

CONTROLLING

Science Replaces Superstition



A 19th century French engraving depicts a man having an epileptic seizure. Taken from the French, the term for this type of seizure, "grand mal," translates as either great evil or great sickness. (Reproduction courtesy of the National Library of Medicine)

The sight of someone having a severe epileptic seizure is hard to forget. The person suddenly cries out, loses consciousness, falls to the ground, and foams at the mouth. Arms and legs jerk convulsively for several minutes.

EPILEPSY

by Margie Patlak

It's no wonder such high drama has inspired supernatural interpretations of epilepsy in the past. During ancient times, most Greeks thought seizures were brief visits from the gods and called epilepsy "the sacred disease." During the Renaissance, in contrast, many people believed demons were behind seizures, and those with epilepsy were burned to death as sorcerers, according to Richard Restak, M.D., author of *The Brain*.

Today science has replaced superstition, and we realize that epilepsy is simply a common neurological disorder that can be diagnosed and treated with devices and drugs regulated by the Food and Drug Administration.

One out of every hundred people in this country has epilepsy. Their seizures stem from overly active nerve cells (neurons) in the brain. The strong and rapid bursts of electrical signals emitted from these hyperactive neurons temporarily disrupt normal functioning, much as a lightning storm can disrupt electrical power in a neighborhood.

The hallmark of epilepsy is recurring seizures—sometimes as many as several hundred a day—under normal circumstances. Anyone can develop a seizure if given the right bodily insult, such as poisoning or a lack of sugar in the brain brought on by diabetes. But in people with epilepsy, seizures can be triggered by something as minor as lack of sleep or the flickering of a light.

What causes epilepsy in all cases is not known. In some people it results from brain damage from head injuries, brain tumors, lead poisoning, meningitis, encephalitis, or measles. Lack of oxygen to the fetus during pregnancy, labor or delivery may cause epilepsy to develop during childhood. Brain damage incurred by a stroke is a common cause of epilepsy in people over 65.

Epilepsy can first appear at any age, although three-fourths of all cases surface during childhood. Epilepsy may run in families, but a genetic predisposition alone probably cannot cause most forms of the disorder; usually other factors, such as a head injury, must also be present.

Types of Seizures

There are more than 20 different types of epileptic seizures, ranging from the dramatic "grand mal" seizure described at the beginning of this article to the slight few-seconds loss of consciousness (known as an absence seizure) that often goes unnoticed. A person with epilepsy can have more than one type of seizure. Accurate diagnosis of the specific types of seizures is critical to determining appropriate therapy.

The kind of seizure depends on where in the brain the electrical signaling has gone awry, and how far that "brainstorm" has spread. If only the portion of the brain controlling movement of a limb is involved, that limb may tremble or jerk uncontrollably. If the affected brain area spreads, more of the body may begin to move erratically.

If the brain section governing hearing or vision is involved, the person may experience auditory or visual hallucinations. Sometimes the emotional centers of the brain are the hardest hit during a seizure and a person starts to cry for no apparent reason, or becomes angry or afraid. These seizures are termed partial because only part of the brain is involved.

Many people mistake a person undergoing a partial seizure as drunk or mentally ill. A complex partial seizure, for example, may cause the person to be dazed, unresponsive and clumsy, and to mumble, pick at clothing, or make chewing movements.

In contrast, during a generalized seizure such as a grand mal seizure (also known as a generalized tonic clonic seizure), the whole brain is suddenly swamped with extra electrical energy so the entire body undergoes convulsions and the person loses consciousness. Another type of generalized seizure called atonic causes abrupt loss of muscle tone, and the person falls to the ground.

Sometimes people, particularly those with complex partial seizures, experience a distinctive warning sign before a seizure, called an aura. The aura is itself a form of partial seizure, but one in which the patient retains awareness. It may be a peculiar odor, "butterflies" in the stomach, or a

sound. One man with epilepsy, an ardent racetrack gambler, always hears the roar of a crowd followed by the name of a favorite racehorse just before falling unconscious. Another person hears rock music.

Although the average individual seizure doesn't appear to have any lasting effects, repeated seizures may be associated with damage such as memory loss. "There's growing evidence that seizures are not good for the brain," says Roger J. Porter, M.D., deputy director of the National Institute of Neurological Disorders and Stroke in Bethesda, Md.

A person may also be injured in a seizure-induced fall. Rarely, a person who has had a convulsive seizure may need resuscitation if breathing does not resume automatically.

Although seizures rarely cause death, they can be life-threatening if they occur in hazardous situations, such as while driving or swimming. Most cases of death from epilepsy stem from a series of seizures in a short span of time, or a seizure that lasts longer than a half hour. Both conditions can deprive the brain of oxygen or cause heart or kidney failure. People experiencing such seizures should receive immediate hospital care.

The diagnosis of epilepsy, clarification of the type of seizures, and determination of possible causes are based on laboratory tests (see accompanying article) and a detailed medical history.

Drug Treatment

Drugs, surgery, a special diet, or a combination of these treatments is used to prevent seizures. Drug therapy alone can control seizures in about three-quarters of all people with epilepsy.

FDA has approved 16 drugs to treat epilepsy. The most commonly prescribed epilepsy drugs are carbamazepine (Tegretol), clonazepam (Clonopin), phenytoin (Dilantin), valproic acid (Depakene or Depakote), phenobarbital, primidone (Mysoline), and ethosuximide (Zarontin). Seizures can usually be controlled with one drug, although, rarely, patients may have to take more than one.

Researchers have yet to pinpoint exactly



These clips from a videotape show a grand mal seizure. The young woman appears normal in the upper left picture, accompanied by an EEG. As the seizure visibly begins (upper right), the patient grimaces and cries. This is followed by vigorous limb movements and jerking (lower left). Moments later (lower right), the patient is unconscious. (Illustration courtesy National Institute of Neurological Disorders and Stroke)

how most epilepsy drugs prevent seizures. Some epilepsy drugs appear to prevent seizures by boosting the amount or actions of certain brain compounds, called neurotransmitters, that inhibit the transfer of electrical impulses from neuron to neuron. Others may influence the passage of electrically charged atoms (ions) through the neuron membrane. These ions trigger the firing of neurons.

Many epilepsy drugs cause unwanted side effects, such as drowsiness, confusion, clumsiness, nausea, increased appetite, and behavioral or learning problems. These side effects can often be relieved by adjusting the dosage or by switching to a different drug.

To find the appropriate dose of medication, doctors usually take frequent blood samples to measure the amount of drug circulating in the patient's bloodstream. The blood levels are monitored at various drug dosages until the dose that best controls seizures with the fewest side effects is determined. Monitoring can take from a week to several months to establish the

optimum dose of the appropriate medicine for a given patient. Children and pregnant women need to continue to have their dosages adjusted.

Pregnancy Risk

Women taking epilepsy medication during pregnancy have about two to three times the standard risk of bearing a child with birth defects. Nevertheless, at least 90 percent of women who take epilepsy drugs during pregnancy give birth to normal, healthy infants. A seizure during pregnancy carries its own risks. The fetus may be deprived of oxygen due to the mother's impaired breathing during a seizure, for example, or both mother and child may be injured from a seizure-induced fall. Therefore, most doctors advise pregnant women with epilepsy to continue taking their medication unless it is likely that a woman will be seizure-free without it.

Many epilepsy drugs are excreted in breast milk, but usually in such small amounts that they are unlikely to affect the

infant. Most physicians recommend that women with epilepsy breast-feed their newborns, although they may suggest alternating breast- and bottle-feeding to lower the infant's exposure to medication.

Drug Interactions

Several drugs interact with some kinds of epilepsy medicine, lessening or intensifying the effects of one or the other drug. To avoid such drug interactions, patients should tell their doctors about any other medications they are taking whenever a new drug is prescribed. Similarly, patients taking an epilepsy drug should check with the pharmacist about possible interactions with over-the-counter drugs they purchase. Birth control pills, the antibiotic erythromycin, some types of asthma, ulcer or heart medicines, and alcohol are known to interact with certain epilepsy drugs.

People taking epilepsy drugs should not change the dose or stop a medication without first consulting a doctor. Suddenly stopping epilepsy medicines can prompt a series of seizures that can be fatal.

Most epilepsy medicines need to be stored in a dry place because any moisture that seeps into the drugs can dramatically alter the medicine's strength. "In general, you shouldn't keep epilepsy drugs on a bathroom shelf where they might be exposed to steam from showers," says Russell Katz, M.D., deputy director of FDA's division of neuropharmacological drug products.

Epilepsy drugs are taken daily by mouth for a period of years or, for some patients, a lifetime. Recent research reveals that when epilepsy drugs are slowly withdrawn after a person has been free of seizures for a few years, most people can stay free of seizures without medication. This is especially true for children. On the other hand, people with certain forms of epilepsy, such as those that cause partial or mixed seizure types, are less likely to be seizure-free after stopping medication.

If drugs cannot control a person's seizures, a doctor may prescribe a ketogenic diet. This high-fat diet produces a chemical condition in the body called ketosis, which in some people, particularly children, prevents seizures. Most people find the ketogenic diet hard to swallow, however, because it makes them nauseous and is expensive and difficult to administer. Moreover, the diet often doesn't work, according to Porter.

Surgical Cures

When all else fails, some people with epilepsy may benefit from surgical removal of the malfunctioning brain cells that spark their seizures. To benefit from such surgery, patients' seizures must begin in one fairly small area of the brain that is not responsible for speech, language, hearing, or other major faculties and that can be detected with an imaging technique (see accompanying article).

Between a half to nearly three-quarters of patients with epilepsy who undergo such surgery are relieved of their seizures for at least five years, according to a recent consensus statement published by the National Institutes of Health. Some of these patients, however, may still require epilepsy medication to stay seizure-free. The surgery carries a less than 5 percent risk of death.

Occasionally, surgery is performed to sever the connections between the two halves of the brain to try to prevent the spread of abnormal discharges from one side of the brain to the other. Although this surgery doesn't entirely prevent sei-

Pinpointing Epilepsy

When diagnosing epilepsy, physicians first try to rule out short-term causes of seizures that may be treated directly. Tests of the patient's blood, urine, or cerebrospinal fluid, which bathes the brain, may reveal uncontrolled diabetes, poisoning, a kidney disorder, or an infection.

Doctors use the electroencephalograph to help diagnose epilepsy. This machine detects, via electrodes taped to the head, electrical charges that pass between the brain cells near the electrodes. These charges are recorded as a series of wavy lines (brain waves) in what is known as an electroencephalogram (EEG). If a person has a seizure during an EEG recording, the device may reveal special brain wave patterns that help the doctor decide whether a person has epilepsy and what type it is. Some forms of epilepsy are associated with specific EEG patterns that can be seen between seizures. An EEG recording session may last as little as 35 minutes or as long as 24 hours.

Some clinics have small TV cameras set up in the EEG test area to film the person's actions during the test. Review of the film together with the EEG results may give added clues to the kind of seizure occurring. Patients may also be given a portable EEG device that records their brain waves continuously for a day while they are in their normal environment.

To induce a seizure during an EEG recording, patients may be asked to breathe deeply during the session, limit their sleep the night before, or to fall asleep during the session. (Some types of seizures are more likely to occur with a lack of sleep, whereas others occur more often during sleep.) Patients may also be exposed to flashing lights or other images or sounds that can prompt a seizure. Electroencephalography is a painless, safe procedure.

A device similar to the EEG, called the magnetoencephalograph is being used experimentally. This device records the magnetic signals that accompany the electrical discharges of neurons. A recording from this device resembles that of an EEG, but a magnetoencephalograph can detect seizure activity from deeper in the brain than is possible with the standard EEG.

Sometimes computerized tomography (CT) and magnetic resonance imaging (MRI) are used to provide pictures of the brain that may reveal tumors, cysts, or excess fluid. If these conditions can be treated successfully, the seizures may stop.

CT scans and MRI images are also used to detect damaged areas or scars in the brain that may be sparking seizures. Such information determines the type of epilepsy a person has and guides therapy.

PET (positron emission tomography), which is being used experimentally, can also point to the origin of epilepsy by measuring sugar uptake. In the responsible brain region, sugar uptake increases during a seizure and falls below normal between seizures. ■

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zures, it does appear to lessen their severity or frequency.

The decision to have surgery depends on the frequency, type and severity of seizures, possible brain damage or injury from frequent seizures, and the effect seizures have on quality of life, according to the NIH consensus statement. Drug therapy must be tried before surgery is considered.

Scientific knowledge about epilepsy has banished the demons and ancient stigmas surrounding the disease. Modern drugs, diet or surgery have made possible normal

lives, free from frequent seizures, for most people with epilepsy. ■

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For more information on epilepsy, contact:

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