



W-F Professional Associates, Inc. 400 Lake Cook Rd., Suite 207 Deerfield, IL 60015 847-945-8050

---

July 2008 "Seizures & Anticonvulsant Drugs" 707-000-08-007-H01-P

---



*Seizure Disorders &  
Anticonvulsant Drugs*

**MISSING A LESSON? IT'S EASY TO GO TO OUR  
WEBSITE, & DOWNLOAD WHAT YOU NEED.  
([www.wfprofessional.com](http://www.wfprofessional.com))**

**WHEN YOU SEND IN QUIZZES, ALWAYS KEEP A COPY.  
YOU MAY EMAIL OR FAX THEM. FAX # IS 847-945-5037.  
OR SEND A CONVENTIONAL EMAIL WITH YOUR  
ANSWERS TO [INFO@WFPROFESSIONAL.COM](mailto:INFO@WFPROFESSIONAL.COM)**

**HAVE YOU RECENTLY MOVED? PLEASE NOTIFY US.**

---

A number of topics seem to be recirculated in our lessons; however, that is your suggestion. Seizure disorders & anticonvulsant therapy is always near the top of the list of requests from participants. Our goal is to provide useful information that can be shared with patients. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings. **The program ID # for this lesson is 707-000-08-007-H01-P. Pharmacists completing this lesson by July 31, 2011 may receive full credit.**

**To obtain continuing education credit for this lesson**, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

---

**The objectives of this lesson are such that upon completion the participant will be able to:**

---

1. Describe the epidemiology, diagnosis, triggers & complications associated with seizures.
  2. List the types of seizure disorders & state the characteristics of each.
  3. Identify the goals of therapy.
  4. State the advantages of the newer anticonvulsant drugs.
  5. List the adverse effects associated with the anticonvulsant drugs.
- 

**All opinions expressed by the author/authors are strictly their own and are not necessarily approved or endorsed by W-F Professional Associates, Inc. Consult full prescribing information on any drugs or devices discussed.**

Epilepsy is a neurological disorder that results in unprovoked, recurring seizures impacting upon motor, sensory or mental functions and usually occurring as a result of disturbances in the normal function of the brain. Today, the term "seizure disorder" is often used to collectively describe patients who suffer from this and other related maladies. Neurons in the brain communicate between each other via firing electrical charges in a normal pattern. A seizure, which is a symptom of epilepsy, is triggered by an abnormal burst of excessive neural firing, or when disruption in the transmission of electrical signals between the neurons in the brain takes place. The discharge of intense electrical energy will change the normal pattern of these charges and may result in muscle jerks in the arms and legs, sudden falls, visual disturbances, staring spells, confusion or unusual sensations or emotions. Thus, physical changes that take place are termed epileptic seizures. If the outburst of energy flashes occurs across a specific area of the brain such seizures are termed **partial**. It is termed **generalized** when the neurons of the entire brain are affected. Bodily and brain functions return to normal once these outbursts subside. The occurrence of a single seizure does not necessarily indicate the presence of epilepsy, since such a seizure may occur as a result of an illness like head injuries, high fever or hypoxia. However, if the seizure recurs because of an unknown reason, the condition is epileptic in nature.

### EPIDEMIOLOGY

Seizures are one of the most prevalent neurological disorders worldwide. Even though there is no central registry of cases in the U.S., it is estimated that they affect 0.5 – 1% of the population. Surveys indicate that about 300,000 people have a first seizure every year, with 120,000 of them being 18 years of age or younger, and the remainder are under the age of 5 whose seizures are due to fever or acute illnesses. Annual incidence rate is 40-70 per 100,000 in industrialized countries and somewhat higher in the developing countries. About 200,000 new cases are diagnosed annually in the U.S., with the incidence higher among children 2 years of age and younger, as well as in the elderly 65 years of age and older. Incidents are slightly more common in males than females. Prevalence appears to increase with age. It is estimated that there are 320,000 cases among children through age 14, and 500,000 over the age of 65.

Socially and economically disadvantaged populations are at a higher risk to develop symptoms. About 10% of children with mental retardation and 10% of children with cerebral palsy, 10% of Alzheimer patients and 22% of stroke patients may develop seizures. About 70% of patients who are seizure-free on medication for 2 to 5 years can successfully stop medication intake. However, 10% of patients fail to respond to treatment.

### DIAGNOSIS

Seizure disorders are typically characterized by **recurrent unprovoked episodes**. Careful medical history of the patient, in particular about description, duration, intensity of the seizure, as well as description of the feeling preceding the seizure, must be recorded. Results of an electroencephalograph (EEG), which records electrical signals from the brain cells, will give a clue to the presence or absence of abnormality. The pattern of the graph taken between and during a seizure will indicate the nature of the abnormality, and will assist in diagnosing the seizure type and pattern. Scans obtained from tools such as computerized tomography (CT) or magnetic resonance imaging (MRI) may assist in detecting growth, scars or any other physical condition in the brain that may trigger the seizures. Positron emission tomography (PET) imaging is helpful in identifying the areas of the brain that cause seizures. Single photon emission computerized tomography (SPECT) is an imaging technology that may assist in seizure localization. It is used mainly for patient evaluation prior to surgery.

*CE PRN*<sup>®</sup> (ISSN 0199-5006) is owned and published by W-F Professional Associates, Inc. 400 Lake Cook Road, Suite 207, Deerfield, Illinois 60015.

William J. Feinberg, President *CE PRN*<sup>®</sup> is published eleven times per year, monthly, January through November. Subscription rate is \$99.00 per year. Second-Class Postage paid at Deerfield, Illinois 60015 and at additional mailing offices. © 2007 by W-F Professional Associates, Inc. All rights reserved. None of the contents of this publication may be reproduced in any form without the written permission of the publisher.

POSTMASTER: Send all address changes to

W-F Professional Associates, Inc., 400 Lake Cook Road, Suite 207, Deerfield, IL 60015.

July 2008

### TRIGGERS OF SEIZURE ACTIVITY

Many patients do not associate a seizure with a trigger as most types of seizure disorders occur without provocation. Others are aware of certain circumstances that act as triggers. Menstruation, hyperventilation, alcohol intake or failure of the patient to comply with medications all might trigger a seizure event. Others include lack of sleep, fever or presence of illnesses. Eating certain foods is patient specific. Flickering light pattern may act as a trigger in a small percentage of patients.

### COMPLICATIONS

During a seizure, the patient may fall and cause injuries, in particular, to the head. Likewise, there is a risk of drowning while swimming or bathing. Seizures that cause loss of awareness and control, as well as intake of anticonvulsant drugs that cause drowsiness may affect patient's ability to drive or operate machinery.

In many states, licensing restrictions are placed on patients. While female patients can become pregnant, it is important to keep in mind that seizures may pose danger on both mother and baby. Since some anticonvulsant drugs may cause birth defects, it is essential that pregnant patients comply with the physician's directions concerning dose and monitoring. Patients, who suffer from status epilepticus, where the seizures are prolonged and continuous, are at risk of brain damage and even death.

### TYPES OF SEIZURES

The clinical and electrophysiological manifestations of seizure disorders are varied. The proper diagnosis and choice of therapy depend largely on identification of the type of seizure, which may be classified into **generalized** and **partial** types.

#### Generalized Seizures

These seizures include **grand mal**, **absence**, **myoclonic**, **tonic** and **atonic** types.

**Grand mal seizures** are characterized by unconsciousness, convulsions and muscular rigidity. Usually the onset is immediately preceded by an aura, a sensation of fear, epigastric distress, an unpleasant odor, various visual and auditory hallucinations and sensory illusions, such as objects changing in size. This is followed by loss of consciousness and muscular contractions. The patient may fall to the floor, and the body becomes rigid in an arched position with feet and head on the floor (opisthotonos position). The jaw becomes locked and a brief cessation of respiration (apnea) may lead to cyanosis. Multiple jerks, excessive salivation and frothing from the mouth may occur. The episode may last from 2 to 5 minutes, after which the patient gradually regains consciousness. Upon recovery, the patient may experience muscular pain and drowsiness.

**Absence seizures (petit mal)** are characterized by a brief loss of consciousness; it occurs primarily in childhood, and diminishes during puberty. The seizure consists of a short period of unconsciousness or cessation of ongoing conscious activity, such as stopping speaking in mid-sentence, followed by a fixed stare, eye blinking, lip smacking or chewing. The attack may last from 10 to 30 seconds. During the seizure, there is no convulsive muscular activity and no loss of muscular tone.

**Myoclonic seizures** are characterized by sporadic, brief, single or repetitive, mild to violent involuntary jerks involving a single muscle or several muscle groups, especially those of the extremities. These seizures are not accompanied by loss of consciousness. Myoclonic jerks may occur in healthy individuals during drowsiness or early stages of sleep.

**Clonic seizures** are characterized by repetitive, rhythmic, jerking movements, whereas tonic sequences cause muscle stiffness and rigidity.

**Atonic seizures** are brief, sudden losses of consciousness and muscle tone. Muscular contraction is usually absent. The seizures lead to head drop or slumping of the body, and the person may fall abruptly to the floor for no apparent reason.

#### Partial Seizures

Partial seizures are classified into two subgroups: **simple partial** and **complex partial seizures**. In **simple partial seizures**, no loss of consciousness is involved. They may appear as a jerking muscle movement of a single part of the body such as a finger, or a limb, but usually end spontaneously. Sensations affecting vision, hearing, smell, taste and stomach may occur.

**Complex partial seizures** are manifested by a change in behavior, confusion and a brief unconsciousness. The attack may evolve into a grand mal seizure.

### CAUSES OF SEIZURES

The underlying neuronal abnormality is unknown. Any factor that causes alterations in the electrical discharge pattern may precipitate a seizure. Genetic factors play an important role and also affect EEG patterns. The incidence of seizures is higher in families with primary generalized seizures than in the general population. The likely cause of recurrent seizures may be age-related. Congenital malformation, birth injury, asphyxia, metabolic defects, or maternal infections, such as rubella, can cause cerebral abnormalities, and later seizures. Brain infections such as meningitis, encephalitis and abscess can trigger seizures during the course of the infection and later on as a result of cerebral scars. Febrile convulsions, which are usually tonic-clonic in nature, are encountered in children between the ages of 3 months and 5 years of age, and occur as a result of high fever (above 38°C) in an otherwise neurologically normal child. The likelihood of developing recurring seizures as a result of febrile convulsions is minimal, if the seizures are short in duration and are not accompanied by EEG abnormalities. However, if the seizures are prolonged and focal, and EEG abnormalities are detected, cerebral damage may follow, and the risk of developing a chronic condition becomes significant. Brain tumors, cerebral vascular diseases, or cerebral degenerative disorders are the most common causes of seizures in older age groups. In young adults, withdrawal from alcohol or other sedative-hypnotic drugs may act as triggers. A number of metabolic diseases such as uremia, hepatic failure, hypo- or hypercalcemia, hypo- or hyperglycemia, or hypo- and hypernatremia may be precipitants at any age. Individuals who suffer from these disorders may experience attacks that may be experienced with fatigue or lack of sleep, emotional or physical stress, fright, fever, constipation, use of stimulant drugs, hyperventilation, stimuli such as blinking lights, noises, or certain odors. Increased seizure activity may occur in women immediately prior to or during menstrual cycle. Pregnancy may increase or decrease the frequency of seizure activity.

### GOALS OF THERAPY

The ideal goals of seizure therapy are to:

1. eliminate or reduce acquired causes;
2. control or eliminate recurrences while producing minimal disruption in lifestyle and normal cognitive function of the patient;
3. deal with psychological effects that may result from the seizures and their aftermath; and
4. minimize the adverse effects of anticonvulsant drugs.

To achieve these goals, the type of seizure must be identified and each drug therapy must be individualized. If the diagnostic tests indicate the seizures occur as a consequence to the presence of an acquired disease, then treatment of the offending factor may lead to reduction or elimination of seizure recurrence. Despite the fact that many patients respond positively to therapy and live a relatively normal life, some lifestyle adjustments may be necessary. Depending on the type of seizures, patients may have to restrict some activities such as driving, swimming unattended or operating potentially hazardous machinery. Likewise, patients who are predisposed to seizures should avoid stimuli such as stress, active exercise, lack of sleep, and intake of CNS stimulants such as caffeine.

Patients often feel embarrassed and become withdrawn to avoid humiliation if the episodes occur in public. Successful control can restore the patient's self-esteem and confidence and enhance social interaction.

Selection of medication should be based on the type of seizure, potential adverse effects of the drug, pharmacological spectrum and pharmacokinetic features. Adherence to these principles can result in control of up to 75% of cases. In spite of rigorous treatment, some patients continue to experience seizures. An ideal drug should be: effective with low incidence of adverse reactions; therapeutically effective against more than one type of seizure; non-sedating; and effective with minimal limitations of lifestyle. None of the currently available drugs possess all of these characteristics. In most cases, single therapy (monotherapy) is more advantageous than multiple drugs (polytherapy), due to reduction in the potential for adverse drug reactions and unwarranted drug interactions, ease of blood monitoring of a single drug, and improved compliance. Once an anticonvulsant drug is selected, the therapeutic, toxic, and adverse reactions must be monitored. The drug's pharmacokinetic, as well as plasma drug levels, play an important role in clinical effectiveness. Monitoring plasma drug levels is important because they may vary from one patient to another, even if the same dose is given. Plasma drug levels determine to a large extent the therapeutic as well as toxic effects. Thus, dosage adjustment is essential. The variation in blood levels is primarily due to pharmacokinetic factors such as absorption, distribution, metabolism, and excretion. However, utilizing blood levels to determine the optimal dosage can compensate for variations from one patient to another. Other factors that influence plasma drug levels are renal and hepatic impairment, presence of other illnesses, diet, and general health of the individual and patient compliance. Serum half-life of these drugs depends largely on rate of metabolism and excretion.

Drug compliance is an important aspect of therapy. Many patients do not realize the importance of steady blood levels and half-life. Thus, they may take the medication occasionally to avoid the side effects that the drug may cause, or they may increase the dose hoping to avoid an attack. It is essential that patients and family members be educated about the chronic nature of the disease and the importance of taking the medication as directed. Likewise, it should be understood that these drugs do not cure, but can eliminate or reduce recurrent episodes and must not be discontinued abruptly. Adverse effects such as drowsiness, ataxia, nausea, vomiting, weakness and headache should be reported to the physician. Generally, it is recommended that medications be taken with meals to avoid gastric irritation. Patients should consult with a physician or a pharmacist prior to taking other medications in order to avoid the risk of interactions. Medical identification tags are recommended, and caution should be exercised when driving a car.

### ANTICONVULSANT DRUGS

These medications may be classified into three major categories: **older** generation, **new** generation and **newer** generation. **Older** generation anticonvulsants include: phenobarbital, primidone, phenytoin, ethosuximide, valproic acid and carbamazepine. **New** generation drugs are felbamate, gabapentin, lamotrigine, topiramate and tiagabine. The **newer** generation group includes oxcarbazepine, levetiracetam and zonisamide.

### OLD GENERATION ANTICONVULSANTS

The use of **phenobarbital** in the control of convulsions was recognized in 1912, and since then it has become one of the most widely used medications. Because of its CNS depressant effect and the sedation it causes, phenobarbital has been replaced by other drugs that are more effective and have lesser side effects. It is used mainly when other medications fail. Unlike many barbiturates, which act as sedative-hypnotic drugs, phenobarbital has anticonvulsant properties in sub-hypnotic doses, which causes no or minimal sedation. The mechanism of action of the anticonvulsant activity of phenobarbital is not fully understood. It has been postulated that the drug elevates the seizure threshold and prevents the spread of the discharge mainly by potentiation of the inhibitory action of gamma aminobutyric acid (GABA), and by inhibition of the excitatory effect of the neurotransmitter glutamate. Phenobarbital is well absorbed from the GI tract, and about 50% of the drug in the blood is bound to plasma protein. Peak concentration level is reached in less than four hours. The half-life is approximately four days, and because of this, about 2 to 3 weeks may be needed in order to achieve steady-state levels.

Phenobarbital is used primarily in tonic-clonic seizures, and may be helpful for other types, but usually not absence seizures. The main adverse reactions are related to sedation, which occurs in the vast majority of patients during the initial phase of therapy. Some degree of tolerance to sedation may develop with continued use, but impairment of cognitive skills and motor performance may continue. In some patients, particularly children, the drug may cause hyperexcitability and agitation. It may impair memory and performance on intelligence tests. Other problems include skin rash, megaloblastic anemia, and osteomalacia due to interference with metabolism of vitamin D. Like all barbiturates, phenobarbital may cause physical dependence.

**Primidone** is an analog of phenobarbital, and, consequently, both share the same pharmacology. It is used for the management of tonic-clonic and partial seizures, but is ineffective against absence seizures. A large portion of the dose is quickly absorbed from the GI tract and is slowly metabolized in the liver and slowly excreted by the kidneys. The adverse reactions are similar to those of phenobarbital. Like phenobarbital, it is infrequently used because of the higher incidence of side effects compared to other drugs.

**Phenytoin** was introduced in 1938, and today it is considered one of the most useful anticonvulsant drugs because of its activity against all forms of seizures, except absence. Even though absorption rate is variable, depending on formulation and manufacturer, orally administered phenytoin is well absorbed from the GI tract. Approximately 90% of the drug that reaches circulation is bound to plasma protein in adults. The average half-life is 22 hours, but it may vary from one individual to another depending on renal and hepatic functions. The drug is metabolized mainly in the liver by oxidation, a process with limited capacity. Because of this, any increase in dosage above that needed to achieve therapeutic effects may result in a significant increase in blood levels.

Phenytoin appears to exert its anticonvulsant properties by inhibiting the spread of seizure activity from the focus to other parts of the brain. It does not prevent the initiation of abnormal discharge at the focus itself. Inhibition of the spread of discharge is believed to be due to normalization of abnormal fluxes of sodium across neuron cell membranes during and after depolarization. This tends to render the neuron less excitable and raises the seizure threshold.

Adverse effects are dose-related and include dizziness, confusion, mood alterations, drowsiness, diplopia (double vision), nystagmus (frequent back and forth movement of the eyes), and decreased cognitive function. Phenytoin may pro-

duce gingival hyperplasia (increased growth of the gum tissue), especially in children. The gums become swollen and bleed easily. Good oral hygiene may minimize the gum lesions. Other side effects include nausea, vomiting, cardiac arrhythmia and hypotension following IV administration, skin rash, hirsutism in females (overgrowth of hair), vitamin deficiencies, and blood dyscrasias.

**Ethosuximide** is the most widely used of the succinimide-derivative anticonvulsants because it is more effective and possesses fewer side effects. It is used in the control of absence seizures, but has no effect against tonic-clonic, complex and partial seizures. It is well absorbed from the GI tract. The half-life is 30 hours in children and 60 hours in adults. A large portion of the drug is metabolized in the liver and excreted in the urine. The mechanism of action is not well established. It has been suggested that ethosuximide raises the seizure threshold and suppresses the EEG spike-and-wave pattern of absence seizures. Adverse effects include drowsiness, especially during the initial phase of treatment, dizziness, nausea, vomiting, abdominal cramps, epigastric distress, and blood dyscrasias.

The chemical structure of **valproic acid** is different from other anticonvulsant drugs. In 1978 the FDA approved its use only in the management of absence seizures. However, the drug has a broad activity against tonic-clonic, partial, atonic, and myoclonic seizures.

Valproic acid is rapidly and almost completely absorbed from the GI tract. Peak blood levels are reached within 1 to 4 hours. About 90% of the drug becomes bound to plasma protein. Elimination half-life is between 6 to 18 hours. The onset of the therapeutic effects is attained within several days following the start of therapy. The mechanism of action is not clearly understood. It appears that it achieves its anticonvulsant activity by increasing the concentration of the inhibitory neurotransmitter GABA. This increase is believed to be due to inhibition of GABA breakdown and reuptake.

Hepatotoxicity, which rarely results in fatality, is the most serious adverse effect. Thus, valproic acid is contraindicated in the presence of hepatic disease. Even though it is more tolerated than other anticonvulsant drugs, valproic acid possesses a number of side effects, the most frequent of which targets the GI tract, and manifests as nausea, vomiting and abdominal discomfort. These symptoms are usually transient, and tolerance may be achieved by using enteric-coated tablets. Hyper salivation, appetite level fluctuation, and constipation have been reported in some patients. Neurological adverse effects such as sedation and drowsiness are usually dose-related and depend largely on whether or not valproic acid is administered concomitantly with other anticonvulsants. Behavioral and cognitive effects are not as frequent as with some drugs. Hematological function parameters should be established before and during therapy, as the drug may cause blood dyscrasias.

**Carbamazepine** was first introduced as an anticonvulsant in the early 1970's, and before that it was used primarily for trigeminal neuralgia. The mechanism of action is unknown, but appears to be similar to phenytoin. It reduces polysynaptic responses in the CNS and depresses seizure propagation.

The drug is absorbed slowly from the GI tract, and its peak blood concentration is reached in 2 to 8 hours. The rate of absorption varies with the oral dosage form employed. There appears to be a variation in steady state plasma concentration depending on the daily dosage. Between 70% to 90% is bound to plasma protein. Plasma half-life of the drug is variable, usually ranging from 25 to 65 hours. During the initial therapy, the half-life is long. However, as therapy progresses, it can decrease to 12 to 17 hours. Carbamazepine is an inducer of hepatic drug-metabolizing enzyme, and, consequently, it tends to cause its own metabolism. Because of these changes, several days may be required to attain effective therapeutic serum levels.

Carbamazepine is effective in the control of tonic-clonic, simple partial, and complex partial seizures, but ineffective against absence, myoclonic or atonic seizures.

The most common adverse reactions are related to the GI tract and the CNS. Sedation, ataxia, nausea, vomiting, diplopia, and mild nystagmus occur at the beginning of therapy, and are dose dependent. Such effects tend to diminish within the first week of therapy. It has been associated with potentially life-threatening blood dyscrasias such as aplastic anemia, leucopenia, thrombocytopenia, and agranulocytosis. Blood count should be taken before and during therapy. Other adverse reactions that have been reported include abnormal liver function, rashes, birth defects and photosensitivity.

### NEW GENERATION ANTICONVULSANTS

New generation drugs are felbamate, gabapentin, lamotrigine, topiramate and tiagabine.

**Felbamate**, which was approved by the FDA in 1993, is used in both partial and generalized seizures, either alone or in combination with other drugs. It is a second-line anticonvulsant due to its adverse effects. It is related to meprobamate, but has different pharmacology. It is available in 400 mg and 600 mg tablets, as well as in suspension. The usual maintenance dose is 1200-3600 mg daily. Felbamate therapy should be initiated at low dose and titrated up slowly at incre-

ments of 300 mg to 400 mg. Since it is an inhibitor of the cytochrome 450 enzyme system, it inhibits metabolism of phenytoin, phenobarbital, valproic acid, and the carbamazepine metabolite, carbamazepine epoxide. It has a half-life of 14 to 24 hours, and 40% - 50% of the dose is excreted unchanged in the urine. Its mechanism of action is unknown. Rare reports of fatal aplastic anemia and hepatic failure limit its use to patients for whom no other treatment alternative exists. The manufacturer recommends biweekly complete blood cell count and hepatic function tests for the first six months of therapy. Adverse effects include anorexia, nausea, insomnia, headache, dizziness, fatigue, weight loss and diplopia.

**Gabapentin** is chemically related to the inhibitory CNS neurotransmitter GABA. However, its anticonvulsant effect is not fully recognized. It was approved in 1994 as adjunct therapy for the management of partial seizures, but not in other seizure types. It is well absorbed after oral administration, and 95% of the dose is excreted by the kidneys. It is available in 100 mg, 300 mg, and 600 mg capsules, as well as 600 mg and 800 mg tablets. Additionally, it is available in a suspension form. It has a relatively short half-life (5 – 7 hours). The usual adult maintenance dose is 900 – 4800 mg daily. When compared with other anticonvulsants, gabapentin is well tolerated and has a low adverse profile. Due to its elimination through the kidneys, gabapentin should be given in lower doses in patients with kidney impairment. Sedation, dizziness, ataxia and nystagmus have been reported. The drug is useful for partial seizures in older children.

**Lamotrigine** was introduced in the late 1980's. It has a broad spectrum of activity and is used as adjunctive therapy in the management of partial seizures, generalized tonic-clonic seizures, absence and myoclonic seizures, and generalized seizures in Lennox-Gastaut syndrome (absences, infantile spasms, juvenile myoclonic convulsions). It can be used as monotherapy in adults. Lamotrigine is available in 25 mg, 100 mg, 150mg and 200 mg tablets as well as in 2 mg, 5 mg, and 25 mg chewable tablets. The usual adult maintenance dose is 300 – 500 mg daily when given with enzyme inducing anticonvulsants (phenobarbital, phenytoin, and carbamazepine) without valproate, and 100 – 400 mg daily if given in combination with valproate. Approximately 10% of the dose is excreted unchanged in the urine, and 85% undergoes hepatic metabolism. Nausea and vomiting, as well as rash, are the most common adverse effects that may occur at high dosage. Other potential problems include dizziness, ataxia, drowsiness and hepatotoxicity.

**Topiramate** is also a broad spectrum anticonvulsant that is used in the control of partial seizures, primary generalized tonic-clonic seizures, atonic, tonic, and tonic-clonic seizures in Lennox-Gastaut syndrome. It is available in 25 mg and 100 mg tablets. The usual adult dose is 200 – 600 mg daily. About 70% of monotherapy dosage is excreted unchanged in the urine. The adverse reactions include weight loss, rare incidence of kidney stones, cognitive changes, drowsiness and fatigue. These reactions may be minimized with a small initial dose, followed by gradual dosage increase.

**Tiagabine** is an effective anticonvulsant for partial seizures in children older than 12 years of age. It is rarely used effectively in generalized seizures. It is available in 2 mg, 4 mg, 12 mg, 16 mg, and 20 mg tablets. The half-life is 7 – 9 hours in monotherapy, and only 2 – 3 hours in those on enzyme inducers, thus the drug should be administered at least three times daily. Elimination occurs mainly through hepatic metabolism. Consequently, the drug should be avoided in the presence of liver impairment. Maintenance adult dose is 32 – 56 mg daily. The adverse reactions include dizziness, unsteadiness, drowsiness, irritability and difficulty with concentration.

### NEWER GENERATION ANTICONVULSANTS

**Oxcarbazepine** is a keno-analogue of carbamazepine, and has been marketed as an alternative to carbamazepine because of its efficacy in the control of partial seizures in children older than 4 years of age and in adults. It does not undergo auto induction, and it is not extensively metabolized by the CYP450 enzyme system. The likelihood is less that it will result in side effects, especially rashes. It is used in the management of partial seizures or primary generalized tonic-clonic seizures. It is available in 150 mg, 300 mg, and 600 mg tablets as well as in suspension. The adult maintenance dosage is 1200 – 2400 mg daily. The main adverse effects include sedation, dizziness, nausea, diplopia, ataxia, and headache. Hyponatremia may be encountered in elderly patients. This side effect rarely affects children.

**Levetiracetam** has shown good results when used for treating partial seizures in adults, and appears to have potential for managing clonic seizures, absence and generalized tonic-clonic seizures. Its use in children is not clear. It is available in 250 mg, 500 mg, and 750 mg tablets. The usual adult maintenance dose is 1000 – 3000 mg daily. Approximately 66% of the drug is excreted in the urine in the unchanged form. The half-life range in normal renal function is 6 – 8 hours. Patients with renal impairment should take a reduced dose. The only side effects reported are mild neurological disturbances that include headache, dizziness, drowsiness, and nervousness.

**Zonisamide**, which possesses pharmacological activities that resemble those of phenytoin, carbamazepine and valproate, has a broad spectrum of anticonvulsant activity. Studies revealed that partial seizures, generalized tonic-clonic seizures, atypical absences, infantile spasms and seizures of the Lennon-Gastaut syndrome have responded positively to the use of zonisamide. The drug is available in 100 mg capsules. The usual adult maintenance dose is 200 – 600 mg daily.

The drug is excreted through renal and hepatic routes. Its half-life is 50 – 70 hours when administered alone, but it diminishes to 25 – 40 hours when taken with enzyme inducers. Since the drug is a sulfonamide derivative, its use should be avoided in patient allergic to sulfonamide drugs. Additionally, patients should be advised to drink plenty of fluids to minimize the risk of kidney stone formation. Adverse reactions of this drug include drowsiness, dizziness, anorexia, nausea, headache, agitation, weight loss and kidney stones.

### **SUMMARY**

Convulsion disorders are common neurological syndromes that result from irregular electrical discharges in the brain. They affect people of all ages and manifest in various types. The current drugs can cause remission but not cure. Anticonvulsant drugs possess adverse effects, some of which are serious.

### **REFERENCES**

- Sander, JW, " The Epidemiology of Epilepsy Revisited", Curr Opin Neurol, 10:165 (2003)
- Kelley, K and Theodore, WH, "Prognosis 30 years after temporal Lobectomy." Neurology, 64: 1974 (2005)
- Meisler, M.H., Kearney, J.A., "Sodium Channel Mutations in Epilepsy and other Neurological Disorders" J. Clin. Invest. 115:2010 (2005)
- Tierney, L.M., McPhee, S.J., Papadakis, M.A.," Current Medical Diagnosis and Treatment 2003". 42<sup>nd</sup> Ed. Lang Medical Books / McGraw Hill (2003)
- Kasper, D.b., Braunwald, E.B., Fauci, A.S., Hauser, S.L., Longo, D.L., Jameson, J.L. " Harrison's Principles of Internal Medicine" 16<sup>th</sup> Ed. (2005)

Fill in the information below, answer questions and return **Quiz Only** for certification of participation to:  
 CE PRN®, 400 Lake Cook Road, Suite 207, Deerfield, IL 60015.

NAME \_\_\_\_\_ (ID # 1st line on label) \_\_\_\_\_

ADDRESS \_\_\_\_\_ CITY \_\_\_\_\_ STATE \_\_\_\_\_ ZIP \_\_\_\_\_

CHECK IF NEW ADDRESS  **ARE YOU LICENSED IN FLORIDA? IF YES FL LIC** \_\_\_\_\_

**EMAIL Address (we need this)** \_\_\_\_\_

**LESSON EVALUATION**

- |   |  |  |  |  |  |     |    |
|---|--|--|--|--|--|-----|----|
| 1. Does the program meet the learning objectives?                                       |  |  |  |  |  | Yes | No |
| Describe the epidemiology, diagnosis, triggers & complications associated with seizures |  |  |  |  |  | Yes | No |
| List the types of seizure disorders & state the characteristics of each                 |  |  |  |  |  | Yes | No |
| Identify the goals of therapy   |  |  |  |  |  | Yes | No |
| State the advantages of the newer anticonvulsant drugs                                  |  |  |  |  |  | Yes | No |
| List the adverse effects associated with the anticonvulsant drugs                       |  |  |  |  |  | Yes | No |

2. Was the program independent & non-commercial Yes No

		Poor		Average		Excellent	
3. Relevance of topic	1	2	3	4	5	6	7

4. What did you like most about this lesson? \_\_\_\_\_

5. What did you like least about this lesson? \_\_\_\_\_

**Please Select the Most Correct Answer**

- |  |   |
|--|---|
| <p>1. What is true about a seizure?</p> <p>A. It is a symptom</p> <p>B. It is usually provoked</p> <p>C. It is generalized when it affects the entire body</p> <p>D. Occurs due to brain damage</p> <p>2. Magnetic resonance imaging assists in:</p> <p>A. Identifying areas of the brain that cause seizures</p> <p>B. Evaluation prior to surgery</p> <p>C. Detecting growth in the brain</p> <p>D. Correcting scar tissue in the brain</p> <p>3. Which of these may provoke a seizure?</p> <p>A. Overeating</p> <p>B. Gender</p> <p>C. Warm environment</p> <p>D. Fever</p> <p>4. Grand mal seizure</p> <p>A. Usually lasts for seconds</p> <p>B. Causes repetitive jerking movements without loss of consciousness</p> <p>C. Is characterized by unconsciousness, convulsions &amp; muscular rigidity</p> <p>D. Is characterized by brief, sudden loss of consciousness</p> <p>5. All of the following are goals of seizure therapy, except:</p> <p>A. Eliminate or reduce acquired causes</p> <p>B. Achieve a cure</p> <p>C. Control or eliminate recurrences</p> <p>D. Minimize adverse effect of drugs used</p> | <p>6. Which statement is correct about phenobarbital?</p> <p>A. Has anticonvulsant properties in subtherapeutic doses</p> <p>B. Poorly absorbed from GI tract</p> <p>C. Improves memory</p> <p>D. With continued use, patients become more susceptible to sedation</p> <p>7. Overgrowth of hair is termed:</p> <p>A. Nystagmus</p> <p>B. Hyperplasia</p> <p>C. Diplopia</p> <p>D. Hirsutism</p> <p>8. Which of these is an inhibitor of cytochrome 450 enzyme?</p> <p>A. Gabapentin</p> <p>B. Felbamate</p> <p>C. Lamotrigine</p> <p>D. Topiramate</p> <p>9. Which of these possess pharmacological activities similar to those of phenytoin, carbamazepine &amp; valproate?</p> <p>A. Levetiracetam</p> <p>B. Tiagabine</p> <p>C. Zonisamide</p> <p>D. Oxacarbazepine</p> <p>10. Which of these is used for trigeminal neuralgia?</p> <p>A. Ethosuximide</p> <p>B. Primidone</p> <p>C. Phenytoin</p> <p>D. Carbamazepine</p> |
|--|---|

**Contributing Author**

Farid Sadik, Dean Emeritus  
University of South Carolina  
College of Pharmacy  
Columbia, SC

**Executive Editor**

William J. Feinberg,  
BS Pharm, MBA

**CE PRN**<sup>®</sup> is a publication of W-F Professional Associates, Inc. This program is in printed format.



W-F Professional Associates, Inc. is approved by the Accreditation Council for Pharmaceutical Education (ACPE) as a provider of continuing pharmaceutical education.

Providers who are approved by ACPE are recognized by the following states: Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin and Wyoming.

Pharmacists completing this course by July 31, 2011 may receive full credit.

This program has been approved by the State Boards of Pharmacy in Alabama and Oklahoma.

This lesson furnishes 1.25 hours (0.125 CEUs) of credit.

**Program ID #707-000-08-007-H01-P.**

CE Provider Registered # with CE Broker.com is 50-3170.