

Epilepsy

Epilepsy is one of the most common neurological disorders in the world. It is characterized by recurring seizures caused by abnormal electrical activity in the brain. A single seizure or recurring seizures due to a correctable cause may not necessarily be evidence of an epileptic disorder.

Epileptic seizures are caused by a disruption in the communication between neurons in the cerebral cortex, the most highly developed part of the human brain. Comprising about two thirds of the brain's mass, the cortex is responsible for thinking and perceiving and for producing and understanding language. Specific areas within the cerebral cortex are responsible for vision, hearing, touch, movement, and smell.

Nerve cells communicate with each other through signals between neurons. During nerve cell transmission, or "firing," chemicals called neurotransmitters are released into the space between neurons (the synapse) to carry the signal. Neurotransmitters influence the action of neurons, either by triggering (exciting) or discouraging (inhibiting) a neuron's firing. The brain has billions of neurons in constant communication with one another.

Epileptic seizures range in severity from mild sensory disruption to a short period of staring or unconsciousness to a seizure. About 2.5 million people experience epilepsy in the United States, and about half of the new cases diagnosed every year occur in children. Roughly 3 percent of the general population will experience epilepsy by age 75 (American Epilepsy Society 2005).

Currently, treatment for epilepsy is based on antiepileptic drugs (AEDs). Often patients must undertake significant experimentation to find a regimen that works. In recent years, research has shed light on new aspects of epilepsy that remain untreated by conventional AEDs.

One effective approach to epilepsy is known as the ketogenic diet. This special diet encourages the creation of ketones in the body and has been shown to reduce seizure activity. However, the ketogenic diet has been linked to specific nutrient deficiencies that must be addressed through aggressive supplementation.

Although the specific underlying cause of epilepsy and seizures is often unknown, research has found that damage caused by free radicals can predispose the brain to seizures. The high fat content of myelin sheaths that surround neurons and the high rate of oxidative metabolism (about 20 percent of the total oxygen demand of the body) make the brain a target for free radical damage. Many factors can induce excess production of free radicals, including head trauma and neurodegenerative diseases (Halliwell B 2001). This means that antioxidant therapy may represent an important adjunct therapy to conventional drugs.

INTERACTION OF THE NERVOUS SYSTEM AND EPILEPSY

The nervous system has two major divisions: the central nervous system and the peripheral nervous system. The central nervous system consists of the brain and the spinal cord. The peripheral nervous system also has two parts: the somatic nervous system and the autonomic nervous system (which is further divided into three parts: sympathetic, parasympathetic, and enteric). The autonomic nervous system exercises control over automatic or involuntary functions in the body, such as heart rate and respiration, among others. Although seizures emanate from the brain, there is a complex interaction between the autonomic nervous system and the central nervous system with regard to seizures.

Some seizures have a preliminary phase, known as an aura. An aura is a brief electrical discharge in the brain that can signal a person with epilepsy that a larger seizure is imminent. Epilepsy auras can range from a nonspecific strange or peculiar sensation to feelings of extreme fear or euphoria to the experience of strange lights or strange sounds. (Epilepsy auras are different from migraine headache auras.) A seizure episode might start with autonomic symptoms: cardiac palpitations or other irregular rhythms; respiratory apnea (breathing stops); hyperventilation (breathing rate increases); hypoxia (breathing rate decreases); nausea, vomiting, and fecal incontinence; genital symptoms; urinary urgency (incontinence); flushing, erythema, and cyanosis; dilated or constricted pupils; and perspiration, salivation, and tearing (NINDS 2006).

People with epilepsy have a mortality rate substantially higher than the general population's. This phenomenon is known as sudden unexplained death in epilepsy patients (SUDEP). SUDEP is unexpected and nontraumatic. It does not involve drowning, may or may not be witnessed, and has no anatomical or toxicological cause. In the United States, SUDEP may account for 8 to 17 percent of all deaths in individuals with epilepsy, and the incidence in younger persons is higher. The incidence of SUDEP also rises in the third to fifth decades of life. The male-to-female ratio can be as high as 7:4 (Nouri S et al 2004).

Epilepsy is typically diagnosed on the basis of a combination of findings, including patient history, physical examination, and laboratory testing. During an office visit, a patient will typically undergo a standard neurological examination, which includes evaluation of the patient's orientation, reflexes, motor control, nerve function, coordination, and sensory perception. It is often helpful for a physician to examine the person as soon after seizure activity as possible.

The most common lab test to detect epilepsy is the electroencephalogram (EEG), which detects electrical activity in the brain. However, brain activity may be normal when the patient is not experiencing a seizure, so a normal EEG does not rule out a diagnosis of epilepsy. Other brain imaging studies, including MRI and computed tomography (CT) scanning, are sometimes used to identify possible physical causes of seizures, such as tumors or malformations in the brain's vasculature.

STANDARD ALLOPATHIC TREATMENT

Conventional treatments for epilepsy often rely on AEDs such as carbamazepine (Tegretol®, Carbatrol®), lamotrigine (Lamictal®), phenytoin (Dilantin®), and valproic acid (Depakene®, Depakote®), which may be taken for many years.

AEDs are grouped by main function: sodium channel blockers, calcium current inhibitors, gamma-aminobutyric acid enhancers, glutamate blockers, carbonic anhydrase inhibitors, and unknown mechanisms. Drug selection is based on clinical diagnosis as well as characteristics of the AED and its side effects. The choice of AED also depends on the personal preferences and experiences of the treating physician as well as the clinical context (e.g., in an emergency room, intravenous administration would be a typical approach). In an outpatient setting, many choices are available.

Becoming seizure free is very difficult. Treatment outcome is optimal when a patient becomes seizure free by taking one AED (monotherapy). Unfortunately, it is estimated that most epilepsy patients achieve only satisfactory seizure control, meaning they still have seizures and experience side effects from medication(s). When successful seizure control with monotherapy cannot be achieved, other AEDs are added to the treatment regimen. Each medication should be titrated upward in dosage until either seizures are eradicated or side effects become intolerable. Certain individuals with intractable seizures can be treated with as many as four different AEDs concomitantly.

In most instances, careful blood monitoring must be performed to determine the blood levels of each AED or other pharmaceuticals, especially when a patient is taking multiple AEDs or other pharmaceuticals that alter metabolism, because a significant increase or decrease in blood levels of AEDs might occur as a result of drug interactions. AEDs are selected on the basis of their mechanism of action. Polypharmacy is then based on a combination of the various known mechanisms of action of each AED (Ochoa JG et al 2005). Only when a patient fails to respond to an AED protocol should surgery be considered.

Epilepsy patients should also be aware that long-term use of AEDs can negatively affect their vitamin and mineral status. For instance, patients taking carbamazepine and related AEDs have significantly lower levels of vitamin D and a higher rate of bone loss, which raises the risk of osteoporosis (Mintzer S et al 2006). AEDs have also been shown to reduce levels of the B vitamins and raise homocysteine levels. Elevated homocysteine is a risk factor for heart disease, and there is evidence that homocysteine itself may raise the risk of epileptic seizures. Some studies have indicated that elevated homocysteine may contribute to AED resistance. Based on these findings, some researchers call for routine supplementation with the B vitamins, especially folic acid, to reduce homocysteine levels (Morrell MJ 2002).

In the future, a number of promising AEDs may become available. One such drug, called lacosamide, is in clinical trials and is expected to be available in 2008 or 2009. This drug has been shown to reduce electrical seizure activity in the brain without affecting other areas of brain function (Duncan GE et al 2005). A number of other promising agents are also in advanced clinical trials in the United States, including brivaracetam, seletracetam, remacemide, retigabine, rufinamide, and safinamide.

Vagal nerve stimulation. The vagus nerve relays information to and from the brain and has many connections to areas in the brain that are instrumental in producing seizures. Vagal nerve stimulation (VNS) is the only form of electrical treatment for epilepsy approved by the US Food and Drug Administration (FDA). VNS was approved by the FDA in July 1997 as an adjunctive treatment for partial-type seizures in adults and adolescents more than 12 years of age who are resistant to treatment. In VNS, a small electrical device about the size of a small tape measure is implanted under the skin in the left upper chest area. A connecting wire is also implanted under the skin. Small leads are attached to the vagus nerve on the left side of the neck. The implantation takes about two hours. After implantation, the stimulator device is programmed to deliver electrical stimulation automatically 24 hours a day (usually every few minutes).

VNS can reduce seizure severity and frequency. The precise mechanism of action of VNS is not known, but it is believed to interrupt excessive electrical discharges in the brain and to either reset them or decrease excessive electrical output. VNS has been found to be safe and effective. Long-term use has been effective in up to 50 percent of cases (Rielo D et al 2006). Reduction of AED use was reported in 43 percent of patients following VNS for intractable epilepsy, and subjective improvement in quality of life occurred in 84 percent (McLachlan RS et al 2003).

The most frequently reported side effects of VNS are voice hoarseness, throat irritation, cough, and shortness of breath. Side effects are considered mild 99 percent of the time and as having insignificant impact on quality of life compared with other methods of treatment (specifically, VNS produces no associated depression, fatigue, dizziness, insomnia, confusion, cognitive impairment, weight gain, or sexual dysfunction). Side effects tend to diminish over time. VNS has been described as an on-demand therapy that is hassle free and long lasting. It has no interactions or known risks concerning potentially life-threatening adverse effects (Rielo D et al 2006).

Although the FDA has not approved VNS for children younger than 12 years of age, VNS is gaining popularity and credibility as a treatment option for children with intractable epilepsy. Trials indicate VNS is well tolerated and might be an important nonpharmacologic treatment option for children who do not tolerate medical therapy or are not surgical candidates (Amar AP et al 2001; Wakai S et al 2001). VNS offers several advantages for children: it is effective in prolonged use; seizure control improves over time; it has no associated cognitive impairment and no adverse drug interactions; the computer-controlled device allows complete and involuntary treatment compliance; and it is a potentially reversible form of treatment.

Tolerance and efficacy of periodic VNS using an implanted vagal nerve stimulator was studied in 12 children with medically intractable epilepsy. Greater than 90 percent reduction in number of monthly seizures was observed in five of the children. None showed deterioration from baseline, and a considerable number had improved status. The number of AEDs could be reduced in four children. No significant adverse reactions were noted. The study concluded that the vagal nerve stimulator was well tolerated in children with intractable epilepsy and might have a role in medical management (Murphy JV 1999).

A similar small study of implanted VNS systems in five children reported reduced overall seizure frequency in four out of five; reduced major convulsive seizures and nonconvulsive seizures in two; fast recovery after a generalized tonic seizure and improved cognitive function in two; and reduction of AEDs from three to one in one child (Wakai S et al 2001). No child had adverse effects.

Some report that VNS is the second most frequently used form of treating epilepsy (Wheless JW et al 2001). The advent of newer AEDs and VNS has reduced the use of surgery in epilepsy.

SURGICAL INTERVENTION

Surgery for epilepsy is a very highly specialized operation. It should be performed only by the most experienced teams of neurosurgeons, epileptologists (neurologists specializing in epilepsy), and other physicians in major academic centers. Successful surgery for epilepsy is dependent on finding a "focal lesion," an abnormality that can be seen on a radiological imaging scan. Common examples of focal lesions include masses; less common focal lesions include scars or fibrosis. The best surgical outcomes occur in individuals who have a diagnosis of temporal lobe epilepsy, a well-circumscribed focal lesion, or abnormal EEG data that are focal in nature to match the imaging abnormality.

In these cases, the success rate, or seizure-free outcomes, ranges from 80 to 90 percent. For individuals who do not have matching lesions on EEG and imaging, the success rate falls to about 50 percent (still considered favorable). Complications are few and insignificant compared to the improved quality of life as a result of seizure reduction (Alarcon G et al 2006).

DIETARY MANAGEMENT: THE KETOGENIC DIET

The ketogenic (i.e., ketone-producing) diet, consisting of high intake of fats (80 percent) and low intake of protein and carbohydrates, was developed in the 1920s (Francois LL et al 2003; Stafstrom CE et al 2003). Dietary management of epilepsy with the ketogenic diet is regarded as a strict medical regimen (Sheth et al 2002; Mady MA et al 2003).

Ketones are produced when fats are the primary dietary source of energy. Because the ketogenic diet is very low in carbohydrates (the usual source of energy), fat becomes the primary energy source for the body. A typical ketogenic diet (also called a long-chain triglyceride diet) is carefully calculated to provide 3 to 4 g fat for each gram of carbohydrate and protein; 75 to 100 calories for each 2.2 pounds of body weight; and 1 to 2 g protein for each 2.2 pounds of body weight (Freeman JM et al 2000). Laboratory testing can detect the level of ketones in the urine, and this level will indicate whether the body is effectively in ketosis through dietary measures.

The ketogenic diet has been used in the treatment of epilepsy in both adults and children with varying degrees of success (Nordli DR et al 2001; Wheless JW et al 2001). In children following the diet, approximately one-third become seizure free, one-third experience a reduction in seizures, and one-third experience no reaction. The diet appears to affect all types of seizures, although the response of children who have atonic seizures is often quicker. Adults frequently experience difficulty with the restrictive ketogenic diet, perhaps because of societal dietary norms (e.g., frequent carbohydrate intake) or concerns about excess consumption of dietary fats. However, the health benefits of a low-carbohydrate diet for individuals with epilepsy (especially regulation of blood sugar) along with a growing number of recipes that offer more-palatable low-carbohydrate, high-fat selections may improve compliance in adults.

Despite its common use and longevity, many questions remain about the ketogenic diet and its mechanisms of seizure prevention (Stafstrom et al 2003). What is known about its mode of action is that the relative state of ketosis induced by low consumption of carbohydrates can prevent wide fluctuations in blood sugar, thereby preventing hypoglycemia, a well-known cause of seizures. Another explanation credits a reduced intake of seizure-triggering allergenic substances.

Children on the regimen must be carefully screened and followed closely by a comprehensive medical team in order to ensure success. Typically a child is admitted to a hospital to start the diet and determine whether it will have any negative ramifications. Under close medical supervision, the regimen is started in the evening with fasting (except for water) that lasts 38 hours for children and 24 hours for infants. The urine is then tested to see if ketones are present. If ketones are found, the ketogenic diet is started. Close monitoring is continued in a hospital for two or three more days.

Side effects that can occur from following the ketogenic diet for a long time are weakened bones, nausea, diarrhea, constipation, dehydration, abnormal liver function, kidney stones, high blood cholesterol levels, behavioral changes, and slowed growth rate (Freeman JM 2000). The diet lacks several important vitamins, which must be supplemented. Intensive parental involvement and supervision are also needed for the diet to succeed (Sheth et al 2002; Stafstrom CE et al 2003).

Reviews of available evidence from studies of the efficacy of the ketogenic diet are consistent: the evidence is sufficient to determine that the diet is efficacious in reducing seizure frequency in children with refractory epilepsy, i.e., epilepsy resistant to treatment (Lefevre F et al 2000). The diet can also be helpful for children with status epilepticus (continuous seizure activity). In a report of experiences of 29 children with refractory epilepsy for whom no surgical option was available, 12 patients experienced improved seizure control from the ketogenic diet; in six with epilepticus, three responded. Compliance with the diet was good. Adverse effects compared favorably with those from AEDs (Francois LL et al 2003). The diet allowed a decrease or discontinuation of AEDs in some children (Hemingway C et al 2001).

When someone with epilepsy adopts a ketogenic diet, vitamin supplementation is important to replenish essential nutrients that are not provided by foods in the diet. A modified form of the ketogenic diet incorporates MCT oil, a substance that helps induce ketosis. Although the MCT diet is more flexible, it is generally less well tolerated and less effective. High fiber content is also important for individuals with epilepsy because fiber (unlike processed foods) must be broken down. This slows the absorption process, thereby slowing sugar intake and avoiding drastic fluctuations in blood sugar. Less-processed foods (e.g., beans and unrefined starches such as brown rice and rolled oats) also help slow the absorption of sugar.

NUTRITIONAL THERAPY FOR EPILEPTICS

Epilepsy is a highly variable disease, and its ideal management requires close supervision and cooperation with a physician. For some individuals, however, nutrient supplementation can reduce the number of seizures or minimize the amount of prescription medication they require. **The dosages given at the end of this chapter are designed for adults. Parents should not initiate antiepilepsy nutrient supplementation on their own. Please consult a physician before adding supplements to a child's epilepsy program.**

The B vitamins are essential for many functions in the central nervous system. Vitamin B6 and folate are critical cofactors in the production of many neurotransmitters. Of particular relevance in epilepsy, B6 is required to convert the principal excitatory neurotransmitter, glutamate, into the primary inhibitor neurotransmitter, gamma-aminobutyric acid. Vitamins B1, B3, B12, and carnitine are required in the maintenance of the myelin sheath that surrounds neurons and affects their ability to conduct coherent impulses.

Oxidative stress has also been identified as a major factor in epileptic seizures. It appears that the brains of people with epilepsy are under considerable oxidative stress from free radicals. Studies have shown that epileptics are low in many antioxidants, including intrinsic antioxidants such as glutathione and superoxide dismutase and extrinsic antioxidants including vitamin E, vitamin C, and vitamin A (Liao KH et al 2004). Although large human studies have not yet been conducted on the use of antioxidants in people with epilepsy, it is already known that vitamins A, C, and E are vital to brain function (Almeida SS et al 2002; Frederickson CJ et al 2000; Savaskan NE et al 2003). Studies have found that the combination of vitamin E and vitamin C protects nerve cell membranes from oxidation in people with posttraumatic seizures (Yamamoto N et al 2002).

Levels of vitamin E are reportedly lower in children with epilepsy than in controls (Ogunmekan AO 1979). In one small study of children not responding to standard drug treatment, the addition of vitamin E to the treatment regimen produced a significant reduction in seizures (Ogunmekan AO et al 1989).

Polyunsaturated fatty acids, including linolenic acid and the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have also been shown to protect the brain from seizure activity. In an animal study, linolenic acid protected animals from seizures after treatment with a seizure-producing drug (Lauritzen I et al 2000). This study was duplicated two years later with similar results. The animals in this study experienced significant protective benefits from linolenic acid (Blondeau N et al 2002). Other animal studies have found that omega-3 fatty acids can increase seizure thresholds and lower markers of inflammation. In a recent human study, 57 epileptic patients were given 1 g EPA and 0.7 g DHA daily. Seizure activity was reduced over the first six weeks, although the effect was temporary. The researchers called for more in-depth studies, with larger doses and larger observational groups (Yuen AW et al 2005).

In many cultures, including African and Asian cultures, epilepsy is commonly treated with herbal preparations from a wide variety of plants. While some of these herbs have anticonvulsive properties, many are hard to locate in the United States. Ginkgo biloba, however, has been identified as a possible anticonvulsant and is widely available. People should be aware, however, that Ginkgo biloba may prevent or cause seizures, and the doses of different brands of ginkgo vary significantly. People should approach this herbal remedy with caution (Harms SL et al 2006). Other herbal remedies have been shown to interact with AEDs. St. John's wort, for example, has been suggested to lower blood pressure in conjunction with carbamazepine.

In Western medicine, some people also self-treat their epileptic seizures with cannabis, or marijuana. In one Canadian survey, 24 percent of patients in an epilepsy care center reported using marijuana or cannabinoids to treat their disease (Gross DW et al 2004). Researchers are investigating active ingredients in marijuana to see if novel drugs can be isolated that may aid in seizure therapy. However, because of psychoactive side effects associated with marijuana, and possible legal repercussions, it is not practical or recommended for the treatment of epilepsy (Wallace MJ et al 2003).

SEIZURE TRIGGERS

Many factors can affect the excitability of brain neurons and increase the possibility of seizure activity. In susceptible individuals, seizures can be precipitated by the presence of certain factors referred to as triggers. Seizure triggers include low blood sugar, dehydration, fatigue, lack of sleep, stress, extreme heat or cold, depression, and flashing or flickering lights. Potentially sensitive individuals can have additional triggers consisting of food and environmental sensitivities.

- **Diet.** Nutritional deficiencies and electrolyte imbalances can cause seizures.
- **Aspartame.** Aspartame has been implicated as a possible cause of seizures; its metabolite phenylalanine can be neurotoxic at high levels, and it interferes with the production of inhibitory neurotransmitters, providing a logical mechanism for its effect. Clinical studies, however, are conflicting. In a study of people with an apparent history of seizures after exposure to aspartame, no seizures were produced under controlled conditions of aspartame exposure (Rowan AJ et al

1995). Another study of children with petit mal seizures, however, did demonstrate EEG changes (but not seizures) after oral doses of aspartame (Camfield PR et al 1992).

- **Caffeine and herbal stimulants.** Caffeine is a global stimulant; there is one reported case of a patient's seizure frequency decreasing with the elimination of caffeine from the diet, but little other evidence exists to support such a role (Kaufman KR et al 2003).
- **Environmental toxins.** Many environmental toxins, including certain pesticides and heavy metals, are known to trigger seizures. For instance, mercury and lead, which are present in drinking water and certain foods, are well known neurotoxins that are associated with seizures. Also, insecticides known as organophosphates are known to increase brain activity.
- **Stress.** Stress adversely affects neurons and induces neurotoxic damage in humans, probably through generation of free radicals. It decreases antioxidant enzyme levels and activities (Zaidi SM et al 2004). Stress often functions as a trigger for patients with seizures. The high correlation of stress, sleep deprivation, and fatigue with seizures suggests that they act through common mechanisms to worsen seizure control (Frucht MM et al 2000).

SEIZURE INTERRUPTIONS

Although auras do not occur in all individuals with seizure disorder, some individuals are aware of a change in their sensory perception (whether auditory, olfactory, sensory, visual, or gustatory, sometimes involving malaise, vertigo, or the sense of *deja vu*) that signals the onset of a seizure. Auras can last for several seconds to a few minutes before progressing to the next stage. However, sometimes auras end without evolving into a seizure. The nature of the aura varies for each individual and is dependent on the area of the brain where the seizure originates (Kotagal et al 2003). For example, a person who generally experiences partial seizures that begin in the temporal lobe (where auditory signals are processed) might hear sounds that do not exist. Other individuals might perceive odors (usually unpleasant) or experience visual aberrations.

Anecdotal reports indicate that some people have learned to interrupt their seizure process by replacing the aura-induced perception with another. In these individuals, the aura is a known signal of seizure onset. For example, if the aura is a smell or unpleasant odor, these individuals can often interrupt the seizure by immediately smelling something else (in general, something with a more pleasing smell than the aura). Some are able to take this interruption technique a step further. By simply relying on mental imagery (e.g., remembering a pleasant, positive smell), they can arrest a seizure. Some find that anger can be a positive force to interrupt a seizure. They are able to arrest their seizures by yelling at the seizures. Other individuals who have seizures with an observable onset pattern enlist a support person to shout at them or give them a quick shake when the pattern commences.

LIFESTYLE CHANGES

Lifestyle changes will also reduce the likelihood of seizure activity. Getting a good night's sleep on a regular basis is a very important component of seizure prevention. Some scientists hypothesize that one major function of REM sleep is to reduce the brain's susceptibility to epileptogenic influences (Jaseja H 2004). Stress reduction and relaxation techniques such as meditation may also aid in reducing seizures.

A variety of activities can help people deal with stress and improve the quality of sleep as well (Richard A 1995). Daily exercise is an obvious means of decreasing stress. However, individuals with epilepsy should exercise at a moderate level, focusing on relaxation and muscle tone rather than bodybuilding or strenuous, competition-level exercise. Yoga, low-impact aerobics, moderate weight lifting, dancing, jogging, biking, and swimming are also suitable activities (Ramaratnam S et al 2000).

In addition to exercise, several relaxation techniques are appropriate: progressive relaxation, autogenic training, guided imagery, hypnotherapy (Puskarich CA et al 1992; Noeker M et al 2000; Ramaratnam S et al 2001). Some involve conscious breathing. Deep, full, slow breaths can stimulate the parasympathetic nervous system and block anxiety. Relaxation techniques can facilitate accurate recognition of disease-related symptoms, leading to empowerment to handle acute crises and strengthen self-esteem (Noeker M et al 2000). Progressive muscle relaxation has been successful in reducing seizure frequency. Progressive muscle relaxation techniques are taught in a few sessions. The method is inexpensive and noninvasive. In one study in a neurology clinic (24 participants with epilepsy, 13 receiving relaxation training, 11 using quiet sitting), 11 of the 13 participants using relaxation techniques reported decreased seizure frequency; 7 of the 11 participants in the quiet group reported a decrease (Puskarich CA et al 1992).

Biofeedback, another relaxation technique, can also be helpful. When the autonomic nervous system (or the involuntary nervous system) is in a state of overarousal, the likelihood of seizure activity can increase. When overaroused, the body is in what is called a beta state. Using biofeedback, participants can learn to shift the body to an alpha state—a state of relaxation. Stress is reduced. In some cases, the ability to recognize auras is enhanced. While researchers are divided on its uses for epilepsy, some studies have shown biofeedback to be successful in reducing seizure frequency (Tozzo CA et al 1988; Andrews DJ et al 1992; Ramaratnam S et al 2001).

Acupuncture may also be helpful in seizure prevention. Two acupuncture studies have found that acupuncture at specific sites produces anticonvulsant effects by increasing inhibitory neurotransmitters and other natural substances that may prevent seizures

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Most patients with epilepsy will take AED drugs. These drugs can affect vitamin status and raise homocysteine levels. Patients taking AEDs are advised to supplement with calcium and vitamin D to help prevent AED-induced osteoporosis and to regularly monitor their homocysteine levels. If homocysteine levels are elevated, patients should take steps to reduce homocysteine by using B vitamins, including folate, vitamin B12, and vitamin B6. For more information, see the chapter Homocysteine.

Patients on a ketogenic diet are advised to take a high-potency multivitamin to ensure adequate availability of nutrients. In addition, a high intake of fiber (more than 20 g daily) is recommended to reduce fluctuations in blood sugar levels.

The following nutrients may help reduce seizure activity:

- **B vitamins**—a complete B complex, which should include at least 50 milligrams (mg) daily of all the essential B vitamins, including B1, B3, B6, and B12
- **Glutathione**—50 to 250 mg daily
- **N-acetylcysteine** (to raise glutathione levels): 600 mg daily
- **Vitamin E**—400 international units (IU) daily (with at least 200 mg of gamma tocopherol)
- **Vitamin C**—1 to 3 grams (g) daily
- **Vitamin A**—5000 IU daily
- **Omega-3 fatty acids**—2100 mg EPA and 1500 mg DHA daily

EPILEPSY SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Choline

- Do not take choline if you have primary genetic trimethylaminuria.
- Choline can cause fishy body odor, excessive perspiration, hypotension (low blood pressure), depression, and gastrointestinal symptoms such as nausea and diarrhea.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Folic Acid

- Consult your doctor before taking folic acid if you have a vitamin B12 deficiency.
- Daily doses of more than 1 milligram of folic acid can precipitate or exacerbate the neurological damage caused by a vitamin B12 deficiency.

NAC

- NAC clearance is reduced in people who have chronic liver disease.
- Do not take NAC if you have a history of kidney stones (particularly cystine stones).
- NAC can produce a false-positive result in the nitroprusside test for ketone bodies used to detect diabetes.
- Consult your doctor before taking NAC if you have a history of peptic ulcer disease. Mucolytic agents may disrupt the gastric mucosal barrier.
- NAC can cause headache (especially when used along with nitrates) and gastrointestinal symptoms such as nausea and diarrhea.

Niacin (nicotinic acid)

- Do not take high doses of nicotinic acid (1.5 to 5 grams daily or more) if you have liver dysfunction, an unexplained elevation in your serum aminotransferase (transaminase) level, active peptic ulcer disease, arterial bleeding, or if you consume large amounts of alcohol.
- Consult your doctor before taking high doses of nicotinic acid if you have a history of jaundice, peptic ulcer disease, gastritis, disease of the liver or bile ducts, gout, kidney dysfunction, or cardiovascular disease (especially acute myocardial infarction or unstable angina).
- Consult your doctor before taking high doses of nicotinic acid if you have diabetes. High doses of nicotinic acid can negatively affect glucose tolerance. Monitor your serum glucose level frequently if you take nicotinic acid and have diabetes.
- Have your doctor monitor your serum aminotransferase level if you take high-doses of nicotinic acid.
- Nicotinic acid may cause flushing, principally of the face, neck, and chest. This flushing is thought to be prostaglandin-prostacyclin mediated. Histamine may also play a role in the flushing.
- Nicotinic acid can cause dizziness, palpitations, rapid heartbeat, shortness of breath, sweating, chills, insomnia, nausea, vomiting, abdominal pain, and muscle pain.
- High doses of nicotinic acid can cause blurred vision, macular edema, toxic amblyopia, and cystic maculopathy.

PABA (Para-aminobenzoic Acid)

- Do not take PABA if you are taking sulfonamides or have a kidney disease.
- PABA can cause anorexia, nausea, vomiting, fever, and rash.

Vitamin A

- Do not take vitamin A if you have hypervitaminosis A.
- Do not take vitamin A if you take retinoids or retinoid analogues (such as acitretin, all-trans-retinoic acid, bexarotene, etretinate, and isotretinoin). Vitamin A can add to the toxicity of these drugs.
- Do not take large amounts of vitamin A. Taking large amounts of vitamin A may cause acute or chronic toxicity. Early signs and symptoms of chronic toxicity include dry, rough skin; cracked lips; sparse, coarse hair; and loss of hair from the eyebrows. Later signs and symptoms of toxicity include irritability, headache, pseudotumor cerebri (benign intracranial hypertension), elevated serum liver enzymes, reversible noncirrhotic portal high blood pressure, fibrosis and cirrhosis of the liver, and death from liver failure.

Vitamin B1 (Thiamin)

- Consult your doctor before taking vitamin B1 for a thiamin deficiency, lactic acidosis secondary to thiamin deficiency, Wernicke-Korsakoff syndrome, Wernicke's encephalopathy, or Korsakoff's psychosis.

Vitamin B2 (riboflavin)

- High doses of vitamin B2 (riboflavin) may interfere with the Abbott TDx drugs-of-abuse assay.
- Riboflavin absorption is increased in hypothyroidism and decreased in hyperthyroidism.
- If you are taking nucleoside reverse-transcriptase inhibitors, even a mild riboflavin deficiency can increase your risk of lactic acidosis.

Vitamin B6

- Individuals who are being treated with levodopa without taking carbidopa at the same time should avoid doses of 5 milligrams or greater daily of vitamin B6.

Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron

overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

For more information see the Safety Appendix

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