid hormones also affect ovulation and reproduction. The hormonal regulatory centers for these hormones are connected to the temporal

lobe and, as a result, seizure disorders in this region may affect the regulation of these hormones. There is also evidence that some AEDs may disturb hormonal regulation, but their effects on fertility are not entirely clear.

Preconception counseling is essential for all women with epilepsy who are of childbearing age. If the woman does not want children at the time of consultation, then contraceptive methods should be discussed that are acceptable to the individual. Some AEDs interfere with the metabolism of oral contraceptives, levonorgestrel implants and medroxyprogesterone injections. When a liver enzyme-inducing medication, such as phenytoin, carbamazepine, phenobarbital, primidone or topiramate, is administered concomitantly with an oral contraceptive, the contraceptive will be metabolized more quickly and become less reliable. These women will require at least 35 micrograms of estrogen when oral contraceptives are considered an appropriate option. There are no known drug interactions with lamotrigine and gabapentin. The hormonal relationship with valproate and felbamate with oral contraceptives may lead to a higher level of the hormones, which will also require monitoring. Women should be educated about the reliability of each method, alternative methods and when to notify a healthcare professional. Notification is essential when the patient experiences breakthrough bleeding, menstrual irregularities, changes in seizures or other adverse effects.

Overall, there is a 2% to 3% risk of a woman having a child with an alteration at birth. The risk doubles to 4% to 6% in women with epilepsy [39]. This increased risk is due to a number of factors including genetics, seizures during pregnancy and the use of AEDs. As with many medications, AEDs have the most devastating effects during the first few weeks of pregnancy. Unfortunately, women are not always aware of the pregnancy during this time period. The risks of AEDs are starting to be understood, but the risk of having seizures during pregnancy is less clear. There is some evidence that seizures may

cause abnormal uterine contractions that could account for the increase in miscarriage, stillbirth and hemorrhage seen in women with epilepsy. These issues must be discussed with women and their partners prior to conception.

When a woman expresses her desire to have children, certain considerations are made regarding medication choices and regimens. There must be an appropriate and individualized balance between the risk of medications and the risk of seizures. All women should be counseled to notify their healthcare providers when they become pregnant. Women must be told to continue their medications as prescribed and not to stop or alter the medications on their own. The ideal situation is to have a woman on a single medication that provides adequate seizure control at the lowest dose possible. Multiple metabolic changes occur during pregnancy and these may affect the mechanisms by which the medications are processed. During pregnancy, close monitoring and frequent dose changes may be required. Any women who are currently pregnant and taking AEDs are eligible to enroll in the Antiepileptic Drug Pregnancy Registry. This registry is primarily concerned with studying the potential effects that AEDs may have on fetal development [41]. More information on the registry is available at <http://www.mgh.harvard.edu/aed> or by calling 1-888-233-2334.

In general, all women should be advised to take a multivitamin with folic acid on a daily basis prior to conception. The addition of folic acid to the diet, especially in those women that lack adequate nutrition or those taking AEDs, may decrease the risk of abnormalities in the newborn. The patient should be provided with the reassurance that more than 90% of epileptic women who become pregnant give birth to healthy infants with no abnormalities [4]. Congenital abnormalities that are more common include cleft lip, cleft palate, heart abnormalities and spina bifida. Valproate and carbamazepine appear to pose the greatest risk of neurological abnormalities.



The Scottish Intercollegiate Guidelines Network recommends that all pregnant women with epilepsy be prescribed a daily dose of 5 mg folic acid from preconception until the end of the first trimester.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=5694.

Last accessed May 17, 2007.)

Strength of Recommendation/Level of Evidence: D
(Non-analytic studies, e.g. case reports or case series, or expert opinion)

The pregnant epileptic woman will require early prenatal care and possible genetic counseling. Some neonates develop coagulation disorders that are related to vitamin K deficiency. These disorders are usually noted in mothers taking phenytoin, phenobarbital and primidone throughout the pregnancy. Soon after birth, the newborn should be given vitamin K or the woman with epilepsy should be administered oral vitamin K during the last weeks of pregnancy. The postpartum period will require additional monitoring of medication dosages, blood levels and seizure status. The patient will require support and rest to prevent additional seizures. Although AEDs can be found in breast milk, their presence does not preclude breastfeeding for most women. In some cases, infants of breastfeeding women experience somnolence or irritability, especially with phenobarbital. Supplemental bottle feedings may be recommended.

During menopause, seizure characteristics may change in women. Many women report an improvement in their condition, while others state that the seizures worsen or report no change. Hormonal replacement therapy must be carefully considered and balanced with other risk factors like cardiac disease, osteoporosis, uterine cancer, breast cancer and the patient's epilepsy. In general, patients receiving supplemental estrogen should also receive progesterone to assist with seizure control. More research is required to understand the complex issues related to women and epilepsy. Research should focus on these unique issues in regard to management, medications and treatment. [44]

EPILEPSY IN MEN

Men with epilepsy may also experience cyclic or hormonal fluctuations in their seizure patterns. Fertility and reproductive changes affected by epilepsy in men are not well understood. Sexual problems, however, appear to be common in epileptic men. Approximately one-third of men with epilepsy report having trouble obtaining and maintaining an erection [4]. There is hope that the medications for erectile dysfunction may help with this problem; however, at this time there is insufficient evidence to make an estimate of any benefit. The constraints associated with participation in sports and some occupations, such as piloting an aircraft, can produce a significant psychological problem in some men and should be addressed by the attending physician.

THERAPEUTIC MODALITIES

Although prevention of epilepsy is the ultimate goal, this is not always possible. However, there is a variety of treatment options. Comprehensive treatment is an important aspect of care for all patients with epilepsy. Managing the disorder improves the quality of life, and the consequences of not treating may be great. Seizures that go untreated or are poorly controlled have an increased risk of becoming more severe or more difficult to manage. Treatment recommendations now tend toward more aggressive management and earlier surgical evaluation for patients with epilepsy.

PHARMACOLOGIC MANAGEMENT

The utilization of antiepileptic drugs is currently the mainstay of therapeutic options. The effectiveness of the antiepileptic drugs relies on the ability to classify the seizure type by its clinical presentation, history and diagnostic test findings. It is important to know the correct seizure type, as some AEDs will exacerbate certain seizures or seizure syndromes (**Table 1**). The goal of these medications is to reduce or control seizure activity, not to cure the disorder. In general, partial seizures are more difficult to treat with medications than generalized seizures. AEDs allow approximately

COMMON MEDICATIONS/SEIZURE TYPES						
Medication	Partial Onset	Tonic-Clonic	Absence	Myoclonic	Atonic	Other
Carbamazepine	X	X				
Clonazepam			X		X	Lennox-Gastaut
Diazepam				X		Status Epilepticus
Ethosuximide			X			
Felbamate	X	X				Lennox-Gastaut West Syndrome
Gabapentin	X	X				
Lamotrigine	X					Lennox-Gastaut
Lorazepam						Status Epilepticus
Oxcarbazepine	X					
Phenobarbital	X	X				Status Epilepticus
Phenytoin	X	X				Status Epilepticus
Pregabalin	X					
Primidone	X	X				Psychomotor
Tiagabine	X					Miscellaneous
Topiramate	X	X				Lennox-Gastaut
Valproic Acid	X	X	X	X	X	
Divalproex	X	X	X	X		
Vigabatrin	X					
As medication indications and dosages vary, please consult the latest literature for changes to the recommendations.						
Source: [21]						Table 1

60% to 70% of epileptic patients to achieve seizure control with minimum side effects. Another 25% can achieve good control with current medications, although some adverse effects may be experienced [14]. Kwan and Brodie found that a patient's response to the first AED was an indicator of the success of any AED [9]. If a patient does not respond well with the first medication due to lack of efficacy, then it is likely that the patient may have refractory epilepsy. Only 11% of patients became seizure free with a subsequent AED. However, if treatment failure was due to side effects or an idiosyncratic reaction, then alternative AEDs were more successful [9].

AEDs assist patients by stabilizing nerve cell membranes and by preventing the spread of abnormal electrical discharges. Many of the medications require a therapeutic level of effectiveness to provide the best seizure control with minimum side effects. Treatment with medications usually focuses on using an adequate dose of a single medication rather than smaller doses of several drugs.

Monotherapy is the goal for most patients due to the benefits of improved drug compliance, reduced cost of medication and laboratory evaluations, lower risk of adverse effects and lessened chance of drug interactions. There is an understanding that polytherapy offers no advantage over monotherapy for about 90% of patients with epilepsy [6]. If the first AED that is attempted proves undesirable due to lack of efficacy or adverse effects, the first medication is tapered, while a second is slowly added. After several single medications are used that are consistent with the patient's seizure type, polytherapy may be attempted. It is common for a refractory patient to require a daily regimen of two or three AEDs. Adequate treatment may take several weeks or months to become beneficial. During treatment, healthcare providers must consider the possibility of patient noncompliance, incorrect diagnosis and other factors that may contribute to the ineffectiveness of a medication choice.

AED ADVERSE EFFECTS		
Antiepileptic Drug	Possible Side Effects	Possible Idiosyncratic Effects
Carbamazepine	Dizziness, visual changes, headache, lethargy, anorexia, nausea, ataxia, syncope	Agranulocytosis, aplastic anemia, Stevens Johnson Syndrome
Clonazepam	Drowsiness, ataxia, behavioral changes, movement disorders, speech alterations, hypersecretion in bronchioles, amnesia	
Ethosuximide	GI distress, drowsiness, sedation, headache	Liver disorders, systemic lupus erythematosus, psychosis, depression, leukopenia, Stevens Johnson Syndrome
Felbamate	Anorexia, vomiting, insomnia, headache, somnolence	Aplastic anemia, liver failure
Gabapentin	Somnolence, dizziness, ataxia, nystagmus, weight gain, rash, nausea, vision changes, tremor, slurred speech, peripheral edema	Acute renal failure, cardiac anomalies
Lamotrigine	Fatigue, drowsiness, ataxia, dizziness, headache, GI distress, visual changes, alopecia, pruritis	Stevens Johnson Syndrome, fetal abnormalities
Lorazepam	Sedation, amnesia, behavioral changes	Respiratory depression, withdrawal reaction
Oxcarbazepine	Dizziness, somnolence, nausea, vision changes	Rash
Phenobarbital	Sedation, mental dullness, cognitive impairment, ataxia	Hyperactivity, rash
Phenytoin	Dizziness, drowsiness, nystagmus, ataxia, hypotension, EKG changes	Gingival hyperplasia, hirsutism, coarsening of facial features, acne, rash, peripheral neuropathy
Pregabalin	Dizziness, somnolence, visual disturbances, peripheral edema	
Primidone	Sedation, mental dullness, cognitive impairment, ataxia, cardiovascular	Hyperactivity, rash
Tiagabine	Sedation, dizziness, memory impairment, emotional changes, headache, abdominal pain, anorexia	New-onset seizures and status epilepticus associated with unlabeled use
Topiramate	Difficulty with concentration, fatigue, paresthesia, weight loss, speech and language problems	Psychomotor slowing, urolithiasis, diarrhea, metabolic acidosis, teratogenic
Valproate	GI distress, lethargy, fine tremor, hematologic problems	Weight gain, alopecia, hepatotoxicity, cardiac, pancreatitis
As medication indications and dosages vary, please consult the latest literature for changes to the recommendations.		
Source: [21]		Table 2

Side effects are common with many AEDs. These adverse effects include, but are not limited to, drowsiness, nausea, visual changes and fatigue. Some adverse effects are related to the dose of the medications, while other effects, such as allergic-type reactions, occur regardless of the dose. With some medications, certain side effects are noted when a drug is first initiated or with a change in dosage. Depending on the type of side effect, it may abate with time. For example, drowsiness, a common side effect with carbamazepine, often improves with continuation of the medication (**Table 2**).

Patient education is crucial to obtain medication adherence and to provide optimum patient care. The patient must receive instruction on the type, dose and potential side effects of each medication. The patient must also understand that the medication is to be taken every day, on time and as prescribed. Although brand and generic drugs are comprised of the same active compounds, their absorption may vary and patients are cautioned not to interchange the medications. To avoid undesirable drug interactions, all professionals writing prescriptions, including dentists, should be

AED RANGES AND HALF-LIVES		
AED Name	Reference Range*	Half-Life (Hours)
Carbamazepine	4-12 mcg/ml	Variable (single dose 18-55, chronic dose 12-17)
Clonazepam	20-80 ng/ml	20-40
Ethosuximide	40-100 mcg/ml	50-60
Felbamate	Not established	20-23 (varies by dose)
Gabapentin		5-7
Lamotrigine	0.25-29.1 mcg/ml	25-33
Oxcarbazepine		2
Phenobarbital	20-40 mcg/ml	53-140
Phenytoin	10-20 mcg/ml	7-42 (oral dose)
Pregabalin		6.3
Primidone	5-12 mcg/ml	10-12
Tiagabine	552 ng/ml (maximum)	7-9
Topiramate		21
Valproate	50-100 mcg/ml	9-16
*All ranges presented in this table are for adults.		
As medication indications and dosages vary, please consult the latest literature for changes to the recommendations.		
Source: [21]		Table 3

aware of all medications. The patient should be informed that many of the medications interact with other CNS depressants, including alcohol. Patients should be requested to bring medication bottles with them at each visit.

As mentioned, monitoring of drug levels is an important aspect of anticonvulsant therapy. Patients should be informed of the frequency and necessity of blood draws. Many AEDs have a common range of levels associated with the desired therapeutic effects with the least likelihood of adverse reactions. Occasionally, patients may benefit from a level outside the ranges and have intolerable side effects at low levels (**Table 3**). An overview of several specific medication dosages and indications is available in **Table 4**.

Several drugs have achieved U.S. Food and Drug Administration (FDA) approval in the past several years, and it is hoped that more will be developed to help control seizures with a minimum of side effects. It must be remembered that treatment of seizures and epilepsy is accomplished on an individual basis with each patient. Appropriate drugs, doses and side effects can vary with each individual [45; 46].

Carbamazepine

The mechanism of action of carbamazepine is generally recognized to be the inhibition of nerve impulses by repressing sodium ion influx across cell membranes in the motor cortex. This medication is used for first-line therapy in the treatment of generalized tonic-clonic and partial seizures. There is no indication for the use of carbamazepine in absence or myoclonic seizures. Carbamazepine treatment is initially started with a low dose and tapered upward to prevent the occurrence of adverse effects and to allow stabilization of drug levels. When discontinuing therapy, a down titration is recommended. The primary side effects of carbamazepine are lethargy, dizziness and gastrointestinal side effects. A reduction in these side effects is often noted during the first few weeks of therapy. Other adverse effects include headache, ataxia, visual changes, mood alterations and difficulty concentrating.

AED ADMINISTRATION			
Medication	Indications	Usual Dose*	Dosage Forms
Carbamazepine	Generalized Tonic-Clonic Partial Simple and Complex Mixed Seizure Patterns	Initial: 200 mg twice daily. Increase until optimum response. Maximum: 1600 mg/day	Tablet Chewtab Suspension Extended-Release Capsule
Clonazepam	Generalized Myoclonic Lennox-Gastaut Akinetic	Initial: 1.5 mg in 3 divided doses. Maximum: 20 mg/day in divided doses.	Tablet
Ethosuximide	Generalized Absence	Initial: 15 mg/kg/day in 2 divided doses. Usual maintenance dose: 15-40 mg/kg/day in 2 divided doses.	Capsule Syrup
Felbamate	Partial with or without generalization Lennox-Gastaut	Initial: 1200 mg/day in divided doses. Usual maintenance dose: 2400-3600 mg/day	Tablet Suspension
Gabapentin	Generalized Tonic-Clonic Partial	Initial: 300 mg 3 times/day Maximum: 3600 mg/day	Capsule Suspension Tablet
Lamotrigine	Generalized Partial Simple and Complex Lennox-Gastaut	Initial: 25 mg/day for 2 weeks; then every day for 2 weeks as adjunct. Maintenance: 225-375 mg/day in divided doses.	Tablet
Lorazepam	Status Epilepticus	4 mg/dose IV over 2-5 minutes. Maximum: 8 mg/dose; may repeat in 10-15 minutes.	Tablet Solution Injection
Phenobarbital	Generalized Tonic-Clonic Partial Simple and Complex	1-3 mg/kg/day in divided doses or 50-100 mg 2 to 3 times/day.	Capsule Tablet Elixir Injection
Phenytoin	Generalized Tonic-Clonic Partial Complex	Initial: 15-20 mg/kg in 3 divided doses, every 2 to 4 hours. Maintenance: 5-6 mg/kg/day in divided doses.	Capsule Chewtab Suspension Injection
Pregabalin	Partial	Initial: 150 mg/day in divided doses. May increase until optimum response. Maximum: 600 mg/day	Capsule
Primidone	Generalized Tonic-Clonic Partial Simple and Complex	Initial: 125-250 mg at bedtime Maximum: 2 g/day in divided doses. Usual: 750-1500 mg/day in divided doses.	Tablet Suspension
Tiagabine	Partial	Initial: 4 mg once daily for 1 week. Increase until optimum response. Maintenance: 32-56 mg/day in divided doses.	Tablet
Topiramate	Generalized Tonic-Clonic Lennox-Gastaut Partial	Initial: 25-50 mg/day for 1 week. Increase slowly. Maintenance: 100-200 mg twice daily Maximum: 1600 mg/day	Tablet Sprinkle Capsule
Valproic Acid and Divalproex Sodium	Generalized Tonic-Clonic Absence Myoclonic Partial Complex	Initial: 10-15 mg/kg/day in divided doses. Maintenance: 30-60 mg/kg/day in divided doses. Maximum: 60 mg/kg/day	Capsule Syrup Tablet Injection
Vigabatrin	Partial Complex Infantile Spasm	Initial: 1-2 g/day Maintenance: 2-3 g/day Maximum: 3 g/day	Tablet
*All doses presented in this table are for adults, and doses may vary.			
As medication indications and dosages vary, please consult the latest literature for changes to the recommendations.			
Source: [21]			Table 4



According to the Scottish Intercollegiate Guidelines Network, carbamazepine, valproate, lamotrigine and oxcarbazepine can all be regarded as first-line treatments for partial and secondary generalized seizures.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=5694)
Last accessed May 17, 2007.)

Strength of Recommendation/Level of Evidence: A
(At least one meta-analysis, systematic review of randomized controlled trials, or randomized controlled trial rated as high quality and directly applicable to the target population, or a body of evidence consisting principally of studies rated as well conducted, directly applicable to the target population, and demonstrating overall consistency of results)

Idiosyncratic side effects include hepatitis, hyponatremia, skin photosensitivity and systemic lupus erythematosus. The life-threatening side effects of carbamazepine are agranulocytosis and Stevens-Johnson syndrome. Patients will require monitoring of the complete blood count and for the appearance of a rash.

Most of the absorbed carbamazepine is metabolized to carbamazepine 10, 11 epoxide (CBZ-E) by the liver. The metabolism of carbamazepine changes with the duration of treatment, and after several weeks of dosing the half-life is often reduced [6]. Monitoring of the parent drug and epoxide levels is important to evaluate the drug's metabolism and to provide the appropriate dose. Carbamazepine is an effective inducer of drug metabolism and there are drug interactions with a variety of medications. These interactions can raise or lower carbamazepine levels.

The absorption of carbamazepine can be slow and erratic, resulting in peak levels of the drug at various time intervals. Tegretol XR and Carbatrol are long acting forms of carbamazepine. Patients often have improved tolerance to side effects with the delayed release capsules and the improved steady state drug levels. Carbatrol is believed to have less variability in regard to the absorption of

carbamazepine. Carbatrol is not effective and may have negative effects for generalized absence and myoclonic seizures.

Clonazepam

Clonazepam is a benzodiazepine that is useful for the treatment of Lennox-Gastaut Syndrome, myoclonic, absence and atonic seizures. Clonazepam is most often used in combination with other AEDs. It is also used in the treatment of absence seizures after other medications have proved ineffective. All benzodiazepines act as CNS depressants by facilitating the action of gamma-aminobutyric acid (GABA). The enhancement of the action of GABA increases the seizure threshold by reducing the ability of neurons to depolarize and suppressing the spread of seizures. This medication should be started at a low dose then slowly titrated upward. Drug monitoring is not frequently completed due to large individual variations between therapeutic clinical outcomes and adverse effects. Drowsiness and ataxia are very common side effects, often resulting in intolerance to the medication. Other common adverse effects include behavioral disturbances, cognitive impairment, hypersecretion of bronchial fluid, weight gain and excessive salivation.

Patients develop tolerance to the medication's antiepileptic effects, which often necessitates an increase in dosing. However, higher doses do not always correspond with increased seizure control. Removal of the medication must be considered cautiously, as abrupt discontinuation may lead to poor seizure control or status epilepticus. Drug intolerance and difficulty with discontinuing this medication make clonazepam an unpopular first choice for most seizure types. Drug interactions are less common with clonazepam compared to the majority of AEDs.

Diazepam

Diazepam is a benzodiazepine that is beneficial during uncontrolled seizure activity and status epilepticus. This benzodiazepine is not used for the chronic treatment of epilepsy, but is essential for the acute treatment of seizure events. Diazepam suppresses generalized seizure activity and limits

the spread of electrical discharges. The mechanism of action is related to increasing the effects of GABA, an inhibitory neurotransmitter.

Diazepam is a CNS depressant and somnolence is a common adverse effect of the medication. The potential for abuse is greater for benzodiazepines than many of the other anticonvulsant medications. Idiosyncratic side effects include a paradoxical excitement. Respiratory suppression is a rare, but life-threatening possibility.

In addition to tablet and intravenous injection formulations, rectal diazepam is available for administration as a gel. This formulation is useful for patients who experience severe seizures with the potential of status epilepticus. The administration of this benzodiazepine may shorten the duration of seizures and prevent recurring seizures. Ultimately, the patient may have a reduced number of emergency visits with an improved quality of life. A well-trained caregiver and close supervision are essential. Dreifuss and colleagues concluded that rectal diazepam "...is an effective and well-tolerated treatment for acute repetitive seizures" [3].

In April of 2006, an advisory was issued for users of the diazepam rectal gel AcuDial delivery systems due to the potential for cracked applicator tips. Cracks in the tip of the syringe may alter dosage and impede the effectiveness of the medication. Patients and/or caregivers are urged to inspect the prefilled syringes at least once a month. Directions on how to inspect the applicators without removing the cap are available at the Valeant Pharmaceuticals website at <http://www.diastat.com> [28].

Ethosuximide

Ethosuximide is effective in suppressing the paroxysmal spike and wave pattern that occurs in absence seizures. Furthermore, it has been found to depress nerve transmission in the motor cortex and increase the seizure threshold [21]. Ethosuximide is effective for the treatment of absence seizures; however, it is not efficacious for other forms of generalized seizures or partial seizures. Due to the documented hepatotoxicity of valproate in

children, ethosuximide is often the preferred first choice. The medication is begun at a low dose, and then increased to a maintenance dose. Administering ethosuximide in an incremental fashion decreases gastrointestinal side effects. Nausea, anorexia, drowsiness and headache are the primary adverse reactions. These symptoms often decrease with continued dosing of the medication or by reducing the dose. Unusual reactions, such as psychosis, depression, leukopenia and rash, have been reported with this drug. No harmful effects on intellectual functioning have been reported. There are also fewer drug interactions with this medication, especially with other AEDs.

Felbamate

In 1993, felbamate was one of the first "newer" antiepileptic drugs to be approved by the FDA. As of 2006, however, it was not recommended as a first-line AED [46].

The mechanism of action in felbamate is believed to involve the antagonistic effect of N-methyl-D-aspartate (NMDA) receptors. The inhibition of NMDA receptors may block excitatory amino acids and suppress seizure activity. These actions result in an increase in seizure threshold and a reduction in the spread of seizures.

It has been used as an adjunctive medication for partial seizures, partial seizures with secondary generalization and Lennox-Gastaut syndrome in children. The medication is now approved as an adjunctive or monotherapy agent for partial seizures with and without secondary generalization, but is more often used as second-line treatment for those patients who do not respond adequately to initial treatment [21; 46].

Common side effects include anorexia, headache, insomnia, weight loss, fever and ataxia. Life-threatening side effects include aplastic anemia, acute liver failure and Stevens-Johnson syndrome. There are reports of severe aplastic anemia associated with the use of felbamate, which have resulted in a decreased use of this medication. Consistent follow-up with a complete blood count is essential for patients receiving felbamate.

Gabapentin

Gabapentin, also approved by the FDA in 1993, is indicated as an adjunctive therapy for patients with partial seizures, with and without secondary generalization in those who are older than 3 years of age. The exact mechanism of action is unknown, but is believed to be related to a novel binding site on neurons. It has been postulated that its effect may be related to an action involving the neurotransmitter gamma-aminobutyric acid (GABA). Common side effects include somnolence, ataxia, nystagmus, amnesia, mood changes, dizziness, fatigue and tremor. Idiosyncratic side effects include leukopenia. In general, gabapentin is well tolerated and many side effects decrease within two weeks with continued dosing [46].

Lamotrigine

Lamotrigine was approved by the FDA in 1994 and has become known as a broad-spectrum AED.

The exact mechanism of action of lamotrigine is unknown. However, it is believed to block calcium and sodium channels and stabilize nerve cell membranes. Lamotrigine is indicated as an adjunctive therapy for partial seizures, and is approved as monotherapy for partial onset seizures in patients older than 16 years of age. The medication is approved as an adjunctive therapy in children with Lennox-Gastaut syndrome who are more than 2 years of age. Research reports that this drug is effective across the complete range of seizure types, including partial seizures, generalized seizures of no known cause, and Lennox-Gastaut [4; 46].

This medication must be initiated at a very low dose and titrated upward slowly. A therapeutic dose may take several weeks to achieve, especially if given with valproate. A slow titration decreases the risk of developing a serious rash. Common side effects include dizziness, somnolence, headache, visual changes and ataxia. Life-threatening reactions include disseminated intravascular coagulation, multi-organ failure and serious cutaneous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis. Dermatologic reactions requiring hospitalization occur in 0.3% of adults and 1.1% of children within the first 8 weeks

of therapy [25]. Cutaneous reactions have been reported as long as six months after the initiation of drug treatment. Lamotrigine must be discontinued at the first indication of a drug-related rash.

Drug levels have not been definitively established for lamotrigine, but a suggested range is available. Drug interactions are common with carbamazepine, phenobarbital, phenytoin, primidone and valproate.

Levetiracetam

The indication for this medication, which was approved in 1999, is for adjunctive therapy of partial onset seizures in adults. Its effects appear to be against the usual targets of the common AEDs. Frequent side effects include somnolence, difficulty with coordination and dizziness. Side effects most commonly occur during the first four weeks of treatment. There has been no significant interaction reported with the co-administration of other AEDs. This drug should not be discontinued abruptly due to the risk of increased seizures, unless warranted by severe side effects [46]. Its benefit is still being evaluated.

Lorazepam

Lorazepam is another traditional benzodiazepine that has been used in the treatment of uncontrolled seizures and status epilepticus. It can be administered intravenously or intramuscularly deep into a muscle mass, if necessary. The mechanism of action is similar to diazepam and clonazepam and the other medications in this class of drug. As with diazepam, lorazepam is typically reserved for emergency situations and not utilized for the chronic treatment of seizures. Common side effects include respiratory depression, hypotension and CNS depression.

Midazolam

This benzodiazepine has several possible side effects. If it is used, it is suggested that cardiopulmonary resuscitation (CPR) should be immediately available.

Buccal administration is possible, with the medication placed between the cheek and gum. This application of midazolam was compared to rectal diazepam by Scott and colleagues [15].

Midazolam was as effective as diazepam in the acute treatment of seizures. This treatment may be more acceptable due to the convenience and the avoidance of a socially difficult situation. However, this is not a commonly prescribed option at this time.

Oxcarbazepine

Oxcarbazepine was approved in 2000 as monotherapy in adults and as an adjunctive treatment in adults and children as young as four years of age with partial seizures. It is an analog of carbamazepine and was designed to be similar in effect, but to have fewer adverse effects. Primary side effects include dizziness, nausea, headache, diarrhea, vomiting, upper respiratory tract infections, constipation, dyspepsia, ataxia and nervousness. Precautions must be taken with patients allergic to carbamazepine, due to similarities in the drugs' structures.

Phenobarbital

Phenobarbital has been used for the treatment of seizures since the early 1900s. Barbiturates, as a class of drugs, contain anticonvulsant properties. Phenobarbital and primidone are the most commonly used barbiturates; other barbiturates are usually not used due to the sedative and hypnotic effects. The exact mechanism of action is unknown, but phenobarbital elevates the seizure threshold and prevents the continuation of seizure activity. Phenobarbital may assist in the action of certain inhibitory neurotransmitters and repress the action of some of the excitatory agents. Phenobarbital is useful for the treatment of tonic-clonic and partial seizures. This medication is usually tolerated well and can be initiated at the maintenance therapy dose, or alternatively, a loading dose can be administered. The maintenance dose is often taken at bedtime, due to the sedative effect of the medication. The primary side effects of phenobarbital are sedation, dizziness, cognitive impairment and ataxia. The sedative effect may lessen over several weeks of therapy. It has been accepted that phenobarbital has a negative effect on cognitive function

and behavior. Some patients may experience idiosyncratic hyperactivity. A rare, but serious, adverse effect is a rash that may progress to Stevens-Johnson syndrome.

As with many of the AEDs, drug interactions are common. Phenobarbital drug levels and monitoring for clinical alterations are essential when combining this medication with the other AEDs or other drugs.

Phenytoin

In recent years, this long-time standard anticonvulsant has been found to have other uses, including as an antiarrhythmic agent.

The mechanism of action of phenytoin is the reduction of voltage and spread of electrical discharges in the motor cortex by altering ion, sodium and calcium transport. Phenytoin is effective in patients with simple partial, complex partial and tonic-clonic seizures. Phenytoin is usually tolerated well when started at a maintenance dose, without a tapering upward of the dose level. There are idiosyncratic adverse effects associated with phenytoin, including gingival hyperplasia and hirsutism, which make this medication unpopular for young females. A life-threatening adverse reaction associated with phenytoin is the possibility of Stevens-Johnson syndrome.

Phenytoin has a narrow therapeutic margin and levels of the drug must be periodically monitored. Phenytoin is approximately 90% bound to plasma proteins. The unbound portion, or free drug, is the component that exerts the therapeutic and toxic effects. Certain situations that reduce plasma protein binding, such as renal failure, may increase the free fraction. Blood levels of the bound and unbound (free) levels may be necessary to interpret the total phenytoin concentration with the patient's clinical status. There are many drug interactions with phenytoin; therefore, care must be used with other medications, including oral contraceptives, and all prescribing practitioners should be aware that the patient is taking phenytoin.

The intravenous form of phenytoin must be given with normal saline because a solution containing dextrose will cause a precipitation. Hypotension is an adverse effect with phenytoin and the medication must be given via a slow infusion. A related medication is a parenteral form of phenytoin called fosphenytoin sodium. Fosphenytoin is a rapid-acting form of phenytoin that can be administered intravenously or intramuscularly. Fosphenytoin is indicated for the treatment of status epilepticus, as a substitute for phenytoin and can be utilized during neurosurgery. Dosing is based on phenytoin equivalents.

Pregabalin

In 2004, the FDA approved pregabalin as adjunctive therapy for patients with partial-onset seizures. It has structural similarities to GABA, but does not appear to mimic its functional properties. This medication binds to a subunit of calcium channels in the brain, preventing the neurotransmitter release associated with a seizure event [21]. Therefore, pregabalin tends to decrease the frequency of seizures when added to an AED regimen. Common side effects include dizziness, somnolence, ataxia, and blurred vision. Adverse effects may be dose-dependent or related to interactions with other medications. However, studies have found no interactions with carbamazepine, valproic acid, lamotrigine, phenytoin, phenobarbital, or topiramate [40]. Pregabalin should not be immediately discontinued, but rather diminished gradually, due to a risk of increased seizure activity. The dosage should be tapered off over a period of at least one week [21].

Primidone

The chemical structure of primidone is similar to that of barbiturates. The two primary metabolites of primidone are phenobarbital and phenylethylmalonamide (PEMA). It is primarily used as an adjunctive treatment and is effective in patients with partial and generalized tonic-clonic seizures. Primidone is initiated at a low dose followed by incremental increases to prevent common gastrointestinal and sedative effects. Laboratory monitoring should include primidone and phenobarbital levels.

Adverse effects are similar to those for phenobarbital. Primary differences regarding primidone include neurotoxicity with long-term therapy and decreased libido. Serious adverse reactions are rare. Drug interactions are common with AEDs and other medications. If primidone is to be discontinued, it should be tapered slowly to avoid rebound seizures or other negative effects.

Tiagabine

Tiagabine was introduced into clinical use in 1997 and is indicated as an adjunctive treatment for patients with partial seizures who are older than 12 years of age. Clinical trials have shown that the drug has modest efficacy for partial-onset seizures. The precise mechanism of action is unknown, but tiagabine is believed to enhance the inhibitory neurotransmitter GABA by blocking its reuptake into neurons and glial cells. Common side effects include difficulty with concentration, ecchymosis, ataxia and confusion. Idiosyncratic reactions are rare, but include generalized weakness and rash [46].

Topiramate

Topiramate is another broad-spectrum AED that has had clinical usage for over a decade. It appears to have multiple mechanisms of action, including sodium and calcium channel blockage, GABA potentiation and glutamate receptor antagonism.

Topiramate is indicated as adjunctive therapy in patients as young as 2 years of age with partial and generalized tonic-clonic seizures and for seizures associated with Lennox-Gastaut Syndrome. The medication is initiated at a low dose, and then titrated upward slowly. Topiramate may take weeks to achieve a therapeutic level. Common side effects include somnolence, dizziness, ataxia, speech disorders, confusion, visual changes, memory problems and difficulty with concentration and attention. Idiosyncratic side effects include mood changes and renal calculi. Renal calculi occur in 1.5% of patients, which is 2 to 4 times the incidence in the general population [26]. Patients are told to take topiramate with a full glass of water to prevent renal calculi formation. As with many of the AEDs, drug interactions are common [46].



The American Academy of Neurology and the American Epilepsy Society assert that topiramate may be used to treat drop attacks associated with Lennox-Gastaut syndrome in adults and children.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=5183.)

Last accessed May 17, 2007.)

Strength of Recommendation: A (Established as useful/predictive for the given condition in the specified population)

Valproate

Valproate, or valproic acid, has extensive activity for a variety of seizure disorders of both generalized and partial onset. Valproate is efficacious in the management of primary generalized tonic-clonic, absence, myoclonic and partial onset seizures. The mechanism of action is not entirely known, but the activity of valproate appears to be related to increasing the levels of GABA. As noted, this inhibitory neurotransmitter appears to have properties that help prevent the spread of seizures.

Valproate is available in two forms, Depakene and Depakote. Depakene is valproic acid and is available in capsule and syrup form. Depakote is divalproex sodium that is changed to valproate in the gastrointestinal tract. Depakote is available in enteric-coated tablets and sprinkle capsules, which may be opened and emptied onto food. The enteric-coated tablets minimize gastrointestinal side effects. Valproate is started with a small dose then titrated upward to an effective dose. Regular and sustained-release formulations are available.

The primary side effects of valproate are gastrointestinal upset, including nausea, vomiting, anorexia and diarrhea. Up to 35% of patients taking Depakene report adverse reactions related to the gastrointestinal tract [6]. The incidence of neurological adverse effects, such as behavioral and cognitive changes, is less with valproate than many of the other AEDs. Idiosyncratic side effects of valproate include tremor, weight gain and alopecia. Weight gain occurs due to an increase in appetite and may appear in 50% of patients [6].

The amount of weight increase can be significant, as some patients gain 50 or more pounds over several weeks of therapy. Fulminant hepatic failure leading to coma and death is rare, but has been reported, especially in children less than 3 years of age. Liver enzymes must be monitored prior to initiating therapy and periodically during the dosing of this medication.

Drug interactions with valproate are common; valproate is believed to inhibit hepatic drug metabolism. Valproate drug levels must be monitored, especially during concomitant uses with other AEDs, including phenytoin.

Zonisamide

Zonisamide has been available in the United States since 2000 as adjunctive therapy for patients with partial onset seizures. Reports suggest this drug may have special benefit for the treatment of myoclonic seizures and is now being tested for use in patients with primary generalized tonic clonic seizures [4]. The medication is approved for patients 16 years of age or older. The mechanism of action of zonisamide is the blockade of sodium and calcium channels in the neurons. The most frequent adverse effects include drowsiness, anorexia and alterations in coordination and thinking. Cytochrome P450 3A4 (CYP3A4) inducers, such as those that are present in carbamazepine and phenobarbital, may decrease the effectiveness of zonisamide [21].

Discontinued Medication

Mesantoin was an AED first introduced in the 1940s. The manufacturer, Novartis Pharmaceuticals, discontinued this medication because most patients receive other therapies for the types of seizures for which mesantoin was beneficial.

AED Withdrawal

When a patient is seizure free for more than 2 years, the patient is considered to be a candidate for AED withdrawal. Patients with generalized seizures and an improved EEG have a more favorable prognosis to remain seizure free without medications. If the healthcare team and patient agree that this is a viable alternative, a schedule of gradually withdrawing the medications is considered. The medi-

cations are typically slowly tapered over several months, while the patient is closely monitored.

EPILEPSY SURGERY

Although surgical techniques have improved markedly over the past few years, epilepsy surgery is rarely considered a first-line treatment and is currently considered only after years of medication treatment. A surgical approach is deliberated sooner if the patient's ability to function is hampered by frequent or severe seizures and a specific epileptogenic focus, such as mesial temporal sclerosis, is identified. Other focal lesions, including arteriovenous malformations, tumors and areas of cerebral trauma have also been successfully resected. The objective of a surgical approach is to obtain a significant decrease in seizure frequency, intensity or duration with the least sequelae. As a result of new surgical techniques and new ways of identifying affected areas, more of these operations are being done than ever before, and with greater success [45].

As noted, a large percentage of patients continue to experience seizures despite treatment with medications. It is estimated that in the U.S., more than 60,000 people are candidates for surgery for epilepsy [27]. If the patient is a good candidate, seizure surgery is successful for 40% to 87% of patients [28; 29; 30]. At the University of Florida, approximately 80% of patients had a 90% reduction of seizures or no seizures after surgery [27]. Wyllie and colleagues studied the result of seizure surgery in 136 children between 1990 and 1996. More than 60% of the infants, children and adolescents studied became seizure free. The conclusion of these investigators was that "children should be considered for surgical evaluation at whatever age they manifest with severe, intractable, disabling, localization-related epilepsy" [20].

Not all patients are eligible as surgical candidates. Those with significant medical problems or progressive neurological disorders are rarely considered surgical candidates. Several diagnostic and prognostic procedures are available to determine an individual's suitability for surgery. The presurgical testing commonly includes the patient's seizure

history, a physical examination, laboratory tests and simultaneous video/EEG monitoring. An MRI, PET, SPECT, neuropsychological tests, sphenoidal electrodes and an intracarotid sodium amobarbital test are also commonly used screening methods.

Simultaneous video/EEG monitoring may continue for several days to several weeks, depending on the frequency of the patient's seizures. As mentioned, sphenoidal electrodes are inserted through the skin above the jaw and assist with locating seizure activity in the temporal lobe. The goal of this monitoring procedure is to determine the patient's seizure type, location of seizure onset and to evaluate the position of vital areas for speech and memory. The patient is kept in a controlled environment in which seizures can occur with consistent monitoring and with the oversight of experienced personnel. The patient's AEDs are usually tapered, and aggravating factors are instituted. Aggravating factors may include sleep deprivation, hyperventilation or physical exertion.

Neuropsychological tests analyze a patient's memory, attention, concentration, language, motor skills, intelligence quotient (IQ) and other problem-solving abilities. These tests are lengthy and may take five or more hours to complete, but they can assist in the localization of a lesion. Testing also gives the healthcare team a better understanding of the patient and how the patient may progress through the surgical process to rehabilitation.

The intracarotid sodium amobarbital test, often referred to as the Wada test, combines neuroimaging and neuropsychological testing methods. The purpose of this test is to determine areas of the brain that are important in speech, thinking and memory. This information helps the surgical team determine a proper surgical approach and ascertain any anticipated surgical complications. The patient is conscious throughout the procedure, during which carotid angiography is performed, usually through a femoral approach. One hemisphere of the brain is anesthetized for several minutes with sodium amobarbital or a similar barbiturate. After the injection, the patient is tested for speech and memory. This consists of reading words, identifying

objects or pictures and answering questions. The patient is then asked to remember what is shown. Arm and hand strength is also tested. The entire side of the body contralateral to the injection site will be momentarily paralyzed. Either one or both sides may be tested in the same manner.

If additional information is required, a second hospital admission may be necessary for the surgical placement of epidural or subdural electrodes directly onto the surface of the brain. Depth electrodes, fine wires positioned directly into the deep brain matter, may also be placed. These invasive electrodes are capable of transmitting seizure information that is not detectable by a scalp electrode. While the invasive electrodes are placed, functional mapping may be completed. Functional mapping involves stimulation of the electrodes while the patient is performing certain tasks. These interventions assist in eliciting the seizure focus and determining the involvement of important brain functions.

After presurgical testing is complete, further consultations must occur to determine the patient's eligibility for surgery. In this stage, the patient is evaluated to determine the potential benefits versus the risks of a surgical procedure. There are many important questions to consider, such as whether the seizures impair functioning, the severity of the toxicities of the medications and whether the seizures or the sequelae are harmful to the patient. Finally, the patient's quality of life issues must be addressed.

There are several commonly accepted procedures for the removal of a focal epileptogenic focus. Open surgeries include lobectomy, hemispherectomy, corpus callosotomy and multiple subpial transection. The use of radiation therapy to ablate the area of abnormality has been increasing in popularity in the past several years and is now available in many medical centers. A linear accelerator, which has been widely known by its trade name the Gamma Knife, is commonly used as a radiation source. The end result of all of these procedures is the interruption of seizure pathways or the removal of the seizure focus [47].

Lobectomy

With improvements in diagnostic methods, it is estimated that approximately 30% of people with seizures that are not well controlled with medication could benefit from lobectomy [22]. The lobectomy can include removal of all or part of the temporal, frontal, parietal or occipital lobes. A frequent surgical procedure for epilepsy is a cortical resection, usually of the anterior temporal lobe. Mesial temporal stenosis, identified on MRI, has been successfully treated with a temporal lobectomy [45]. The patient must have a seizure focus that is identifiable and localized, and that is easily accessible. These patients generally experience complex partial seizures. The benefits of undergoing a temporal lobectomy can be dramatic. On average, 65% to 85% of patients will be seizure free after this procedure [31]. Surgical complications can occur and may include alterations in vision, movement, memory and/or speech. As with any invasive procedure of the brain, infection and edema are potential adverse reactions. Complications from the surgery are estimated at 4% [31].



EVIDENCE-BASED
PRACTICE
RECOMMENDATION

Patients referred to an epilepsy surgery center for disabling complex partial seizures, with or without secondarily generalized seizures, who have failed appropriate trials of first-line antiepileptic drugs, who meet established criteria for a temporal lobe resection, and who accept the risks and benefits of this procedure, as opposed to continuing pharmacotherapy, should be offered surgical treatment.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=4108.
Last accessed May 17, 2007.)

Strength of Recommendation: A (Established as useful/predictive for the given condition in the specified population)

Hemispherectomy

A hemispherectomy involves the removal of all, or almost all, of one hemisphere of the brain. This procedure is generally reserved for children with very severe and frequent seizures that occur unilaterally. The remaining brain tissue may compensate

for the missing hemisphere by gaining additional functions. The negative consequences of the hemispherectomy are residual paresis, loss of some motor function and visual changes. The potential risks of this surgery include infection and hemorrhage. Surprisingly, the results of this operation are often reported to be very successful and the child often maintains excellent seizure control [31].

Corpus Callosotomy

A corpus callosotomy, or corpus callosum section, splices the innervations between the left and right brain by interrupting the corpus callosum. This type of surgery may be useful for generalized seizures to prohibit the spread of epileptic discharges. Uncontrolled myoclonic, atonic and tonic-clonic seizures may be reduced in severity or frequency after this procedure. In some patients, generalized seizures may stop while other patients may have a worsening of partial seizures. Complications such as infection, cerebral edema, impaired muscular activity, visual defects, memory and speech disorders occur more often after this type of surgery. The rate of complication is approximately 20% [31].

Multiple Subpial Transection

Multiple subpial transection is a process whereby small incisions are made in the brain to interrupt the spread of seizures without the removal of brain tissue. This may be performed as a single procedure or combined with any of the other surgical methods mentioned above, including a corpus callosotomy.

Radiation Ablation

Gamma knife radiosurgery has been used for many years for the treatment of cerebral abnormalities. It is now available in many large medical centers and university hospitals. One of the primary benefits of the procedure is the elimination of the necessity of a craniotomy, making it essentially a noninvasive procedure. The treatment is often performed in one session with a collimated beam of ionizing radiation focused on the area of abnormality. It can be performed on an outpatient basis, but an overnight stay is recommended. In some centers the results have been comparable to standard surgery for patients with temporal lobe epilepsy, but in others the beneficial results were only short term.

This difference may be related to the dose of administered radiation.

Side effects have included verbal memory decline, which has been reported to be as high as 60%. However, the technique shows promise, especially in patients with a localized epileptogenic focus and those who cannot tolerate open surgery [47].

Postsurgery Follow-up

During any surgical procedure for seizures, electrocorticography is completed before the patient leaves the operating room to determine if any EEG abnormalities remain after the resection or alteration of the epileptogenic focus. After surgery, the majority of patients will remain on antiepileptic medication for 1 to 2 years. Patients must be counseled that the first 1 to 2 years after the surgical procedure is a crucial time period to avoid seizure activity. Continuing AEDs is essential in providing the most beneficial long-term outcomes.

ELECTRICAL STIMULATORS

The vagus nerve stimulator, first approved by the FDA in July 1997, was the first successful medical device for patients with uncontrolled partial onset seizures. Jacob Zabara, a biophysicist, discovered that breathing techniques could stimulate the vagus nerve and decrease muscular contractions in the abdomen. Because the vagus nerve has an effect on the brain stem, hypothalamus, hippocampus and amygdala as well as innervating several organs, Zabara postulated that vagus stimulation could decrease seizures [10].

The stimulator is an implanted device, similar to a cardiac pacemaker, that is connected to the vagus nerve in the neck and stimulates the nerve with electrical impulses. The device is programmed to send electrical discharges at specific intervals automatically and periodically throughout the day. The device is adjusted according to each patient's individual requirements and tolerance. The stimulator can be programmed externally by the attending physician or controlled, if necessary, by the patient with the use of a handheld magnet.

Fisher and Handforth reviewed clinical trials involving more than 300 patients with the stimulator and reported that the device is safe and effective [5]. On average, patients had a 25% decrease in number of seizures, and more than 50% indicated an improvement in quality of life. Not all patients are candidates for the device, and the device is approved for use in adults and adolescents only. The stimulator is used as an adjunctive therapy to medications and surgery, not as a first-line consideration. The most common adverse reactions were hoarseness, alterations in speech, cough, shortness of breath and throat discomfort. Most patients consider the adverse effects to be tolerable.

Research is being conducted on the direct implantation of electrical stimulators in the basal ganglia and thalamic nuclei in an attempt to control seizures in patients with refractory epilepsy. In addition, work is being done on a device that can analyze an EEG and automatically deliver a dose of an anti-epileptic drug in time to abort a seizure [45].

TREATMENT OF PSYCHOGENIC PSEUDOSEIZURES

Psychological interventions are important for the patient with psychogenic pseudoseizures. Patients will require counseling and support throughout this process. Psychogenic pseudoseizures often develop as a defense mechanism in response to difficult situations. If this coping strategy is challenged, patients may feel depressed, angry and vulnerable. Extreme sensitivity and caution are required to achieve a positive outcome for the patient. Prior to a definitive diagnosis, patients may be prescribed AEDs. The medication may continue until psychological counseling is instituted, after which they are tapered off. A firm schedule of follow-up visits should be established. While the diagnosis of psychogenic pseudoseizures is as real as a diagnosis of epileptic seizures, the etiology, pathophysiology and treatment are very different. Patients who have documented epileptic seizures may concurrently have psychogenic pseudoseizures. These patients will require psychological intervention as well as care for the epilepsy.

ALTERNATIVE THERAPY

Patients and families often seek alternative treatments in order to manage epilepsy naturally or if other treatment methods have been unsuccessful. The ketogenic diet is an alternative approach to standard medications and epilepsy care. It is being so widely recommended that it is becoming a mainstream form of therapy. There are some assertions in the lay literature that suggest vitamin E and selenium are helpful for some kinds of seizures, although these claims have not been supported by scientific research.

KETOGENIC DIET

The theory behind the ketogenic diet is that it has the same effect on the body as fasting; that is, the body is forced to utilize fat as energy instead of glucose. This can increase ketosis, with a subsequent rise in serum ketones.

In the 1920s, this diet was studied as a treatment for patients with intractable epilepsy. As newer medications were discovered, the diet became perceived as a less favorable treatment option. Today, there are many respected centers located throughout the United States that prescribe and monitor the ketogenic diet as a complementary approach to standard AEDs [32]. If a patient's seizures are not controlled on usual medications or if the adverse effects of medications are numerous, the ketogenic diet may be considered. This diet must be prescribed and monitored by a physician in collaboration with a nutritionist.

This diet is high in fat, very low in carbohydrates, low in protein, and fluids are restricted. The usual ratio is three to four parts fat to one part protein and carbohydrates. The diet is said to be helpful in tonic-clonic, complex partial, myoclonic and minor motor seizures. The latter two types of seizures respond to the ketogenic diet with the most success. The ketogenic diet appears to be most effective for children between 1 and 10 years of age. However, it must be noted that the diet is nutritionally very inadequate, and children will require vitamin and mineral supplementation.

The results of the diet can be immediate, or it may take several months to be effective. At the Stanford Medical Center, more than 50 patients between 11 months and 19 years of age were placed on the ketogenic diet between 1995 and 2000, with two-thirds of the patients remaining on the diet. This center found that 19% of the patients became seizure free, and 90% of the patients had a 50% or greater reduction in seizure activity [17]. If the diet is helpful, the child may continue it for two years and then be subsequently weaned. This duration of therapy is similar to treatment with AEDs. Side effects include poor linear growth, hypercholesterolemia, poor weight gain, constipation, kidney stones and gallstones.

Other Alternative Regimens

Patients must be cautioned against the use of herbal remedies with AEDs. There are known interactions between the benzodiazepines and the herbs hawthorn, kava-kava, skullcap and valerian [8]. These combinations may result in CNS depression. Antiepileptic drugs may also have an effect on the levels of certain vitamins in the body. Phenobarbital and phenytoin may reduce activity of vitamins B6, B9, C and D [7]. The implications for these alterations are not well understood at this time.

Certain forms of reflex epilepsy are responsive to complementary or behavioral techniques. Epilepsy caused by flashing lights, reading or hearing certain sounds may be responsive to techniques such as biofeedback. As research continues in these areas, patients may have a more comprehensive and holistic range of treatment options in the future.

PROGNOSIS

Approximately 60% of patients with epilepsy will achieve a remission during the first year of therapy. Another 15% will achieve a remission at a later time, after treatments have been instituted for a number of years. The remaining 25% will develop intractable epilepsy despite treatment [37]. Patients with underlying neurological disorders, such as multiple sclerosis and cerebral vascular disease, tend to have epilepsy that is more difficult to control. Patients should continue with regular office visits because seizure disorders may change with

age in an unpredictable manner. Some seizures may be outgrown, while others worsen with time. Some patients improve for a period of years and then worsen. It is hoped that some of the newer modalities, including surgery and electrical stimulators, will have a synergistic effect with the AEDs and improve prognosis in the near future.

MANAGING AN ACTIVE SEIZURE

There are many misleading and inappropriate concepts about how to care for a person who is having a seizure. It is important for all healthcare professionals to know the basic tenets of care and to teach as many people as possible the proper way to handle a seizure patient.

The first rule is to “do no harm.” Many individuals witnessing a seizure will try to restrict movement or otherwise restrain the patient. The Epilepsy Foundation stresses that this can cause more harm than good and encourages bystanders and professionals to simply take steps to keep the person safe [4]. For a person who is having a partial or nonconvulsive seizure, this merely requires guiding the individual away from a source of danger, such as a busy highway, steep stairway or hot stove. In general, it is best to gently guide the person, as grabbing or holding may cause a struggle and aggravate the situation. Speak to the individual in a calm and reassuring way, and stay with him or her until the episode is over, especially if there is a period of unconsciousness.

When assisting a person who is having a generalized tonic, clonic (*grand mal*) seizure, it is vital to remember to keep calm and reassure others in the vicinity that there is no need to interfere. However, bystanders can assist in removing any sharp or dangerous objects in the immediate area. Loosening a patient’s tie or any other object that may cause impairment to respiration may also be helpful. Removing loose dentures or food that is expelled from the mouth is recommended, but forceful removal or shoving an object into the mouth may cause injury and is contraindicated. Placing something soft and flat under the individual’s head may prevent an injury, and turning the victim gently onto his or her side can help to clear the airway and avoid aspiration. There is no need for artificial

respiration except in the very rare cases when respiration ceases and does not resume after the seizure ends. If in a care center, supplemental oxygen should be available and provided if indicated. The individual should not be left alone until the seizure ends naturally. One should be prepared to offer assistance to a possibly confused or somnolent postictal individual when the seizure activity ceases.

Timing the length of the seizure can provide useful information for the patient's future management. It would also be helpful to assess the patient's breathing and determine if there are any apneic periods [4].

COMPLICATIONS OF SEIZURES

Complications from seizures are varied and numerous. Patients can sustain injuries, both physical and neurological. A patient with any type of seizure may sustain a physical injury, especially during impaired consciousness. Patients may experience abrasions, bruises, broken bones, burns and oral lacerations, including tongue and cheek injuries. Other patients may experience a severe head injury or other trauma with sudden falls to the floor or falls from heights.

During a seizure, there is an increase in metabolic requirements associated with heightened cerebral oxygen consumption, glucose consumption and cerebral blood flow. In animal studies, the repetitive discharge from an epileptic focus produced long-lasting and permanent changes in neuron excitability in local and distant areas of the brain. These studies suggest that the initial seizure may cause additional seizures to occur and can cause secondary brain injury. The longer patients continue without good seizure control the more difficult the seizures are to manage.

Patients may also develop complications due to AEDs. Adverse drug reactions and idiopathic and life-threatening reactions are possible with these medications. Some adverse reactions are related to the dose, while others might occur without toxicities.

STATUS EPILEPTICUS

Status epilepticus, or status, is defined as uninterrupted seizure activity or frequent succession of seizure activity. It often requires medical intervention, because there can be a mortality rate of 20% [34]. The time variable for status varies greatly depending upon the sources cited. In general, a patient is considered to be in status if a single seizure continues for greater than 15 minutes or if there is a rapid succession of seizures lasting more than 30 minutes. Convulsive status epilepticus involves tonic-clonic seizures. Nonconvulsive refers to absence or complex partial seizures. Although nonconvulsive seizures are serious events, the most dangerous form is the tonic-clonic type. Cerebral complications occur from high metabolic demands, changes in calcium influx, brain edema, acidosis, hyperthermia, hypoglycemia, hypotension, prolonged autonomic dysfunction, hypoxia, arrhythmia, acidemia, aspiration and, ultimately, brain damage.

Due to these life-threatening complications, emergency care is often necessary in cases of status epilepticus. As with any emergency situation, the first priority is the maintenance of a clear airway. The patient sustains a rapid depletion of oxygen and other nutrients during status. Often, the individual is intubated to assist with oxygenation and the prevention of aspiration. The patient will usually require supplemental oxygen. Continuous assessment of all vital functions and neurological status is necessary. Cardiac monitoring is required to identify dysrhythmias and to allow for appropriate intervention. The patient must be protected from injury and provided a safe environment with close supervision. Laboratory evaluations may be completed to assess AED levels and to check for any metabolic changes. The patient will require additional glucose, which is administered intravenously, to meet increased metabolic requirements.

Anticonvulsant medications will be prescribed for intravenous injection and infusion. These medications may include diazepam, lorazepam or midazolam. Currently, diazepam is considered the drug of choice for the immediate treatment of status epilepticus. In 90% of cases of status

epilepticus, diazepam or lorazepam stops the seizures within 3 minutes of intravenous administration [6]. The primary adverse reaction in this situation is respiratory depression, and caution must be maintained with the administration of this drug. Diazepam has a short half-life, and repeat dosing is often necessary while additional medications, such as phenytoin or phenobarbital, are added. If the use of these medications is not successful and the patient continues to seize, other alternatives must be considered. These alternatives may include general anesthesia with a neuromuscular blockade or a barbiturate coma, with a medication such as pentobarbital. Barbiturate anesthesia offers reliable, albeit aggressive, therapy for status epilepticus.

The patient's family members will require support and education during this time. When the patient is stabilized, the family members may be helpful in assessing the cause of the patient's status epilepticus and in finding solutions for the prevention of future events. The most prevalent cause of status epilepticus in epileptic patients is failure to comply with AEDs.

MORTALITY AND SUDDEN DEATH

Patients with epilepsy have a mortality rate that is higher than the average population. Mortality may occur due to the etiology of epilepsy, which may include a malignant brain mass or a genetic abnormality that is the underlying cause of death. Death can also result from a seizure or a complication of a seizure. As noted, patients who develop status epilepticus may not recover. Other patients may have serious injuries or accidents that may lead to death, including falls or burns.

Sudden unexpected deaths in epileptics are most common in young male patients with a long history of generalized seizures, history of head trauma, alcohol use and refractory seizures. These patients usually take several AEDs. The deaths commonly occur at home and without a witness. Autopsy reports often reveal pulmonary edema and cardiac ischemic damage with normal coronary arteries. Cardiac ischemia may occur from vasoconstriction during the current or past seizure events. The exact cause is uncertain.

PATIENT EDUCATION

Epilepsy is a chronic disorder and often requires long-term management. The patient and family should be encouraged to obtain information about epilepsy through self-education. Local epilepsy organizations often provide written materials and information on videotape. Frequently, the patient's family members or other significant persons require as much education as the patient does because they will be observing the patient during the actual events. These significant persons should be educated to care for the patient during and after a seizure. These individuals should be instructed to stay with the patient until he or she is conscious, to time the seizure duration and to provide for the patient's safety. If consciousness returns without further incident and the seizure ends in less than five minutes, then the convulsion is considered to be uncomplicated and emergency attention is not necessary. In general, after a period of rest, the patient is able to resume caring for him or herself. The spouse or other significant person is a crucial asset for the patient and can assist in differentiating between an emergency and an uncomplicated seizure, even though, to the general public, all seizures may appear to be emergencies. The assisting person is important in the prevention of injury and can also help the patient maintain an accurate seizure calendar and ensure medications are taken appropriately.

An ambulance should be called if a seizure lasts longer than five minutes or if seizures continue to reoccur without the patient regaining consciousness. Other situations when emergency assistance is required include seizures that:

- Occur in water, due to likelihood of cardiac or pulmonary damage
- Have related signs of injury
- Result in physical distress
- Occur in patients with diabetes
- Arise in a pregnant patient
- Are the first seizure in a patient without epilepsy or if the health history is unknown

If consciousness does not return after the seizure appears to be over, then emergency assistance will also be required.

As previously described, the Epilepsy Foundation has basic suggestions for caring for a person who has a seizure. These should be related to first responders and those who may be present when a seizure occurs [4].

Patients with a seizure disorders should wear identification wristbands or necklaces. These items are helpful in situations in which a seizure occurs in public. Identification jewelry acts to alert bystanders and healthcare personnel regarding the patient's medical condition and appropriate treatment. Identification is also important to prevent unnecessary or inappropriate interventions, such as the initiation of CPR. Additional information may also be carried by the patient, including the name and telephone number of healthcare providers, types of medications and known allergies.

On an individual basis, a significant other may be requested to administer medications, such as rectal diazepam or oral lorazepam. Therefore, these individuals will require education regarding multiple aspects of patient care and seizure control. Often, the significant other will require emotional and psychological support. Watching any person, especially a loved one, having a seizure is a stressful experience.

Teaching patients about their medications is essential. AEDs and other medications must be taken regularly and continuously. Some patients may require medications for a lifetime, and they should be informed of this possibility. The patient must receive information about the name and type of the medication, the dose and schedule of administration, the side effects and when to call healthcare providers. For most patients, a written schedule and pillbox are helpful. The patient should also be aware of the appropriate action to take if a dose is missed. Many persons taking AEDs require therapeutic drug monitoring of the drug levels as well as blood tests for other laboratory values. Patients should be informed of the necessity and frequency of laboratory monitoring.

Some individuals are susceptible to a seizure that is provoked by a simple sensory experience. The most common sensation is flashing lights or shifting patterns. Sleep deprivation and sudden noises are other precipitating factors. The susceptibility to these phenomena is most commonly noted in the benign, primary, generalized epilepsies of childhood, but may occur in all epileptic seizure types. Patients should be told to avoid situations in which these provoking factors may be present. Those who are sensitive to flashing lights should avoid driving, as light flickering through trees or fence posts may precipitate a seizure event. Very rarely, seizures are elicited by more complex situations, such as from music or when doing mental calculations.

In addition to the education of patients and their families, other individuals may require knowledge that would enable them to provide the best quality of life for the patient. The education of teachers and/or coworkers may enhance the care of the epileptic person by providing a supportive and safe environment. These individuals should be aware of appropriate interventions and telephone numbers, should a seizure event arise. The patient or healthcare providers, upon the patient's request, may contact other significant individuals. Patients may also require support in everyday situations; for example, a bus driver having knowledge of a patient's condition can ensure the patient's safety during the bus ride.

SAFETY EDUCATION

Injuries are the primary complication of seizures. Patients with epilepsy often cause harm to themselves by biting their tongues or falling down and hitting a piece of furniture. As noted, the patient must be safeguarded and monitored from injuries and falls. Injury prevention is a key aspect of patient education and the maintenance of quality of life. The patient and family should be instructed on constructive methods of safety planning without being overburdened with unnecessary restraints and concern. If possible, the environment should be altered during a seizure rather than restraining the patient. A helmet may be a reliable alternative to provide a protected environment.

At home, the patient must evaluate the living situation. General household safety precautions include: applying thick carpeting; padding sharp objects; avoiding lighting of fires; and obtaining automatic shut off switches for space heaters, curling irons and irons. The patient must be informed that smoking is not recommended and certainly not permitted in bed. Bathroom safety measures include setting the water temperature below 120 degrees, using a hand held shower while seated in the bathtub, padding the carpet in the bathroom and preventing the bathroom door from locking. The kitchen can be a perilous environment, and cooking can be especially dangerous for the individual who experiences a change in consciousness. Patients must be cautioned about the risk of falling onto a hot stove or leaving the heating elements and oven on. Kitchen safety measures include: the use of plastic cups, plates and cooking utensils; cooking on the back burners of the stove; using a microwave oven; and sliding containers on the counter top rather than picking them up.

Recreational activities pose a unique challenge for many active epileptic patients. Most individual sports are considered acceptable, with the exception of scuba diving, parachuting or activities involving a motorized vehicle. Patients are generally advised that they may participate in basketball and baseball. Football and boxing are often prohibited. If indicated, a mask worn over the face or a helmet can be necessary and helpful during potentially dangerous activities.

HEALTH PROMOTION

Health promotion of individuals with epilepsy includes the management and reduction of seizure activity. The patient should be instructed to obtain adequate rest, limit alcohol, reduce stress, eat a healthy diet, and exercise. Patients susceptible to the effects of caffeine and aspartame should avoid these products. These interventions assist in the patient's overall well-being and prevent other disease states and assist in seizure control. Any precipitating situations that trigger seizure activity, such as flickering lights, should be identified and

avoided. An accurate and comprehensive seizure diary may assist with revealing these factors. Patients are also guided with regard to medication compliance and the necessity of follow-up visits. The patient and family members should be provided with appropriate resources, including information on the local chapters of epilepsy support groups.

PREVENTION OF EPILEPSY

There are multiple avenues in which epilepsy can be prevented in the general population. Prevention can occur before birth with improved prenatal care. Folic acid supplementation should occur in women of childbearing age prior to conception to prevent neural tube defects. The current recommended allowance of folic acid for nonpregnant individuals is 0.4 mg/day. During pregnancy, care must be taken to avoid maternal systemic illness and infection, which can affect the developing fetus' central nervous system. A reduction in the number of early teenage pregnancies may decrease the incidence of premature and/or low-birth-weight infants and maternal infections. Improved perinatal care in the labor and delivery area can also decrease fetal trauma and hypoxia.

High fevers in children, especially in those susceptible to seizures, should be monitored and treated appropriately. Parents or caregivers of small children should be instructed in how to take an accurate temperature, based on the child's age. Parents should also be instructed about the significance of a fever and how to intervene when necessary; it is important that they understand when to call a healthcare professional regarding an elevated temperature and when to treat the child with antipyretic medications.

The prevention of childhood infection and toxic ingestions is crucial in averting the development of epilepsy. Meningitis, viral encephalitis, measles, mumps and diphtheria can be minimized through appropriate immunization of children and adults. The prevention of toxic poisonings through screening and safety measures is essential. Lead poisoning continues to be problematic in many older homes.

A final area that may minimize the incidence of epilepsy is the reduction of motor vehicle accidents and the prevention of trauma. Traumatic injuries can occur through a variety of accidents and abuse. The utilization of safety belts and restraint devices in all motorized vehicles is essential for children and adults. Avoiding settings where there is a potential for gunshot wounds is also important to prevent the occurrence of head injuries and the subsequent development of epilepsy. Practicing safety during sporting activities is also essential. The prevention of abuse is vital in the reduction of head trauma-related epilepsy. Workplace injuries must be reviewed and reduced. Lastly, the prevention of substance abuse, alcohol and illicit drugs will assist in the reduction in the incidence of epilepsy.

CONSIDERATIONS FOR NON-ENGLISH PROFICIENT PATIENTS

Communication with patients regarding prevention and education is a vital aspect of caring for patients seizure disorders or epilepsy. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required. Frequently, this may be easier said than done, as there may be institutional and/or patient barriers.

Depending upon the patient's language, an interpreter may be difficult to locate. Or, an organization may not have the funds to bring in an interpreter. Also, bringing in an interpreter creates a triangular relationship with a host of communication dynamics that must be negotiated [48]. Many view interpreters merely as neutral individuals who communicate information back and forth. However, another perspective is that the interpreter is an active agent, negotiating between two cultures and assisting in promoting culturally competent communication and practice [49]. In this more active role, the interpreter's behavior is also influenced by a host of cultural variables such as gender, class, religion, educational differences, and power/authority perceptions of the patient [49].

Consequently, an intricate, triangular relationship develops between all three parties. Another factor affecting the communication process is the fact that many interpreters are not adequately trained in the art of interpretation in general health settings, as there are many technical and unfamiliar terms. An ideal interpreter goes beyond being merely proficient in the needed language/dialect [50]. Interpreters who are professionally trained have covered aspects of ethics, impartiality, accuracy, and completeness [51]. The interpreter should be regarded as part of a collaborative team, bringing to the table a specific set of skills and expertise [52].

In a multicultural setting, interpreters are a valuable resource to help bridge the communication and cultural gap between patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter. When providing care for patients for whom English is a second language, the consideration of the use of an interpreter and/or patient education materials in their native language may improve patient understanding and outcomes.

DRIVING RESTRICTIONS

For individuals with epilepsy, the safe operation of a motor vehicle is a complex issue. The caregiver must try to achieve a balance between providing the best care to the patient and providing the patient with the autonomy and freedom that often coincides with driving. Safety must be the highest priority for the patient and for other individuals. This issue is further complicated by a variety of state statutes and regulations. A helpful reference concerning driving restrictions in each state is available on the Epilepsy Foundation website at <http://www.epilepsyfoundation.org> [38]. Each state has specific requirements for obtaining a driver's license and restrictions for persons with certain medical conditions. This website is updated on a regular basis and is an excellent resource. Laws

EXAMPLES OF STATE DRIVING RESTRICTIONS				
State	Seizure-Free Period	Periodic Medical Updates Required	Doctors Required To Report	DMV Appeal Of Denial
Florida	After six months and upon doctor's recommendation	At discretion of medical advisory board	No	Yes
California	3, 6 or 12 months with exceptions	At discretion of department of motor vehicles	Yes	Within 10 days
*Please consult your State Department of Motor Vehicles for more comprehensive information.				
Source: [38]				Table 5

change, however, and each healthcare professional and patient must be aware of the current laws governing the state in which they practice and reside (*Table 5*).

CHALLENGES FACING PATIENTS AND THEIR FAMILIES

Patients with epilepsy face unique challenges. For many individuals with epilepsy, a perceived stigma creates diverse psychosocial issues. A seizure may be referred to as a “fit” and there are corresponding bizarre interpretations of this phenomenon. Historically, seizures have been associated with supernatural powers, demonic possession and insanity [11]. Society places value on self-control, conformity and independence, all of which may be inhibited by a patient's epilepsy. There is confusion on the part of many individuals when a person has a seizure. Observers and the police may consider the individual drunk, disorderly or mentally ill. The patient may be institutionalized or jailed.

O'Donoghue and colleagues surveyed more than 300 patients with epilepsy to assess the psychosocial consequences of this disorder. Their findings indicated patients with active seizures perceived themselves as less healthy and more than 30% of these patients were significantly handicapped by their condition. The seizures and the adverse effects of the medication regimen disrupted the patient's sense of well-being [13]. Unfortunately, the majority of these psychological alterations were not assessed by the general practitioner.

Dalrymple and Appleby conducted a study with patients using questionnaires. The results of their study revealed that those patients with uncontrolled epilepsy measured higher in anxiety, depression and stigmatization than those with less frequent seizures. Frequent seizures impact employment and driving, which have a significant effect on self-esteem and feelings of isolation. There are other associated difficulties with epilepsy including alterations in affect, mood and memory [2].

Children are exceptionally vulnerable to the negative impact on social and intellectual development. Children with epilepsy require medical care and AEDs that often affect academic and personal performance.

Healthcare personnel can help patients identify people that may be supportive and to whom they may explain the seizures and treatment. They may also help the patients to focus on positive aspects of life, rather than limitations. Appropriate referrals to a psychologist or psychiatrist may be indicated. Lifestyle adjustments should be considered without unnecessarily inhibiting the patient's activities and routines. The interdisciplinary healthcare team should anticipate and provide solutions for common social issues, difficulty with self-image, frightening experiences, loss of control and difficulty with independence. Essentially, all members of the team may be vital links to assist each individual to adjust to their personal limitations and difficulties.

EPILEPSY RESEARCH

There is hope for patients with epilepsy as future avenues of treatment and prevention develop. The Epilepsy Foundation of America Epilepsy Gene Discovery Project has facilitated the continued search for the genes associated with epilepsy. This survey involves the completion of a questionnaire by patients with epilepsy or their family members. The project allows international participation and has been completely voluntary and confidential. The goals of the study are to collect data and to connect individuals with qualified genetic researchers. Genetic research may provide a valuable clue for the discovery of epilepsy's etiology. Surgical techniques offering improved precision and reduced complications may be another option. Research regarding the transplantation of fetal pig cells and stem cells directly into the brain is continuing. Other projects have focused upon direct stimulation of areas of the brain, including low magnetic fields. Tergau and colleagues described a pilot study in nine patients in which low-frequency repetitive transcranial magnetic stimulation (rTMS) was applied. The data revealed a temporary improvement in seizure frequency or severity [18].

Improved imaging techniques are another avenue that may assist patients with epilepsy in the future. These techniques involve magnetic resonance spectroscopy (MRS) and functional magnetic resonance imaging (fMRI), which allow the evaluation of brain function.

Pharmaceutical research on AEDs is constantly evolving. Improved medications with refined efficacy and reduced adverse effects are future potential alternatives. Implanted medication delivery devices, such as those used in the delivery of insulin to diabetics, show promise as well. Lastly, an increased understanding of the role of prevention for at risk patients may reduce the incidence of epilepsy.

CASE STUDY

Patient R is a female, 38 years of age, with a history of seizures since birth. She is otherwise in good health. Her current diagnosis is temporal lobe epilepsy. Patient R experiences complex partial and secondarily generalized seizures. She states that she is aware that a seizure is going to occur because she has a very brief "strange sensation." This sensation is her aura. After the aura, the patient cannot recall any other events until the postictal period. During the postictal time, Patient R is fatigued, confused and often experiences headaches.

During her seizure event, witnesses noticed a typical pattern to Patient R's seizures. First, she becomes very quiet and blank. She will not communicate or respond to other individuals. She experiences vocalizations and yells in a very loud voice, "Jesus help me." During the vocalizations, Patient R will experience automatisms that include pulling at her clothing. Usually, the seizure ends after approximately 60 seconds, and she regains consciousness within several minutes. At other times, the seizure will progress, and she will experience tonic posturing followed by clonic movements. The tonic-clonic phase is quite severe and can last several minutes. The postictal period after the secondarily generalized seizure is prolonged and can last for several hours. Patient R experiences disorientation, confusion and somnolence. She has experienced status epilepticus twice in the past.

At times, Patient R's seizures occur almost every day. However, some days will be seizure free, and she may have several days at a time with no seizure events. Unfortunately, this does not occur consistently. Most days she will experience at least one seizure and often she has several during the same day.

She has been on a number of antiepileptic drugs in the past including phenytoin, phenobarbital, valproic acid and experimental medications. Her current medications include carbamazepine and topiramate, with lorazepam as needed. She also takes an over the counter multivitamin and, occasionally, acetaminophen for headache. Her sister has been instructed on administering lorazepam when Patient R is experiencing several consecutive seizures that occur over a 15-minute period or after her second secondarily generalized seizure for the day. Her sister administers the lorazepam approximately once every two weeks. However, Patient R's seizures are quite variable with no known pattern. One week, she may not require any lorazepam; the next week, she may require it several times.

Patient R is very compliant with her medications. She uses a pillbox and can correctly describe her daily medications and doses. Her seizure calendar is a method of tracking her seizures that she has used for years. For each day she records the number of seizures she has and describes them. Patient R has no family history of epilepsy and she has not had any surgical treatments.

During Patient R's physical examination, her physician discovered that the patient had difficulty with coordination. There were deficits in cognitive processes such as calculation and abstract thinking. The exam is otherwise unremarkable.

Patient R has a twin sister who is neurologically normal. The twin sister provides a large amount of social and emotional support and is always present to accompany the patient at her visits. Patient R is a very independent woman who lives in an assisted living center and wears a protective helmet. She has completed the 5th grade. She does not use nicotine products, drink alcohol or use illicit substances. She has experienced difficult situations in the past related to a divorce and loss of her only child.

The patient has been involved in the trial of several new experimental antiepileptic drugs with varying success. The latest study she participated in had a positive effect on her seizure frequency. Unfortunately, the pharmaceutical company discontinued the medication from the study. As a result, other alternatives were sought. Her current healthcare providers evaluated Patient R and placed her in the epilepsy monitoring unit for simultaneous EEG/video monitoring.

In the epilepsy monitoring unit (EMU), Patient R's antiepileptic drugs were slowly withdrawn. She began to experience her typical events, which included vocalizations. During these events, a large amount of motor activity was exhibited and EEG readings were difficult to ascertain. The medical team suspected a diagnosis of pseudoseizures. The patient completed the neuropsychological testing and the evaluation continued for several days. The patient experienced a secondarily generalized seizure and the EEG readings clearly revealed epileptogenic changes. Sphenoidal electrodes were placed to obtain localizing information. Patient R continued to have a large number of seizures and required frequent administration of intravenous benzodiazepines to maintain seizure control.

After more than a week of monitoring, a seizure focus was determined. Unfortunately, multiple focal areas existed in the bilateral temporal and frontal lobes and thus eliminated the surgical option. The patient was restarted on her antiepileptic drugs, stabilized and alternative treatments were discussed. The patient and healthcare team agreed that a vagus nerve stimulator would be a positive option. Alterations in the medication regimen were discussed. The patient and sister were offered the option to attempt dosing with felbamate with close monitoring. Patient R did not want to attempt felbamate and opted for slowly removing the topiramate and attempting a trial with lamotrigine while awaiting the vagus nerve stimulator placement. This medication was somewhat helpful, but the vagus nerve stimulator provided substantial relief.

CONCLUSION

The impact of seizures and epilepsy on a patient's life is significant. While various forms of seizures and epileptic syndromes exist, there is a degree of anxiety associated with each event. Seizures affect all facets of a patient's life as well as the lives of family members, friends and the communities in which they live.

Medical personnel in all practice settings should understand the potential causes and management of epilepsy and seizure disorders to effectively assist their patients. By providing information, support, treatment options and community resources, the disorder's negative impact on all involved can be mitigated. Appropriate interventions and care are critical contributions.

The primary goal for all individuals is the prevention of epilepsy. For cases where total prevention is unlikely, the objective is optimal mental and physical functioning despite the disorder. Other objectives include freedom from seizure-induced injury, the achievement of tolerable side effects from antiepileptic drugs and obtaining satisfactory social and psychological functioning. Through interventions and education, healthcare professionals can make a positive difference in achieving progress towards these goals.

RESOURCES

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

The Epilepsy Foundation of America
<http://www.epilepsyfoundation.org>

The American Epilepsy Society
<http://www.aesnet.org>

National Library of Medicine / National Institutes of Health / MedlinePlus
<http://www.nlm.nih.gov/medlineplus/epilepsy.html>

National Tuberous Sclerosis Association
<http://www.tsalliance.org>

National Library of Medicine
<http://www.nlm.nih.gov>

Centers for Disease Control and Prevention
<http://www.cdc.gov>

American Academy of Neurology
<http://www.aan.com>

International League Against Epilepsy
<http://www.ilae-epilepsy.org>

EFA Epilepsy Gene Discovery Project
<http://www.epilepsyfoundation.org/gene/>

National Institute of Neurological Disorders and Stroke (NINDS) Epilepsy Information Page
<http://www.ninds.nih.gov/disorders/epilepsy/epilepsy.htm>

World Health Organization
<http://www.who.int/topics/epilepsy/en/>

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