Surgery for Difficult-to-Treat

EPILEPSY

A Step-By-Step Guide for Patients and Families

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The content of this book is meant only as a guideline. The views expressed may not reflect those of your health care providers. Please discuss them with your neurology team to obtain their best clinical judgment. Consult complete prescribing information before administering any of the drugs discussed.

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INTRODUCTION

Most epileptic seizures can be managed with a single medication, regular monitoring by a health care provider, and periodic testing—including blood tests, magnetic resonance imaging (MRI), and electroencephalograms (EEGs), which detect electrical activity in the brain. Taking medication as prescribed and avoiding known triggers such as sleep deprivation, alcohol consumption, and illicit drug use are important preventive measures. Yet these approaches, even when carefully carried out, do not always keep seizures in check. When they don’t, your doctor may ask you to consider more aggressive treatment that might involve stronger medications, usually with more side effects; a diet tailored to your needs; or even surgery. Although the main goal of this book is to help you and your loved ones understand and prepare for epilepsy surgery, the final sections describe medical and dietary options that may also help to control seizures. The book’s design highlights certain scientific articles to give readers a taste of the research that informs clinical practice.
Dedicated to our families; our patients; the doctors, nurses, nurse practitioners, physician’s assistants, personal care assistants, social workers, secretaries, therapists, psychologists, housekeepers, electroencephalogram technicians, and all of the other team members who work with us; and to those who have furthered the field of epilepsy and epilepsy surgery, including, but not limited to:

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Many people suffer from poorly controlled seizures and may be unaware of all of the treatment options that are available. There are various reasons for this, including lack of knowledge, fear, and lack of access to an epilepsy center. Other reasons include the belief that certain groups of persons, including children and the developmentally disabled, are not good candidates for more aggressive treatments, including epilepsy surgery. This may also be related to the long held belief that some forms of epilepsy, particularly the syndromes that begin in childhood, are benign, self-limiting and easily controlled. Also, early attempts at surgery did not always result in favorable outcomes.
Fortunately, this situation has changed. Recent scientific and technological advancements—coupled with the realization by experts that about 20 percent of patients with epilepsy cannot be treated successfully with medication—have renewed interest in epilepsy surgery. In even the youngest patients, surgery can help to control seizures and, by extension, improve patients’ behavior, ability to learn, and quality of life.

Epilepsy surgery should be performed only at a nationally certified Level 3 or 4 Comprehensive Epilepsy Center, by a medical team that performs many procedures each year. Pediatric epilepsy surgery should be performed by a pediatric team. Children exhibit a variety of syndromes not often seen in adults, with developmental and quality of life issues, EEGs and seizures that differ from those seen in adults.

For thousands of years, people mistakenly believed that epileptic seizures resulted from mental illness. This is not true! To address this and other misconceptions about epilepsy, we begin our discussion of surgery with a review of the fundamentals.

**What are seizures?**

Put simply, a seizure occurs when there is too much electricity in the brain, and the neurons (nerve cells) fire all at once. The brain contains millions of neurons, which send signals to control the actions of muscles, glands, and other neurons throughout the body. These signals travel through electricity created when electrolytes (substances that conduct electricity) flow in and out of the neurons. The flow of electrolytes is controlled by chemicals called “neurotransmitters.” In people who suffer from seizures, this complex system becomes overloaded. Medications used to prevent seizures act on electrolytes, neurotransmitters, or both, causing the neurons to become less excitable and less apt to fire uncontrollably. This, in turn, reduces seizures.

**What is epilepsy?**

In general, epilepsy is diagnosed when a person has two or more unprovoked seizures—in other words, seizures that are not caused by fevers, injuries, sleep deprivation, illness, or drug or alcohol use. However, epilepsy may be diagnosed after one seizure when there is an abnormal EEG.
The International League Against Epilepsy (ILAE) has proposed a new definition of epilepsy. It states that epilepsy should be considered a disease of the brain defined by any of the following conditions:

- at least two unprovoked seizures occurring more than 24 hours apart
- OR one unprovoked seizure and a risk of further seizures of about 75 percent
- OR at least two seizures in a setting of reflex epilepsies (seizures with specific triggers, such as flashing lights or certain noises)

Each year, there are 61–124 new cases of epilepsy per 100,000 people (adults and children) in developing countries and 41–50 new cases per 100,000 people in developed countries. (The difference is probably the result of a greater number of injuries causing epilepsy in developing countries.) The annual rate of new epilepsy cases is higher in children than in adults. Each year, there are 100–200 new cases per 100,000 children, as opposed to 24–53 new cases for every 100,000 adults.

Of these, 50–65 percent become seizure free with medication, but 10–20 percent will become “medically intractable,” meaning that their seizures cannot be controlled with medication. One-third of people with medically intractable seizures are surgical candidates. This amounts to more than 100,000 epilepsy surgery candidates each year.

About half of all children with epilepsy have other conditions that add to the toll of the disease. These include learning disabilities, mental retardation, developmental delays, mental and behavioral issues, attention deficit disorder, and psychosocial issues. Children whose seizures continue into adulthood are less likely to finish high school, successfully maintain long-term relationships, or live independently, even when compared to children with other chronic diseases such as asthma and diabetes.
Why consider surgery?

The importance of controlling seizures is the first and most important reason to consider surgery for epilepsy. Reducing the severity and frequency of seizures can lessen their harmful consequences. In addition, surgery can prevent continued EEG abnormalities between seizures. These abnormalities, known as “interictal spikes,” indicate excessive activity in the brain neurons that can interrupt sleep and memory and eventually contribute to permanent cognitive, behavioral, and psychosocial problems if left untreated.

Surgery also prevents “kindling” (the spread of seizure activity) by removing, disconnecting, or altering the areas of the brain involved in epilepsy. In patients with widespread seizure activity, disconnection surgeries called “corpus callosotomies” and “hemispherotomies” can prevent the spread of seizures to other areas in the brain. These surgeries are not resective (involving removal of parts of the brain), but rather cut the ties that allow different areas of the brain to signal each other.

Other reasons to consider epilepsy surgery are to decrease the need for medications over time (and thus to reduce their adverse side effects) and to reduce the risk of SUDEP (sudden unexplained death in epilepsy).
Epilepsy surgery is an established, effective treatment in children and should be considered early.

Freedom from seizures after pediatric epilepsy surgery leads to a reduced risk of psychological distress during early adulthood.
Overall, studies indicate either improvements in or no worsening of mental health after epilepsy surgery.

Most studies indicate improvement in social functioning after epilepsy surgery.
Why don't more people undergo epilepsy surgery?

The main reasons people do not consider epilepsy surgery include:

**Fear.** Patients, parents, doctors, and other health care providers resist the idea of surgery involving the brain. Patients and families may not trust their health care team’s judgment in making such a serious recommendation or may lack education about the safety of these procedures.

**Poor access.** There may be limited access to a Level 4 Comprehensive Epilepsy Center.

**Lack of knowledge.** Not all health care providers are knowledgeable about the advantages of surgery. They may not be able to explain the process and available procedures or to help families weigh the benefits and risks. There may also be concern about the possibility of morbidity (resulting illness) and mortality (resulting death) from surgery. In reality, however, the risks of morbidity and mortality are much greater from uncontrolled seizures. Because of this lack of understanding, only about 1 percent of potential surgical candidates are ever referred to an epilepsy center. The number is even lower in nonindustrialized countries.

**Resignation.** There is a tendency for people to learn to live with seizures and accept “good enough” control when they assume that improvement is not possible. Comments such as, “Oh, she only has one seizure a week,” are sometimes heard from patients’ families and caregivers who have become resigned to living with epilepsy.
Provider reluctance. A 2012 survey of neurologists found that only those who specialized in epilepsy and were affiliated with large treatment centers were comfortable referring patients for surgery.

Initially, providers’ worries about epilepsy surgery were caused by several factors:
Few facilities performed surgery.
Referrers unfamiliar with surgery refrained from discussing it as a treatment option.
Referrers were reluctant to lose patients to a major treatment center.
Surgery was considered only after epilepsy was deemed “catastrophic.”
Too many centers were reporting disappointing results.

However, the landscape has changed significantly since the 1990s, thanks to better testing and surgery techniques. Outcomes have improved, and complications have declined, increasing neurologists’ and neurosurgeons’ confidence in the potential benefits of epilepsy surgery.

In addition, a deeper understanding of the natural history of epilepsy supports consideration of surgery as an early treatment option instead of waiting for the discovery of new medications to provide a cure. We now know that surgery is a safe and viable means of preventing the deterioration and associated complications of intractable epilepsy.

Finally, attitudes toward desirable outcomes of surgery have also changed. The goal is no longer to completely eliminate seizures, but rather to improve patients’ quality of life by reducing the number and severity of seizures. This paradigm shift supports referral for surgery earlier in the course of the illness, even before trying every available medication.

**Why should we consider epilepsy surgery sooner rather than later?**

There are several strong reasons to consider epilepsy surgery early in the disease course:

- The adverse psychosocial effects of epilepsy may be eased if a patient becomes free of seizures.
- Because antiepileptic medications can cause adverse behavioral and cognitive side effects, the less time a child is required to take them, and the fewer medications needed for seizure control, the better. Even if seizures are successfully controlled with medication, frequent interictal spikes may still cause permanent neuronal changes that may not show up on MRI.
- Getting surgery sooner instead of later can reduce the risk of SUDEP.
- After two antiepileptic medications have failed to control a patient’s seizures, each subsequent medication is less likely to work. One study showed that only 3 percent of patients become seizure free on a multi-drug treatment regimen.
- Younger patients may recover from surgery more easily than older patients.
Research shows that a young brain, compared to an adult brain, has a greater potential for recovery after brain injuries such as surgery, strokes, or malformations. Younger brains also have a greater capacity to reorganize neurological functioning. The potential for significant recovery is greatest in patients who are between the ages of 3 and 7 years, when synapses and dendrites (parts of the neurons) are most dense and the brain is most “plastic.”

Surgery performed during this period may hasten recovery and cause milder postoperative impairment. Studies have shown that the shorter the duration of epilepsy before surgery, the greater the gain in functioning afterward.

What is epilepsy surgery?

There are several different types of epilepsy surgery. One involves removing the portions of the brain that cause excessive electrical stimulation. Another disables those portions of the brain, and another disconnects the parts of the brain that cause seizures to spread. Other options include the vagus nerve stimulator (VNS), an implanted device designed to prevent seizures by sending mild electrical pulses to the brain through the vagus nerve, and deep-brain stimulation (DBS) and resective neurostimulation (RNS, or NeuroPace), all three of which involve implanted sensors called “electrodes.” Another option is laser ablation (tissue removal), most often used in cases of mesial temporal sclerosis, when one temporal lobe is shrunken and malfunctioning.

Who is a candidate for epilepsy surgery?

Surgery may be an option for patients who have not achieved complete seizure control after trying two appropriate antiepileptic medications at the correct doses. According to a more specific definition of intractable epilepsy, surgery should be considered after the failure of two appropriate first-line antiepileptic medications, with failure defined as the patient experiencing an average of more than one seizure per month for 18 months without having three consecutive, seizure-free months during this time period. When these conditions are present, the chance of becoming seizure free is so remote that other options, including surgery, should be considered sooner rather than later.

Before considering epilepsy surgery, it is important to review all medication options with the primary health care provider. The discussion should cover new medications reserved for difficult-to-control seizures, as well as medications with potentially intolerable side effects.
How long has surgery been used as a means to control seizures?

The first modern epilepsy surgery was done in 19th-century England on a man who experienced intractable seizures as a result of a tumor. The second wave of epilepsy surgery started in the 1940s, after EEGs were invented. However, the procedure became discredited when “the wrong surgeons operated on the wrong patients.” Today, epilepsy surgery is safe and effective. The process involves a team approach to selecting patients carefully, choosing the correct battery of tests, and maintaining close oversight and follow-up, with systematic evaluation of outcomes. Recent improvements in technology have led to better outcomes after surgery.

What are the goals of surgery?

The clinical goals of surgery are to control seizures, lessen the burden of medications, lower the risk of SUDEP, and prevent the cognitive decline that results from continued seizures. With the reduction in seizures comes improvement in quality of life, including better academic performance, increased socialization, and more success in maintaining long-term relationships.

How can we tell if a person might benefit from epilepsy surgery?

Assessing the potential benefit of surgery depends, first and foremost, on confirming that the events a patient is experiencing are indeed epileptic seizures. This is done with video EEG monitoring to capture the events and rule out other diagnoses such as reflux, tics, movement disorders, fainting (also called “syncope” or “vasovagal events”), cardiac events, and pseudoseizures (those related to psychological stress rather than epilepsy).

Next, the cause of the seizures must be determined to predict the appropriateness of surgery compared to other treatments. For example, seizures can be caused by illnesses (such as fever, dehydration, or kidney failure) or by abnormalities in the brain (such as tumors, blood vessel or cortex [gray matter] abnormalities, neurocutaneous syndromes [conditions causing damage to the neurons and on skin], or strokes). Genetic syndromes may also be at play, but the presence of a genetic syndrome does not mean a person with epilepsy cannot have surgery.
What is the process leading to epilepsy surgery?

The health care provider will order a series of tests (in addition to taking a full medical history and performing a neurological examination) when a person first presents with seizures. These tests are usually repeated at intervals, especially when surgery is being considered.

The most important test is an EEG, which involves placing electrodes on the scalp at regular intervals to obtain a good approximation of the area of the brain producing the seizures. The EEG looks at the electrical signals in the brain, detecting abnormalities that cause or increase a person’s chances of having seizures. The EEG tracing is a read-out of lines tracking the signals produced by electrical discharges of neurons (sometimes called “brain waves”). A sharp spike or series of spikes may indicate the area where a seizure starts (also called the “focus”). If a specific point is involved consistently at the start of a seizure, that area may be the focus.

A routine EEG is usually performed for about an hour. In preparation for the test, the person may be prevented from sleeping. Because it is important to check the brain waves while a person is asleep and awake, a longer, ambulatory EEG may be performed for up to 96 hours, during which the person wears the EEG device while going about his or her daily activities. In some settings, this ambulatory EEG can also be videotaped.
The video EEG (considered the gold standard) is a longer test performed in the hospital while the person is being videotaped. The video EEG is typically performed after routine and 24-hour EEGs have been conducted in the outpatient setting. It allows events to be captured on video and correlated with changes that appear on the EEG tracing. This test is especially useful for distinguishing between actual seizures and events that look like seizures but are not (such as reflux, tics, or pseudo seizures). A person’s dose of antiseizure medications may be decreased during the EEG to ensure that seizures occur and are captured. For reasons of safety, the test takes place in the hospital.

![EEG showing interictal spiking leading to a seizure.](image-url)
A child undergoes a video EEG in a hospital.

In addition to identifying actual seizures, the EEG and video EEG measure the speed of a person’s brain waves and the interictal spikes (during both sleeping and waking periods) to help determine the long-term prognosis and whether the abnormalities may be affecting functioning, sleep, and cognition.
What is the difference between a seizure and a spike?

The difference between seizures and spikes may be understood through the following analogy: Think of a man standing in a forest on a bed of dry leaves, lighting matches and dropping them to the ground. Each match that lights is like a spark of electricity—a spike, or abnormality, on the EEG. If the match is dropped and goes out before it reaches and ignites the dried leaves, there is no seizure. If, on the other hand, that lit match drops and ignites the leaves, the whole forest catches fire in a split second. We liken that sudden forest fire to a seizure—a clinical event that we can see or feel. The goal of using antiepileptic medications is to dampen the bed of dry leaves so that the fire does not catch and spread as easily. The medications strengthen the neurons in the brain, making them less likely to become excitable and thus less susceptible to a seizure.

Once it has been determined that the events occurring are actually seizures, attention shifts to pinpointing the seizure type and determining the treatment plan and prognosis. At the same time, the search for causation continues. Seizures are broadly divided into two types: those that involve impaired consciousness and those that do not. EEG findings and the way the seizures look (also called the “semiology”) help to determine whether the seizures are focal (arising in one distinct part of the brain) or generalized.

Focal (or partial) seizures can affect a small area of the brain, an entire lobe, several lobes, or the entire hemisphere. Because different areas of the brain control different functions, seizures present clinically according to where they arise. The type of seizure and the progression of symptoms give us clues to where the seizures start. Sometimes, seizures begin focally and later become generalized, meaning that, eventually, the whole brain “lights up” at once. There are many types of generalized seizures, including:

- **Generalized tonic-clonic seizures.** Alternating stiffness and shaking with loss of consciousness; may be missed by caregivers when they occur briefly or at night
- **Atonic, or astatic, seizures.** Loss of tone or “drop attacks,” often with head drops or falls
- **Absence seizures.** Brief stares, often with eye deviation or blinking and brief alteration of consciousness
- **Atypical absence seizures.** Longer stares with changes in tone and a less-abrupt onset and cessation
- **Myoclonic jerks.** Rapid muscle contractions that are brief and repetitive
- **Tonic seizures.** Sustained extension of one or more extremities
- **Spasms.** Brief head drops or nods with arms up
The ILAE classification scheme for seizures is partially based on these descriptions.

Searching for the cause of seizures involves neuroimaging studies called computed tomography (CT) scans and MRIs. CT scans are often performed when a person presents in the hospital emergency room with a first-time seizure. They are used to quickly rule out brain bleeding or a tumor as the cause. If the patient appears normal and has a normal physical exam, a CT scan may be deferred in favor of an MRI so as not to expose the person to unnecessary radiation. MRIs, through the use of magnetic fields, provide a more extensive picture than a CT and pick up subtler abnormalities.

Metabolic and genetic studies also may be conducted to find the cause of seizures and determine whether epilepsy will respond to medications, surgery, or neither. People who have epilepsy resulting from certain neurodegenerative processes (conditions that damage the brain neurons), including leukodystrophies, metabolic disorders, genetic disorders such as Rett syndrome, and ion-channel disorders (“channelopathies”) such as Dravet syndrome, are less likely to achieve freedom from seizures with either medication or surgery. Other syndromes such as benign rolandic epilepsy and childhood absence epilepsy are age-limited and, with time, may resolve on their own.

Which syndromes and structural abnormalities respond well to surgery?

Fortunately, many syndromes and structural abnormalities do respond well to surgical intervention and, in some cases, respond better to surgery than to medication. These include some of the neurocutaneous syndromes, particularly tuberous sclerosis and Sturge-Weber syndrome. Rasmussen’s syndrome is an infection-related process that also responds well to epilepsy surgery. Following are descriptions of some of the forms of epilepsy that respond best to surgical intervention.
**Tuberous sclerosis (TS).** This is a genetic neurocutaneous disorder that affects many organ systems, most notably the brain, skin, kidneys, lungs, and heart. It occurs in about 1 in 6,000 live births, and about 1 in 9,700 people are carriers of one of the two responsible genes: TSC1 and TSC2. However, about 22 percent of cases occur in the absence of these genes. A telltale characteristic of TS is the presence of skin damage, including discoloration and bumps such as nail bed fibromas (benign tumors), shagreen patches (areas of leathery, dimpled skin), ashleaf spots (white patches), and confetti spots (clusters of small discolored spots). In addition, benign tumors or tumor-like growths may occur in the heart (“rhabdomyomas”), kidneys and lungs (“angiomyolipomas”), brain (“hamartomas,” “subependymal tubers,” and “giant-cell astrocytomas”), and retina.

Epilepsy associated with TS is extremely difficult to control, despite a number of medications that specifically target the related seizures. Tubers and hamartomas, in particular, give rise to very difficult-to-control seizures. Although they do not in themselves cause seizures, the tissue surrounding them is thought to be epileptogenic (capable of causing epileptic seizures). Children with a TSC2 genetic mutation and those with a high number of cortical tubers are at higher risk for seizures, including infantile spasms (a severe form of epilepsy occurring in infancy).

When considering surgery for epilepsy associated with TS, tests can help to determine which tuber or tubers may be causing the seizures. These tests are the same as those performed for any other epilepsy surgery, except for the use of a specialized positron emission tomography (PET) scan. The procedure itself also differs and may result in removal of more than one tuber, sometimes from both hemispheres of the brain. Removal of the tubers most responsible for causing seizures occasionally increases seizure activity from the remaining tubers, necessitating more than one surgery. Surgery can also be resective, removing the area of the brain from which seizures arise. RNS and VNS are also used in people with TS and epilepsy. Subependymal tubers can also lead to obstructive hydrocephalus (blockage of normal spinal fluid drainage from the brain), requiring surgical removal. More information about TS can be found at tsalliance.org.

**Mesial temporal sclerosis (MTS).** In MTS, part or all of the temporal lobe on one side is shrunk and nonfunctional, often as a result of years of seizures, which frequently begin with febrile (fever related) seizures. Evidence-based articles in the medical literature note that surgery is the preferred treatment option for seizures that are caused by MTS.
Developmental lesions. The types of developmental lesions (malformations of the brain’s cortex) listed below are among those that cause epilepsy and respond well to surgery.

- **Cortical dysplasia.** Areas of abnormally formed cortex that are frequently not seen on MRI, but rather are identified through laboratory pathology exams after the surgery has been performed.

- **Heterotopia.** The presence of cortex tissue abnormally positioned in the white matter of the brain or near the ventricles, which are the fluid-containing areas deep within the brain.

- **Polymicrogyria.** Gyri are ridges found in the brain’s gray matter. Polymicrogyria occurs before birth during early brain development and results in many small gyri. When this abnormality is widespread, there may be one area or several small areas that cause seizures.

Tumors. Many tumors that have the potential to cause epilepsy can be mitigated by surgery. These include:

- **Low-grade gliomas.** Usually benign tumors that arise from the brain or spinal cord.

- **Gangliogioma.** Tumors that arise from the ganglion cells in the brain or spinal cord.

- **Dysembryoplastic neuroepithelial tumors.** Usually benign tumors that arise from the cortex of the brain.

- **Hypothalamic hamartomas.** Abnormal collections of cells that attach to the hypothalamus and cause gelastic (laughing) seizures.

Vascular lesions. Surgery may be appropriate in the presence of the following vascular lesions:

- **Arteriovenous malformations.** Abnormal connections between arteries and veins in the brain that rupture, causing bleeding.

- **Cavernous malformations.** Lesions made up of abnormally formed small blood vessels that look like mulberries and may bleed.

- **Angiomatosis from Sturge-Weber syndrome.** A congenital syndrome characterized by abnormal blood vessel growth in the brain that presents with a distinctive facial birthmark called a “port wine stain.”
Injury-related and infectious lesions. Epilepsy caused as a result of injury or infections, such as those listed below, also may be treated surgically.

- **Gliosis.** Scar tissue from a stroke or trauma
- **Granuloma.** Small areas of inflammation resulting from infection
- **Parasitic cysts.** Brain cysts produced by neurocysticercosis, a disease resulting from the accidental ingestion of the eggs of pork tapeworms
- **Rasmussen’s syndrome.** A rare inflammatory autoimmune disease that typically damages one hemisphere of the brain

Focal and partial epilepsies such as those listed above are not the only seizure types for which surgery may be considered. People with atonic or astatic seizures (drop attacks or lack of tone), focal infantile spasms, intractable absence seizures, or generalized seizures associated with apnea may also be considered for surgery.
How does the team confirm the appropriateness of epilepsy surgery as a treatment for a given patient?

Stepwise analysis of the appropriateness of surgery begins with confirmation of the cause of seizures and of whether they are truly intractable (see page 14). The treatment team will address the following key questions:

- Have the appropriate medications been used for the appropriate period of time, in the appropriate combinations, with adequate dosing and therapeutic blood levels (when indicated)?
- Have all therapeutic options (including dietary) been considered and, when appropriate, tried without success?
• Is there a chance of a timely remission (as with electrical status epilepticus in sleep, a rare form of epilepsy) that will not result in long-term learning disabilities?

The team also will consider and discuss with you individual factors to determine whether surgery is the right choice for you and your family. These factors include:

• Risks of anesthesia
• Risks of surgery failure (no improvement in seizure control)
• Risks of harm (such as bleeding, memory impairment, infection, and damage to language or motor skills)
• Time-consuming tests that must be performed leading up to surgery
• Psychological stress to the patient and family
• Difficulty of enduring intentional seizing over the course of at least 1 week in the hospital while the team gathers information to determine the area of seizure onset in the brain
• Brain mapping (electrode testing to locate the areas of the brain that control motor function, sensation, and language and therefore should be protected during surgery)
• Need for about 1 week of recovery time in the hospital after resective surgery
• Stress of hospitalization to the patient, parents, siblings, and other family members
• Loss of income during hospitalization and recovery
• Risk of depression from “forced normalization” (adapting to life without chronic illness)
• Pain
• Recovery support at home
• Need for continued medication after surgery
• Fatigue after surgery
• Months-long waiting period before knowing the long-term outcome of the surgery

We describe the surgical process as a marathon and not as a sprint.
Once surgery is deemed appropriate, what are the next steps?

First, the area of the brain from which the seizures arise (the epileptogenic zone) must be clearly defined. Different methods are used on a case-by-case basis, and, often, the work-up to determine whether surgery is the right approach has already answered questions related to the type of seizures, the location(s) where the seizures begin, and the involvement of crucial areas of the brain, including those affecting speech, motor, and memory abilities.

The following tests may be repeated before surgery:

**Video EEG.** This test of electrical activity in the brain is repeated as the patient is weaned off some or all antiepileptic medications. The goal is to capture typical seizures and their onset. Depending on the type of surgery being considered, the team tries to determine the source of the seizure with respect to hemisphere (lateralization) or lobe (localization).

**MRI.** MRI provides pictures of the brain showing three-dimensional detail in different planes. The sides are reversed, so that the section shown on the right is actually the left side of the brain.

MRI studies show the structure of the brain. A) Image of a normal brain; B) Abnormal brain image showing tubers in tuberous sclerosis (white areas).

MRI should be performed to certain specifications at a dedicated epilepsy center and read by neuroradiologists familiar with epilepsy surgery. Children or patients with developmental disabilities may need to be sedated to obtain optimal results from MRI. In children, a pediatric anesthesiologist should perform the sedation. The epilepsy team orders all tests based on the indication.
Magnetic resonance spectroscopy (MRS) may be performed along with MRI. It noninvasively measures chemical substances such as N-acetyl-aspartate (NAA), choline, creatine, and lactic acid, which may be abnormal within the epileptogenic zone. This test is performed when there is suspicion of a tumor and can help to determine the epileptogenic parameters (for example, the ratio of NAA to choline may be reduced in that area of the brain).²⁰
PET. PET scans look at the metabolism of the brain. Often, the seizure area shows hypometabolism (metabolism slower than in other parts of the brain). PET scans are particularly useful in people whose MRIs are normal. In such cases, the brain structure may be fine, but there still may be metabolic abnormalities at the cellular level.\(^{21}\) From the patient’s standpoint, this procedure is similar to a CT scan.

![PET scan image](image)

The lighter areas (blue) of this PET scan show hypometabolism.
Other tests. Other tests are considered once a patient is clearly a surgical candidate. These include single-photon emission computed tomography (SPECT) scans, functional MRIs (fMRIs), neuropsychological testing, Wada tests, visual field testing, and magnetoencephalography (MEG) scans.

• **SPECT.** This functional imaging study shows areas of the brain with abnormal perfusion (blood flow). This helps in localizing brain abnormalities, particularly when the MRI is normal. The test is usually performed at the time of the video EEG and involves an injection of an isotope (through an IV line) and a trip to the hospital Nuclear Medicine department either at the time of the seizure or between seizures.

SPECT is a nuclear imaging test that uses a radioactive substance to show the areas of the brain that are more or less active.

• **Neuropsychological testing.** This involves an extensive battery of IQ and memory tests performed by a neuropsychologist to help localize areas of impaired functioning in the brain. It also provides a baseline for cognitive functioning and can help to determine related risks from surgery. If the patient is severely impaired, using an abbreviated version of these tests or relying on recent testing done by the school may be sufficient.
• **fMRI.** This test is performed under research protocols and may not be covered by insurance. Its purpose is to locate the portions of the brain that affect language, motor, and sensory functioning to evaluate whether deficits in these areas will be likely after surgery.

• **Wada test.** This test (named for the doctor who first performed it) involves injecting an anesthetic into the carotid artery to inactivate one side of the brain at a time while testing is done to identify which hemisphere controls speech and memory. Because it is an invasive procedure, it is only performed in older children and adults.

• **Visual field test.** This test is important if the area to be resected is near the part of the brain that controls vision. Frequently, patients with epilepsy already have visual field defects (loss of part of the usual field of vision) that they do not even recognize. When considering certain types of surgery (especially mesial temporal lobe and occipital lobe surgery), patients should be told of the risk for new or further visual field defects. In most cases, such defects are not even discernible by the patient, although a few activities of daily living such as driving a car might be affected.
What are the options for surgery, and how does the surgical team decide which route to take?

When the tests have all been done, and the team determines that surgery is, in fact, a viable treatment, the next step is to arrange a meeting with the patient, family, epileptologists, neurosurgeons, advanced practice nurses, neuropsychologists, nurse coordinators, pediatricians, primary care doctors, intensivists, and social workers who will all be involved in patient care.

At this time, the team looks for congruence (whether all tests point to the same area of the brain as the epileptogenic zone). The team also seeks consensus on whether that area can be safely removed without causing impairments. The prognosis is usually better when there is only one problem zone, and removing that area is highly likely to eliminate the seizures. Patients with a structural lesion such as a tumor, cavernous malformation or cortical malformation, encephalomalacia (abnormal brain tissue after injury), cortical dysplasia, or other abnormality detected through MRI are the most likely to become seizure free. Possible scenarios from test results are as follows (see flow chart on page 34):

1. If there is a structural lesion that corresponds to the abnormality on the MRI, a one-stage surgery, with resection of the area of abnormality, may be performed. If the boundaries are not clear, electrocorticography—a type of EEG in which recording is done directly on the brain, in the operating room—may be done.

2. EEG recordings may be placed directly on the brain to assist the epilepsy team in determining exactly where the seizures begin and where they spread. These subdural EEG electrodes are placed directly on the surface of the brain (using grid or strip electrodes) or deep into the brain, a technique called stereo EEG (SEEG). In this case, SEEG depth electrodes are placed, using robot guidance, to sample both cortex and deeper structures. The robotic guidance system assists the surgeon in placing the electrodes, avoiding vascular structures. Use of the robot requires that a special CT scan be done before the surgery and allows for a shorter time in the operating room and under anesthesia. This is particularly useful when seizures are thought to arise from deeper structures of the brain. This first step assists in determining the extent of resection.
At times, brain mapping may be needed. Brain mapping enables the team to send electricity to the parts of the brain presumed to control motor function, sensation, and language. This allows the neurosurgeon to avoid resecting these areas (referred to as “eloquent cortex”).

Robot guidance system allows neurosurgeons to precisely place electrodes deep in the brain for SEEG procedures to pinpoint where seizures arise.

3. If the seizures seem to come from both hemispheres of the brain, the team may decide to place SEEG electrodes in both hemispheres of the brain. Another procedure is a corpus callosotomy, in which the connection between the two halves of the brain is severed. After this, the seizure onset may lateralize, allowing the epileptologist to pinpoint more precisely where the seizures come from. This procedure can be followed by the placement of subdural EEG electrodes directly on the brain to localize the seizure onset and is followed by resection of the epileptogenic zone (provided the seizures localize to one or more areas). The corpus callosotomy can also be used by itself to diminish the frequency of atonic seizures.
The other option is the placement of SEEG electrodes on both sides of the brain, in both hemispheres, as noted above, to determine where the seizures begin. Some centers may place strips of EEG electrodes directly on both sides of the brain, using burr holes, rather than a more extensive craniotomy. This can allow the epileptologist to see which side of the brain the seizures are coming from. This may be followed by: 1) placement of subdural EEG electrodes directly on the brain to localize the seizure onset and 2) resection of the epileptogenic zone if the seizure onset localizes to one or more discrete areas and brain mapping determines that resection can avoid eloquent cortex.

4. If it is already determined that the seizures come from a widespread area in one hemisphere and that there is no lesion or that there is a large area of abnormality, subdural electrodes are placed over that area to localize the seizure onset and determine exactly where the seizures come from. This is followed by resection of the epileptogenic zone if brain mapping determines that resection can avoid eloquent cortex.

Most cases involving MRI-detected abnormalities, regardless of whether the seizure onset zone is clearly depicted, will need a two-stage surgical procedure: first, placement of grid and strip electrodes on the brain to map the seizure activity, and, second, removal of the area(s) from which the seizures arise. Although this sounds fairly straightforward, the process is complex and requires a great deal of work and thought. And even then, things may not line up quickly or easily!

Similarly, in the remaining scenarios described above, in which the initial EEG does not clearly identify the seizure onset area, a two- or three-stage surgical process is needed to better pinpoint the seizure area and then remove it.
Surgical intervention may also be complicated if seizures occur near the functional (eloquent) cortex (the area of the brain that controls movement and language). This would require extensive brain mapping by the epilepsy team and consideration of other types of interventions such as VNS, RNS, or multiple subpial transection (see p. 48).
Once a strategy is set, how does the intervention proceed?

Deciding on a strategy for surgery is a dynamic process. As described above, initial testing often does not provide the surgical team with enough information to be certain about whether a patient’s seizures arise from the right or the left hemisphere or their exact location within a hemisphere. In such cases, an initial surgery is scheduled, sometimes to perform a corpus callosotomy (described in more detail on page 39), but more commonly to implant SEEG electrodes or bilateral strip electrodes. To do this, the neurosurgeon uses the robot guidance system to implant SEEG electrodes into both sides of the brain. Alternatively, the neurosurgeon makes burr holes in the patient’s skull and implants electrode strips between the skull and the brain on either side of the head. The electrodes capture seizures, revealing whether the area of onset is in the right or left hemisphere. Typically, these electrodes remain implanted for a week, although they may be left in for longer periods with the goal of capturing a sufficient number of seizures to definitively determine the hemisphere of onset.

Grid and strip electrodes, which are placed directly on the brain for recording.
During SEEG, neurosurgeons use a robotic guidance system (top) to reach precise locations in the brain where they place ultra-thin SEEG electrodes (bottom).

The next step occurs about 6 weeks later and involves a craniotomy, or opening of the skull, for placement of grid and strip electrodes directly on the affected hemisphere(s) of the brain, as determined by the initial surgery. The goal here is to find out exactly where the seizures begin and where they spread, thus determining how much of the brain needs to be resected and can be removed safely. The electrodes also allow for brain mapping to determine which areas should be avoided because they are too close to the functional cortex. In some cases, depth electrodes may be used. These are placed deeper into the brain in a SEEG procedure (described on page 31).

After electrodes are placed on the brain, the patient is usually admitted to the intensive care unit (ICU) and remains there for at least 1 week. During that time, medication is tapered or discontinued to provoke seizures. A schematic diagram is made of the placement of the grids and strips so the team can locate the seizure onset area(s). When enough seizures have been captured (the exact number is decided case by case), the patient may undergo brain mapping at the bedside (described in more detail on page 37).
Resective surgery occurs most commonly 1–3 weeks after grids and strips are implanted. If SEEG is done and RNS is planned, there is usually a 1-month wait to minimize the risk of infection.

During the hospitalization leading to focal resection surgery, a patient also may undergo additional tests, including CT scans performed immediately after leaving the operating room and sometimes at other times during the hospital stay. These tests allow for precise visualization of the electrode placement in preparation for brain functional mapping.

- Brain functional mapping. If a focal resection seems likely, the seizure zone must be checked to pinpoint its importance to normal functioning such as movement and language. The process for this is called brain functional mapping and involves two additional tests performed at the bedside in the ICU. The first, called somatosensory evoked potential (SSEP) recording, uses the existing EEG leads to determine where sensory (feeling) and motor (movement) areas of the brain meet. The second is brain mapping, in which electrical impulses are sent through the same electrodes to determine more precisely where sensation and motor functions are located. These impulses will cause the patient to feel a sensation or move in certain ways. The stimulation itself can result in a seizure, so rescue medications are readily available during the mapping process. Additional stimulation may also stop a seizure.
Avoiding eloquent cortex (the areas of the brain that control movement, sensation, and language) is of paramount importance throughout epilepsy surgery. The team knows the locations of these areas in a healthy brain but must remain mindful of a possible shift due to bleeding, stroke, or seizures beginning in early in childhood. Mapping the brain allows the team to avoid these areas during the resection.

Language mapping is also performed if there is any suspicion that seizures are arising from areas located near the language centers of the brain. This involves having the patient read and answer questions, identify pictures, count, or recite the alphabet. The testing is geared to the patient’s developmental level. The testers watch for interruptions in speech or difficulty answering questions. The test can be conducted at the bedside with parents present (in the case of young patients) or even during surgery with the patient awake (in older adolescents and adults).

**What other procedures and terminology are important to know before pursuing surgery?**

- **Multifocal resection.** Focal resection is not the only available type of resective epilepsy surgery. Sometimes seizures begin simultaneously in more than one area of the brain. This is called “multifocal onset.” The team may then decide to perform a multifocal resection, meaning that more than one area is removed or one area is removed and another is disconnected so seizures do not spread to or from that area. If there is more than one area of seizure onset linked by white matter fibers, it may be possible to remove more than one area at a time. Brain mapping tells the team whether this can be accomplished safely without causing functional deficits.

- **Mesial temporal lobectomy.** If a preoperative MRI shows that one temporal lobe is sclerotic (shrunken), as may occur after years of seizures, the lobe may be removed in a single procedure called a mesial temporal lobectomy, without the placement of subdural electrodes. The patient may also undergo laser ablation.

- **Hemispherotomy.** This surgery is performed when seizures involve one entire side of the brain. The procedure severs all the connections between the two hemispheres, but leaves the brain intact. In the past, the nonfunctional hemisphere was removed (hemispherectomy), but that practice led to more adverse events. Now, most centers perform only hemispherotomies. Hemispherotomies have better outcomes in terms of seizure control, but may result in weakness of one side of the body. If performed early in life, the weakness is usually minimal.
• **Corpus callosotomy.** The corpus callosum is a large bundle of nerve fibers that connects the two hemispheres of the brain, allowing certain signals (and seizures) to spread. Severing this pathway is a less invasive procedure than resection, with a more limited craniotomy requiring a smaller opening in the skull and having a quicker recovery time. Callosotomies reduce seizure frequency, and this effect is sustained over years. Specifically, this surgery is used to decrease the frequency of atonic seizures (drop attacks) in patients with generalized epilepsy.

![Corpus Callosum Diagram](image)

Corpus callosotomy diagram.

It also decreases the frequency of seizures associated with apnea. The procedure may also be the first step in localizing seizures when onset is not restricted to one hemisphere of the brain. People who have undergone a corpus callosotomy may later experience focal seizures and undergo focal resections. In children with drop attacks, the procedure should be considered at an early age. Potential side effects include weakness immediately after the surgery, which usually resolves quickly. Benefits include improved behavior and cognition.

• **Multiple subpial transection.** This procedure is performed when the area from which the seizures arise cannot be removed without causing damage. The neurosurgeon uses a special instrument to interrupt horizontal intercortical connections, while preserving the descending fibers. This procedure has largely been replaced by RNS.
Are there surgical options that do not require operating directly on the brain?

In some cases, epilepsy surgery may consist of the placement of a device or stimulator rather than operating directly on the brain. The type of device used most extensively is the VNS (vagus nerve stimulator), which has been shown in clinical trials to cut the number of seizures in half in patients. VNS was approved in the United States for treatment-resistant epilepsy in 1997 and for depression in 2005. The VNS and other implantable devices are described in more detail below.

- **VNS Therapy® system.** This system is indicated for use as adjunctive therapy to reduce the frequency of seizures in patients who have partial-onset seizures that are difficult to control with antiepileptic medications. It is also used in an off-label manner in patients with generalized seizures. Consisting of an implanted pacemaker-like generator attached to nerve stimulation electrodes (leads), the device delivers intermittent stimulation to the patient’s left vagus nerve, which sends signals to the brain.

An increase in heart rate that may correspond with a seizure sends an additional electrical impulse to stop the seizure. The surgeon implants the device and the electrodes. The procedure usually requires a 1-day or overnight stay in the hospital and is performed under general anesthesia.

The patient may be discharged with dressings in place (to be removed later either by the neurosurgery or neurology team at a post-operative visit or by the family). In most cases, the two required incisions are barely visible after healing. Initial stimulation (“turning on” the device) is done at a neurology appointment. The settings (duration and intensity) are adjusted at regular neurology visits, usually every 1–2 weeks to start. Alternatively, the latest VNS Therapy technology allows the neurology team to safely schedule the device settings to be automatically adjusted without additional office visits for programming. The battery usually lasts for years and is changed as an outpatient procedure. The most common side effects include hoarseness, shortness of breath, sore throat and coughing. Infection is the most common side effect of the procedure. Side effects typically only occur during stimulation and usually improve over time.
• **NeuroPace RNS® system.** Implantable cranially and connected to one or two leads positioned in the brain near the patient’s seizure focus, this programmable, battery-powered, microprocessor-controlled neurostimulator is designed to detect abnormal electrical activity and deliver a short series of electrical pulses to ward off seizures. Once placed, the health care team programs the device noninvasively. Additional features of the system include the ability to view the patient’s brain electrical activity in real time and to upload the corresponding record (electrocorticogram) from the RNS neurostimulator, to be stored for later review.28
• **Deep brain stimulation device.** This is an implantable pacemaker device that targets specific areas of the brain to deliver an electrical current. Currently used in movement disorders, this surgical technique also shows some promise for seizure control.
Why is pediatric surgery recommended?

The most progressive thinking in terms of the timing of epilepsy surgery is that it should be performed as soon as possible once it becomes evident that seizures are intractable. In the past, the average duration of epilepsy in patients deemed appropriate candidates for surgery was about 20 years—in other words, most patients first endured about two decades of ongoing seizures, cognitive decline, socialization issues, and medication side effects.  

Given what we know now, it is imperative to dispel outdated notions of epilepsy surgery as a “last resort.” In the hands of a skilled team, including pediatric specialists, surgery is a safe and effective procedure. Indeed, research shows that, if indicated, surgery can be performed safely in patients who are 1 year of age or even younger. This is because a child’s brain has a greater potential for recovery after a brain injury (including surgery) and significant capacity to reorganize neurological functioning. Also, early surgery can prevent damage to the opposite side of the brain if seizures are coming from one area.  

Even when seizures are successfully controlled with medication, frequent interictal spikes can cause permanent changes in the neuronal structure at a microscopic level and create a secondary epileptogenic site. Furthermore, intractable epilepsy in the immature brain significantly increases the risk of mental handicap. The harmful effects of prolonged seizures and the possible side effects of antiepileptic drugs on brain, cognitive, and psychosocial development bolster the argument for early surgery in pediatric patients. When performed in very young children (less than 2 years of age), surgery may hasten recovery and alleviate postoperative impairments. In general, the younger the child, the more quickly he or she will get out of bed, eat, walk, talk, and return to normal functioning after surgery.  

In well-selected cases, early surgery has been shown to prevent the negative long-term effects of seizures. This, in turn, enhances the behavioral, cognitive, and developmental domains of life, improving a child’s chances of staying in school, becoming employed, eventually living independently, and building healthy long-term relationships. Seizure control after surgery also lessens the long-term risk of learning disabilities and depression. Emerging data also suggest benefits of surgery in cases of catastrophic epilepsy, including those associated with genetic abnormalities and catastrophic syndromes.  

Finally, one of the biggest fears for patients and families who live with epilepsy is that of SUDEP (sudden unexplained death during an epileptic seizure). The risk of sudden death is about 20 times greater in people with epilepsy than in the general population and is even higher among those who are male, have poorly controlled epilepsy, or are developmentally delayed. The sooner the seizures are controlled, the lower the risk of death from a seizure.
What about developmentally disabled patients?

Historically, patients with developmental delays (ranging from learning disabilities to autism to cerebral palsy) have been less likely to have their epilepsy managed aggressively, much less to be referred for surgery.\(^{34}\) However, we strongly believe that seizures should be managed aggressively in these patients, including those who are wheelchair-bound, nonverbal, living in a group home, or have no chance of living what we deem a “normal” life. Indeed, the person suffering from atonic seizures who must wear a helmet or the individual who suffers apneic spells and needs oxygen for every seizure is no less a candidate for surgery than other patients with epilepsy. Yet, caregivers, providers, and families may become complacent in these situations and inured to the fact that uncontrolled seizures (no matter how often they occur) are distressing to people with developmental disabilities. Seizure control improves many aspects of life for these individuals and their families and reduces their trips to the emergency room, use of rescue medications, medication side effects, missed days of school or work, and overall medical costs.\(^{35,36}\) The table on the table below dispels more myths about the appropriateness of epilepsy surgery in people with developmental disabilities.\(^{37}\)

Common Myths About Epilepsy Surgery in the Developmentally Disabled\(^{37}\)

<table>
<thead>
<tr>
<th>Misconception</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>A normal MRI is a contraindication to surgery.</td>
<td>Other techniques often detect a single epileptogenic zone in patients with a normal MRI.</td>
</tr>
<tr>
<td>Chronic psychosis is a contraindication to surgery.</td>
<td>Such patients will still benefit if seizures are eliminated.</td>
</tr>
<tr>
<td>An IQ less than 70 is a contraindication to surgery.</td>
<td>Outcomes for these patients depend on the type of epilepsy and the type of surgery they have.</td>
</tr>
<tr>
<td>Surgery is not possible if the primary cortex is involved.</td>
<td>Essential functioning can be protected.</td>
</tr>
<tr>
<td>Multiple or diffuse lesions are a contraindication to surgery.</td>
<td>The epileptogenic zone may only involve part of the lesion area(s).</td>
</tr>
<tr>
<td>Autism is a contraindication to surgery.</td>
<td>Such patients can benefit from seizure control, and there are possible behavioral benefits from surgery.</td>
</tr>
</tbody>
</table>
What do the numbers say about the success of epilepsy surgery?

Although there are different published outcomes for different types of surgery, overall seizure-free outcomes after surgery are presented in the table below. Remember that, after a person has tried two antiepileptic medications unsuccessfully, the likelihood of multiple medications working to control seizures is only about 3%. The risk of complications resulting from epilepsy surgery is far less than the long-term risk of living a life with seizures.

Seizure-Free Rates After Epilepsy Surgery

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Seizure-Free Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemispherotomy</td>
<td>57–90%</td>
</tr>
<tr>
<td>Hemispherotomy for cortical dysplasia</td>
<td>33–69%</td>
</tr>
<tr>
<td>Temporal resection</td>
<td>58–67%</td>
</tr>
<tr>
<td>Temporal resection for hippocampal sclerosis</td>
<td>53–87%</td>
</tr>
<tr>
<td>Temporal resection for cortical dysplasia</td>
<td>50–69%</td>
</tr>
<tr>
<td>Temporal resection for tumor</td>
<td>86%</td>
</tr>
<tr>
<td>Extratemporal or multilobar resection for cortical dysplasia</td>
<td>50–55%</td>
</tr>
<tr>
<td>Extratemporal or multilobar resection for tumor</td>
<td>75%</td>
</tr>
</tbody>
</table>
In anticipating the surgery “marathon,” what practical details are important to think about?

Many patients and families wonder exactly what they will go through to get ready for surgery, as well as what will happen on the day of surgery and afterward. As described earlier, the process starts with a meeting with the full neurology team to discuss your case and test results. Any further tests that may be needed will be scheduled at this time. Depending on the institution, you and your family may have met with the neurosurgeon before this meeting.

In most cases, the team will then meet again with you, your family, and anyone else you wish to attend to discuss the test results and specific plans for surgery. This is the time to raise questions, preferably written down beforehand so that nothing is missed. The procedure(s) and their benefits and risks will be discussed. The meeting may conclude with a tour of the ICU and a brief meeting with the pediatricians and nurses who will be responsible for the patient’s care during the hospital stay. Any special needs such as feeding tubes or the use of oxygen should be explained at this time.

Most importantly, this is the time to assess whether you and your family are ready to run this marathon. Consider the following issues carefully.

- The patient will be in the hospital, for the most part in bed, for about 2 weeks.
- There must be more than one person available to stay with the patient (to avoid caretaker “burnout”).
- There is always a risk that the surgery may not work and that the patient will have at least as many seizures after the surgery as before.
- It will likely be stressful for your family to watch numerous seizures occurring during the hospitalization, despite knowing that they are necessary to map the seizure area in the brain.
- Both patient and family will be fatigued after hospital discharge.
- During recovery, the patient may need to stay home, with a caregiver, for 1 month or longer.
- The patient may feel an emotional letdown and will be at risk for depression (“forced normalization”) after surgery.
- It may take 6–12 months to realize the full outcome of surgery.
Specific questions your family should ask before surgery include:

- When is the surgery scheduled?
- At which hospital and on which floor?
- What time do we need to arrive at the hospital, and where do we go when we get there?
- What should we bring (e.g., clothes, medications, special equipment, toys, videos, favorite foods)?
- Who arranges for insurance approval?
- When do we get clearance for surgery from our primary care provider?
- How do we taper medication before admission (or do we?), and exactly what medications should be taken and when?
- What should we do if a seizure occurs during the tapering process?
- Is blood work needed?
- Should we donate blood in case it is needed during surgery?
- Who is the anesthesiologist, and when do we meet him or her?
- Whom do we tell about allergies?
- How often will we see the surgeon, the epileptologist, and other team members?
- Do we need someplace for family members to stay during the hospitalization?
- Who will take care of the patient and help our family each day?
- What emergency numbers should we have on hand in case of problems?

Questions you should ask the day before surgery include:

- **Where do we go?** Usually the operating room personnel will call the night before surgery to tell you where to go, what time to arrive, and when the patient should stop eating. Medications are usually given just before the fasting period begins or may be given at the regular time with just a sip of water. The surgery will be cancelled or postponed if instructions for eating and drinking are not followed, so it is important to pay close attention.

- **Can I walk my family member into the operating room?** Typically, the answer is yes, but every center has its own rules. If you get approval, you will be asked to wear surgical garb.

- **Will shaving the head be necessary?** Shaving the head is not necessary for SEEG or bilateral strip placement and usually not for a corpus callosotomy. For placement of grids and strips, the surgeon can tell you whether it is necessary to shave the whole head or just a small area.
These practical questions about what happens during surgery should also be asked:

- Where does my family wait?
- Who will talk to us as the day goes on?

Finally, the answers to these questions will help you know what to expect after surgery:

- Will we be in the ICU or in a ward?
- What happens immediately after surgery?
- Will the patient go immediately for a CT scan?
- Will the patient go to the recovery room, the ICU, or a ward?
- What will the patient look like?

Although there are individual variations, patients generally emerge from surgery with a dressing on the head. It will be similar to the one used during the video EEG but may have protruding wires to attach implanted electrodes to an EEG machine. A catheter will have been placed for urine and is typically removed the next day, at which time the patient uses a urinal, bedpan, or bedside commode. The patient usually stays in bed, but some surgeons allow patients to use a bedside commode instead of a bedpan for bowel movements.

The dressing is usually not changed unless there is drainage or it becomes loose. The patient usually sleeps for the rest of the first day and the first night and begins to be more alert during the second day. Eating may begin once nausea or vomiting passes and the patient is alert enough to chew and swallow. If the patient is fed via a tube, the medical team will decide when eating can resume, typically when there are bowel sounds. The patient usually has at least two IV drips for the entire ICU stay. They also may be used for taking blood for testing, which happens periodically depending on symptoms and medications.

What is the process for monitoring seizures?

A map showing the electrode placement will have been prepared and discussed with the family. Its purpose is to show the seizure onset zone or zones, as well as other areas to which the seizures quickly spread. Next comes the worst part for many patients and families: watching or experiencing seizures. The number of seizures required to determine the extent of the needed resection varies from patient to patient.
Typically, the seizures must be of the same semiology (that is, have the features of a typical seizure for the patient). The team then determines exactly how many need to be recorded. The length of the seizures may vary depending on how quickly the patient goes into status epilepticus (a long-lasting seizure that does not stop without medication). A rescue plan is put in place when the electrodes are placed. This usually entails using a rescue medication after a seizure has lasted for a certain period of time or after there has been a cluster of seizures. Antiepileptic medications are restarted after enough seizures have been recorded. These may or may not be the same medications that were used preoperatively.

**What other medications are used after electrode grids are implanted?**

Depending on the type of surgery and the center’s protocols, the patient will be on IV antibiotics and steroids to reduce infection, swelling, and inflammation. Usually one or two pain medications will be ordered depending on the level of pain and whether the patient has begun to eat and take oral medications. Pain is minimal with SEEG and usually thought to be worse with placement of bilateral strips than with placement of subdural grids and strips. It is important to keep the team aware of the patient’s pain level. The longer pain is left untreated, the harder it becomes to control. However, the patient needs to be awake and not too drowsy from pain medication. Bowel activity is closely monitored because patients on bed rest tend to become constipated.

**How will my child or loved one look?**

It is common for swelling to occur after electrode placement, and especially with grids and strips. This usually peaks within 2–3 days after surgery and is worst on the side of the implants, especially around the eye or eyelid. The patient also may be drowsier than usual or complain of pain.
What else happens after surgery?

It is important for the patient to stay awake as much as possible so the team can interact with the patient to assess the level of consciousness. Sleep deprivation also is a factor in triggering seizures to record on the EEG. Again, the more seizures occur, and the more quickly they occur, the faster the patient can go back to the operating room for the resection surgery (phase two or three). If the procedure was for SEEG, further surgery (for resection or placement of RNS or VNS) will often necessitate another hospitalization.

What can go wrong during and after surgery?

- **Anesthesia.** Anesthesia poses certain risks, including difficulty awakening from anesthesia and the possibility of something going wrong during the procedure. The risk of complications with general anesthesia is extremely low. The anesthesiologists on your surgery team should be well-versed in neurosurgery and epilepsy surgery, performing these procedures many times each year.

- **No seizures.** As odd as this may sound, patients may be seizure free while the electrodes are implanted. In this case, the electrodes are left in place for as long as is safe (depending on the team’s protocols). A decision may be made to resect based on the interictal spikes or on seizures that show up on the EEG but do not cause any movement or change in consciousness on the patient’s part. There have been times when patients have undergone placement of electrodes, monitoring has been performed, no seizures have occurred, and the electrodes have been removed without a resection. Occasionally, this alone will result in seizure freedom.

- **Brain bleeding.** Although rare, bleeding can occur in the brain after surgery. This could cause a stroke that can lead to weakness, language problems, or even cognitive or visual problems, depending on where it occurs.

- **Infection.** As with any surgery or even any cut made to our skin, there is also a risk of infection. As a safety measure, cultures are taken when the electrodes are placed and watched carefully to make sure that there are no signs of infection. Fever is another sign of infection. Infections are treated with additional IV antibiotics, which are sometimes continued after the patient is discharged. If the patient remains on antibiotics, additional blood tests will be needed in the hospital and after discharge. In extremely rare cases, a chronic bone infection can occur, requiring placement of a prosthetic skull. However, this is more of a nuisance than a danger.
- **Cerebrospinal fluid (CSF) leakage.** There is a risk of a CSF leak from the area where the electrode leads exit the scalp. Should this occur, treatment with antibiotics will be necessary. The patient will be monitored for CSF leakage daily by examining the dressing. If there is an excessive amount of leakage, the dressing may be removed and replaced, using a special type of glue to seal the leak after the area is cleaned. If the leak is small, it usually stops on its own. There is a risk of creating infection if there is excessive unwrapping and inspection of the dressings. Your team will decide the next steps, but it is not uncommon to see some leakage after placement of grids and strips.

- **Brain swelling.** There is a small risk of brain swelling, which can be managed with steroids. Rarely, a patient’s brain does not tolerate having grids and strips implanted. This unusual reaction leads to swelling and may result in the patient becoming unresponsive or appearing very sick. If this is a concern, the team will do an emergency CT scan and determine whether the grids need to be removed immediately or whether a medical treatment such as steroids will suffice. Nurses perform frequent “neuro checks” in the ICU to ensure that patients are easily responsive and to detect rare problems such as brain swelling.

- **Hydrocephalus.** Another very rare side effect that can occur with some surgeries (such as resection of hypothalamic hamartomas, multilobar resections, and hemispherotomies) is an increased risk of hydrocephalus (collection of fluid on the brain), which can be managed in a few different ways. A ventriculoperitoneal shunt or lumbar drain may be placed for a period of time to help drain the fluid.

- **Electrolyte imbalances.** With some surgeries, there is a risk of low sodium levels. This is managed by frequent checking of intake and output and replacement of electrolytes through an IV if needed. Often, just allowing the patient to eat and drink with close monitoring solves the problem. This is why the team will be checking urine output and frequently asking how much the patient has been drinking and eating.

- **Stroke.** There is an extremely low risk of stroke during surgery. Some people experience weakness afterward, including one arm or leg feeling weaker than the other. This occurs when the surgery affects the motor area (the main part of the brain that controls movement) or the supplementary motor area (which also helps to control movement). If the culprit is the supplementary motor area, the weakness should be short-lived and resolve with therapy. If the motor area is affected, recovery may take longer and may not resolve completely.
• **Transient cognitive issues.** There may be cognitive issues after surgery, including difficulty with word-finding, memory, or speech. Again, these can be associated with the supplementary motor area, in which case these issues will get better with time. If surgery affects other areas of the brain that control language, the problems still tend to improve but may require speech-language therapy.

• **Seizures after surgery.** There is a risk of seizures soon after surgery because the brain has been wired for a long time to generate seizures and will need time to calm down. Typically, your team will restart antiseizure medications before surgery, but blood levels can fluctuate. That, combined with the brain being swollen after surgery, places the patient at immediate risk for a seizure. We warn families that these early postoperative seizures are to be expected and are not necessarily a sign that the surgery did not work.

### What happens after the patient goes home?

Usually the dressing is removed in the hospital and the sutures are left exposed. Most surgeons do not allow tub baths at home but do encourage showering and shampooing, with application of bacitracin to the sutures. If there is a tendency to pick at the scalp as it heals, which can result in scarring or infection, the sutures may be covered with gauze and then with a baseball cap or something similar. The patient will almost always go home on a tapering dose of steroids and on antiepileptic medication. Cultures of the surgical site will have been done during the surgery, and it is important that these have tested negative when the patient is discharged. If there is any infection, the patient will be sent home on antibiotics.

Follow-up appointments are scheduled with the neurology and neurosurgery teams. The patient resumes usual activities as soon as possible, typically within 1–2 weeks for children. Therapies should be started right away. Adults may take a little longer to recover and may complain of headaches for a longer period of time. Feeling tired after surgery is to be expected. We tell patients, “For every day you are in the hospital, expect a week of recovery.” In some cases, when surgery has resulted in weakness, the patient may be transferred to a rehabilitation center for intensive therapy before going home.

If an RNS device has been implanted, the hospital stay is even shorter, usually 2 or 3 days. After discharge, monthly visits are scheduled with the epilepsy team to review data and program the device. The patient or family must download data on a daily basis. Placement of a VNS device may only require an overnight stay, and battery replacement is done as an outpatient (same-day) surgery.
When can I tell if the surgery was a success?

Seizures are not unusual after surgery. Thus, it might take up to 6 months to know the full effects of surgery. Remember, too, that the goal of surgery is not always to completely eliminate seizures, but rather to reduce their number and severity.

What are additional common questions for each type of surgery?

Frontal lobe resections:

• **Is this like that movie with Jack Nicolson?** No, the patient will not develop into a character similar to the one in One Flew Over the Cuckoo’s Nest, nor should the patient become disorganized or impulsive. Remember, we do not remove both frontal lobes, so one remains intact and works just fine.

• **Will the patient be able to move his or her legs?** Because movement of the legs and feet is controlled by both sides of the brain, leg movement would only be an issue if there were damage to the motor areas on both sides.

• **Will the patient’s motor functioning remain intact?** As described above, in some cases, swelling occurs after surgery in the supplementary motor area near the motor cortex. This may result in temporary weakness or loss of speech. Fortunately, this usually resolves within 1–2 weeks, but it can take up to 3 months. Physical therapy often helps.
Occipital lobectomy:

- **Will it affect vision?** Depending on the resected area, some surgeries may cause a visual field defect typically involving peripheral vision. The patient may have to turn his or her head to see objects located far to the left or right. The normal human visual field extends about 60 degrees toward the nose (inward) and 100 degrees away from the nose (outward). Surgery may cause “homonymous hemianopia” (loss of one side of the visual field in both eyes) or “quadrantanopsia” (loss of a quarter of a field of vision). Some patients, particularly those who have had a stroke, may already have a visual field loss before surgery.

Temporal lobectomy:

- **Will it affect memory?** A Wada test performed before surgery ensures that the temporal lobe being removed is not the one that supports memory and language. Typically, the affected temporal lobe is doing nothing but causing seizures. If the seizures and spiking are resolved, there is less interference with memory and language.

- **Will it affect language?** The areas of the brain that usually control language (including written language, spoken language, and multilingualism) are well known, although in people with longstanding epilepsy and MRI abnormalities, normal language centers can shift. Language mapping and Wada testing helps surgeons avoid these areas.

Hemispherotomy:

- **Will the patient become paralyzed?** Most people who undergo a hemispherotomy already have some loss of motor function. They may be partially paralyzed or have some weakness already. However, fine motor skills such as hand and finger dexterity may be lost as a result of this surgery.

- **Will the patient’s legs work after a hemispherotomy?** Yes, your legs should continue to be fine. If you were already weak on one side, the weakness will not get better. But both sides of the brain control the legs, so severing the connection should not significantly affect their functioning.
Corpus callosotomy:

• **Will the patient’s behavior worsen?** Typically, behavior improves after a corpus callosotomy. In a high-functioning person who undergoes a corpus callosotomy, the only effect should be what is referred to as split-brain syndrome.

• **What is split-brain syndrome?** After a corpus callosotomy, a person may have difficulty naming (a function supported by the left side of the brain) what the right brain is seeing (a function controlled by the right side of brain). Here’s an example: normally, a person would be able to describe an object placed in his or her hand as round, smooth, and red and then name it “ball.” After a corpus callosotomy, the person would be able to describe the object while holding it in the right hand, but would have to move it to the left hand to actually name it “ball.” There is also a small risk of mutism, a psychological side effect that prevents speaking, which is typically temporary.

RNS and VNS:

• **With RNS, will I feel the device?** No, the RNS device is inserted in the skull. However, you may be able to feel the outline of the battery.

• **With RNS or VNS, will I need battery changes?** Yes, these are usually done as an outpatient procedure, and the time between battery changes depends on the settings on the devices.
Nonsurgical Treatments FOR EPILEPSY

Fortunately, there are many tools for managing epilepsy. The goal is to control seizures with minimal side effects and to do this with as few medications as possible. Although this book is about surgery, familiarity with the dietary and medical options in this section will help in considering different approaches when current treatment is ineffective or poorly tolerated.
What are the medical treatment options for epilepsy?

As background to your discussion of epilepsy surgery with your medical team, the table on pages 57–67 contains information regarding antiseizure medications. Many readers will be familiar with the more commonly used medications and may be worried about using the medications that are perceived to have more severe side effects. This table provides the generic and brand names of the drugs; their approval date; their indications; advantages and disadvantages; monitoring requirements; side effects and contraindications; and interactions with other medications, particularly those used for the treatment of epilepsy.

Medications for the Treatment of Epilepsy*

<table>
<thead>
<tr>
<th>Medication (brand name[s])</th>
<th>Year Approved</th>
<th>Indications</th>
<th>Advantages / Disadvantages</th>
<th>Monitoring Requirements</th>
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<th>Interactions</th>
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</thead>
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<tr>
<td>Carbamazepine (Tegretol, Tegretol XR, Carbatrol)</td>
<td>1964</td>
<td>For treatment of partial seizures, generalized seizures, and mixed seizure types</td>
<td>Used most often for partial seizures; can worsen some types of generalized seizures, including atonic, absence, and myoclonic</td>
<td>Blood levels must be monitored and maintained at therapeutic levels (4–12 μg/mL).</td>
<td>Adverse effects worsen with higher doses and include dizziness, double vision, nausea, vomiting, sedation (usually early in treatment), weight gain, severe rash, cardiac issues, hypertension, anemias, and liver problems, as well as low sodium levels, jaundice, and blood clots. If used during pregnancy, it can cause congenital malformations.</td>
<td>Phenobarbital and phenytoin can increase carbamazepine clearance, lowering its blood level. Valproic acid can increase carbamazepine levels and thus increase its side effects. Carbamazepine reduces the effectiveness of oral contraceptives.</td>
</tr>
<tr>
<td>Clobazam (Onfi)</td>
<td>2012</td>
<td>Used as add-on therapy for certain seizures</td>
<td>Has a rapid onset and wide spectrum of effectiveness, with rare side effects</td>
<td>Usually none; may monitor when used with cannabidiol</td>
<td>Rare side effects include sleepiness, fatigue, behavioral issues, sedation, and cognitive impairment. These can be worsened with depressants such as alcohol and barbiturates.</td>
<td>Can interact with other medications from this class, causing sedation and drowsiness; interacts with cannabidiol, causing sedation and drowsiness.</td>
</tr>
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<tr>
<td>Clonazepam (Klonopin)</td>
<td>1975</td>
<td>For treatment of syndromic and other seizures that fail to respond to conventional medications</td>
<td>Patients can develop a tolerance and require increasing doses.</td>
<td>None in patients without symptoms; those experiencing drowsiness or a sedation effect should be monitored for possible toxic doses.</td>
<td>Side effects include sedation, behavioral and cognitive impairment, drowsiness, ataxia (loss of movement control), personality and behavioral change in children, hyperactivity, blurred vision, aggressiveness, and irritability (usually dose-related). Doses are usually increased slowly, with larger doses given at night to avoid side effects. (Dosing solely at night is often effective for myoclonic jerks.) Withdrawal symptoms can occur if a dose is missed and may include increased pulse, tremor, and general feeling of being unwell. This drug should not be used in people with glaucoma or liver dysfunction. The benefits of breastfeeding are thought to outweigh the risks of doing so while taking clonazepam. Data regarding its use in pregnancy are limited; some small studies showed no increase in major malformations.</td>
<td>Can interact with other medications from this class, causing drowsiness or sedation</td>
</tr>
</tbody>
</table>

Clonazepam (Klonopin) (continued)

Can occur if a dose is missed and may include increased pulse, tremor, and general feeling of being unwell. This drug should not be used in people with glaucoma or liver dysfunction. The benefits of breastfeeding are thought to outweigh the risks of doing so while taking clonazepam. Data regarding its use in pregnancy are limited; some small studies showed no increase in major malformations.
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<tr>
<td>Diazepam (Valium)</td>
<td>1960s</td>
<td>Rescue medication that can be used in the community setting</td>
<td>Available in oral, IV, intramuscular, and rectal gel formulations</td>
<td>None</td>
<td>Adverse reactions are common and include confusion, ataxia, dizziness, dysarthria (unclear articulation of speech), restlessness, and irritability; repeated administration can increase risk of respiratory depression, sedation, and hypotension. Use in the first trimester of pregnancy increases risk of major malformations and cleft palate in infants. Use just before delivery places the infant at risk for respiratory depression (inadequate breathing), hypotonia (poor muscle tone), feeding difficulties, temperature instability, and neonatal withdrawal syndrome. This drug should not be used when breastfeeding.</td>
<td>Oral contraceptives reduce clearance of diazepam from the body.</td>
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<tr>
<td>Eslicarbazepine acetate (Aptiom)</td>
<td>2014</td>
<td>Add-on therapy for complex partial seizures in adults</td>
<td>Extended release formulation; fewer side effects than carbamazepine and oxcarbazepine; typically dosed once daily and has no significant psychiatric or cognitive side effects</td>
<td>None</td>
<td>Adverse effects include rash, depression, low sodium, headache, nausea, vomiting, dizziness, blurred or double vision, insomnia, and changes in liver function and thyroid tests.</td>
<td>Does not interact with most medications used in epilepsy. When used with phenytoin, can increase the phenytoin level; when used with carbamazepine, phenobarbital, and phenytoin, the level of eslicarbazepine can be increased. Side effects can increase with use of other sodium-channel drugs. This drug reduces the efficacy of oral contraceptives.</td>
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<tr>
<td>Ethosuximide (Zarontin)</td>
<td>1958</td>
<td>For treatment of childhood absence seizures</td>
<td>Not effective for generalized tonic-clonic or partial seizures</td>
<td>None, but blood levels should be maintained at therapeutic levels (40–100 μg/mL)</td>
<td>Adverse effects are usually mild and dose-dependent. Gastrointestinal side effects are fairly common.</td>
<td>Interacts with carbamazepine and erythromycin; decreases lamictal levels</td>
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<tr>
<td>Ezogabine (Potiga)</td>
<td>2012</td>
<td>Add-on treatment of complex partial seizures</td>
<td>Unique mechanism of action on potassium channels</td>
<td>Vision monitoring is required because this agent can cause retinal changes; electrocardiogram (EKG) is needed for patients who are at risk for prolonged QT.</td>
<td>The most common side effects are sleepiness, confusion, dizziness, tremor, amnesia, abnormal thinking, vertigo, and speech disorders. It can cause cardiac issues (prolonged QT interval on EKG); urinary retention; discoloration of skin, nails and mucous membranes and the sclera of the eyes; and decreased visual acuity.</td>
<td>Phenobarbital, phenytoin, and carbamazepine can reduce ezogabine levels.</td>
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<tr>
<td>Felbamate (Felbatol)</td>
<td>1996</td>
<td>For use in the treatment of Lennox-Gastaut syndrome involving seizures not controlled with other medications; also used for refractory partial seizures with or without secondary generalization</td>
<td>Usually works well to control seizures but can cause anemias; must be dosed twice daily, usually about 4 hours apart, which means during school for children</td>
<td>Blood should be checked before initiating treatment and monitored at regular intervals thereafter.</td>
<td>Severe adverse reactions include life-threatening aplastic anemia and liver failure. This occurs more commonly if the patient is female, has a history of allergy or anemia on previous antiepileptic medications, or has a history of immune disorders, especially lupus. Common side effects include anorexia, nausea, vomiting, and weight loss, as well as insomnia and irritability in children, and are most likely to occur within the first 3 months. The medication should be given at 8:00 a.m. and noon to avoid insomnia.</td>
<td>For patients on a ketogenic diet, the tablet formulation should be used instead of liquid because there is a large amount of sorbitol in the liquid preparation. Felbamate increases phenytoin levels when both are used.</td>
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<tr>
<td>Gabapentin (Neurontin)</td>
<td>1993</td>
<td>Add-on therapy in adults and children older than 3 years of age for treatment of partial seizures</td>
<td>Helps with pain and sleep problems, but may be sedating</td>
<td>None</td>
<td>Side effects include central nervous system depression (drowsiness, sedation), which is generally short-lived. Other side effects include emotional lability and hostility and rare rashes. This drug should not be used in pregnancy, and its use should be limited while breastfeeding.</td>
<td>None</td>
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<td>Lacosamide (Vimpat)</td>
<td>2008</td>
<td>Add-on therapy for partial-onset seizures in patients older than 16 years of age</td>
<td>Works well in refractory patients and has a low potential for interaction with other drugs</td>
<td>None</td>
<td>The most common side effect is dizziness. It can also cause EKG changes in patients with cardiac conduction problems or cardiac issues. It should not be used during pregnancy or while breastfeeding.</td>
<td>May interact with cardiac medications</td>
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<tr>
<td>Lamotrigine (Lamictal)</td>
<td>1995</td>
<td>Used as an add-on therapy for partial-onset seizures in adults and children or as mono-therapy in partial-onset seizures; generalized seizures associated with Lennox-Gastaut syndrome; and tonic-clonic seizures in generalized epilepsy; also frequently used to treat absence seizures in children and adolescents</td>
<td>Advantages include that it is usually well tolerated, does not worsen cognition, and works synergistically with valproic acid; the main disadvantage is the risk of a severe rash (but this risk is much lower when it is started at a low dose and increased slowly)</td>
<td>Monitoring of blood levels is rarely necessary except during pregnancy.</td>
<td>Common side effects include dizziness, ataxia, somnolence, headache, double vision, blurred vision, nausea, vomiting, and insomnia. When used in pregnancy, there is a slight increase in the risk of congenital malformations, including oral clefts.</td>
<td>Lamotrigine levels are reduced by carbamazepine, phenytoin, and other enzyme-inducing antiepileptic medications. This drug can lower the efficacy of oral contraceptives.</td>
</tr>
<tr>
<td>Levetiracetam (Keppra)</td>
<td>2001</td>
<td>Primary treatment for partial-onset seizures in adults and children older than 6 years of age and add-on therapy for partial-onset seizures in adults and children older than 1 month of age; used for myoclonic seizures, photo-sensitive seizures, status epilepticus, and neonatal seizures</td>
<td>Well tolerated when used with steroids (as in patients with brain tumors).</td>
<td>Monitoring is required during pregnancy and after delivery.</td>
<td>Side effects include sleepiness, irritability, nausea, headaches, depression, emotional lability (mostly with higher doses and previous history of behavioral problems or psychiatric diagnosis). Blood concentrations are lower during pregnancy and increase rapidly in mothers after delivery. Cases of major congenital defects are rare when used during pregnancy. When used during breastfeeding, blood concentrations are low in the newborn, but elimination is slowed.</td>
<td>None</td>
</tr>
<tr>
<td>Brivaracetam (Briviact)</td>
<td>2016</td>
<td>Primary treatment for partial-onset seizures in patients older than 16 years of age and add-on therapy for partial-onset seizures in adults and children older than 1 month of age; used for myoclonic seizures, photo-sensitive seizures, status epilepticus, and neonatal seizures</td>
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<td>Lorazepam (Ativan)</td>
<td>1997</td>
<td>First-line treatment for status epilepticus, usually given by injection; also used in adults for anxiety and sedation</td>
<td>Less risk of hypotension than with diazepam (also used for status epilepticus), but there is a tendency for patients to develop a tolerance</td>
<td>Watch for addiction, sedation, and hypotension; cannot be taken with alcohol</td>
<td>Common reactions include respiratory depression, sedation, dizziness, vertigo, weakness, and unsteadiness. Less common are disorientation and depression. It should be used in pregnancy only in life-threatening situations and should not be used when breastfeeding.</td>
<td>Interacts with other benzodiazepines</td>
</tr>
<tr>
<td>Midazolam (Versed)</td>
<td>1975</td>
<td>For treatment of status epilepticus; given nasally, intra-venously, or through the buccal mucosa; also used for conscious sedation, anesthesia, and sedation in hospital intensive care units</td>
<td>Considered an alternative to Diastat (rectal diazepam); short-acting and easier to use in patients in wheelchairs</td>
<td>Used only for status epilepticus and as a rescue medication</td>
<td>Severe adverse reactions of respiratory depression and variations in blood pressure and pulse are only reported with IV use in inpatient settings. Side effects include gastrointestinal disturbances, jaundice, anaphylaxis, drowsiness, hallucinations, laryngospasm, ataxia, amnesia, fatigue, dizziness, and vertigo. There have been no fetal malformations reported when used in pregnancy. It readily crosses into breast milk, but there is no evidence of harm to infants.</td>
<td>Can interact with other medications in its class, causing increased sedation, but usually is used only as rescue or to promote sedation</td>
</tr>
<tr>
<td>Oxcarbazepine (Trileptal, Oxtellar XR)</td>
<td>1991</td>
<td>Mono-therapy or add-on therapy for partial-onset seizures</td>
<td>Advantages include that it does not have carbamazepine’s serious side effects of anemia and agranulocytosis and has fewer drug interactions than carbamazepine; also causes no cognitive impairment</td>
<td>Blood levels should be monitored in people who have kidney disease and during pregnancy.</td>
<td>The most common side effects include drowsiness and low sodium levels (more common in adults). More serious reactions include anaphylaxis, angioedema, rash, and anemia. The rates of major congenital malformations were comparable to the rate in pregnancies in other women with epilepsy or off antiepileptic medications. Effects in breastfeeding are unknown.</td>
<td>This drug can lower the efficacy of oral contraceptives.</td>
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<tr>
<td>Medication (brand name[s])</td>
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<tr>
<td>Perampanel (Fycompa)</td>
<td>2013</td>
<td>For treatment of partial seizures</td>
<td>Severe aggression and RARE homicidal and suicidal ideation have been reported.</td>
<td>Monitor for mood/aggression.</td>
<td>Side effects include aggression, hostility, depression, abuse, dizziness, sleepiness, headaches, nausea, and low sodium. It should not be used in pregnancy unless the benefits outweigh the risk. There are insufficient data to assess the risk of use while breastfeeding.</td>
<td>Topiramate, oxcarbazepine, clobazam, and carbamazepine can each lower perampanel levels. Carbamazepine levels can also be decreased by perampanel.</td>
</tr>
<tr>
<td>Phenobarbital (Luminal)</td>
<td>1912</td>
<td>Used for febrile seizures, tonic-clonic seizures, status epilepticus, and eclampsia; a first-line for treatment of partial and generalized tonic-clonic seizures in developing countries because of its low cost and once-daily administration</td>
<td>Tolerance may develop with long-term use.</td>
<td>Blood monitoring is recommended when the patient is on multiple antiepileptic medications; this drug should be maintained at a blood level of 15–40 μg/mL.</td>
<td>Common side effects include drowsiness, mood changes, and impairment of cognition and memory. At high doses, side effects may include nystagmus (involuntary rapid eye movement), ataxia, slurred speech, disinhibition, and anemias. Serious reactions include respiratory depression. If used in pregnancy, the baby may experience withdrawal and trouble breathing; there is also risk of congenital malformations. It should not be taken when breastfeeding.</td>
<td>Valproate increases phenobarbital concentrations. Phenobarbital interacts with a variety of medications, including steroids, warfarin, and some antibiotics and antihistamines. It also interacts with oral contraceptives, causing contraceptive failure and breakthrough bleeding.</td>
</tr>
<tr>
<td>Phenytoin (sold under many names, including Dilantin, Phenytek, Prompt, and Di-Phen; IV formulation is called fosphenytoin and sold under the name Cerebyx)</td>
<td>1938</td>
<td>Used to treat partial-onset and generalized seizures and for status epilepticus</td>
<td>Inexpensive and long-lasting</td>
<td>Blood levels must be closely monitored and often fluctuate; the therapeutic level is 10–20 μg/mL.</td>
<td>Side effects include gum hyperplasia, hirsutism, ataxia, slurred speech, anemias, and impotence. Long-term use can lead to peripheral neuropathy and osteoporosis. It should not be used in pregnancy, but if its use is necessary, the lowest dose possible should be given. It is usually considered safe in breastfeeding.</td>
<td>Phenytoin interacts with many medications, including (but not limited to) psychiatric medications, calcium channel blockers, digoxin, cholesterol-lowering agents, warfarin, antifungals, antibiotics, felbamate, isoniazid, topiramate, carbamazepine, phenobarbital, and vigabatrin.</td>
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### Medications for the Treatment of Epilepsy* (continued)

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<tr>
<td><strong>Pregabalin (Lyrica)</strong></td>
<td>2005</td>
<td>Add-on therapy for focal epilepsies in adults and children older than 12 years of age; also used for neuropathic pain</td>
<td>Works on calcium channels; can cause sedation</td>
<td>Patients should be monitored for drowsiness.</td>
<td>May cause sedation.</td>
<td>There are few interactions, except with carbamazepine, which may lower pregabalin blood concentrations.</td>
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<tr>
<td><strong>Primidone (Mysoline)</strong></td>
<td>1954</td>
<td>Used for treatment of generalized tonic-clonic seizures and complex partial seizures and as second-line treatment for juvenile myoclonic epilepsy</td>
<td>Efficacious in some patients, but requires blood monitoring and may cause sedation</td>
<td>Check blood levels. Primidone partially breaks down to phenobarbital. Plasma levels are usually maintained at 5 – 12 μg/mL</td>
<td>Common (but usually transient) side effects include drowsiness, listlessness, visual disturbances, nausea, headaches, dizziness, vomiting, nystagmus, and ataxia. Serious reactions include anemias, elevated liver enzymes, arthralgia (joint pain), and osteomalacia (bone softening). When used during pregnancy, it can cause low maternal folate levels and coagulation disorders in newborns. There is some evidence that it may cause congenital malformations. When used during breastfeeding, it can cause somnolence and drowsiness in the infant.</td>
<td>Interactions with numerous medications may occur, similar to those with phenobarbital. It also interacts with oral contraceptives, at times causing breakthrough bleeding and failure of contraceptive therapy.</td>
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<td><strong>Rufinamide (Banzel)</strong></td>
<td>2008</td>
<td>Add-on therapy for partial-onset seizures and seizures associated with Lennox-Gastaut syndrome</td>
<td>Well-tolerated and useful for Lennox-Gastaut syndrome, but may cause abdominal upset</td>
<td>Do not use if prolonged QT syndrome exists.</td>
<td>Common side effects include dizziness, fatigue, nausea, vomiting, double vision, and somnolence. Rufinamide can also cause shortening of the QT interval, a cardiac side effect. It is not indicated for use during pregnancy or while breastfeeding.</td>
<td>Valproate increases the rufinamide concentration, and rufinamide increases serum concentrations of carbamazepine, lamotrigine, and phenobarbital. It decreases the efficacy of oral contraceptives.</td>
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<td>Stiripentol (Diacomit)</td>
<td>2018</td>
<td>Used for treatment of severe myoclonic epilepsy in infancy (Dravet’s syndrome)</td>
<td>Has some efficacy in Dravet’s syndrome but must be imported and is therefore difficult to obtain, expensive, and not covered by insurance</td>
<td>Complete blood count and liver function tests should be performed before treatment and every 6 months during treatment.</td>
<td>Common side effects are anorexia, weight loss, drowsiness, ataxia, nausea, lethargy, vomiting, tremor, and, in rare cases, aplastic anemia. No studies exist on its use in pregnancy and breastfeeding.</td>
<td>When used with clobezam or carbamazepine, the doses of the other medications should be decreased.</td>
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<td>Tiagabine (Gabitril)</td>
<td>1998</td>
<td>Add-on therapy for partial seizures with or without secondary generalization in adults and children older than 12 years of age</td>
<td>Advantages include minimal interactions with other antiepileptic drugs. Disadvantages include the need for slow titration because of potential adverse side effects and the possibility of aggravating generalized seizures.</td>
<td>There is no evidence to recommend routine monitoring of blood level, but patients seem to respond best with trough levels of 20–40 μg/mL.</td>
<td>Side effects include dizziness, weakness, nervousness, tremor, diarrhea, depression, and emotional lability. These usually can be managed by slow titration and dosing multiple times per day. It is not recommended for use in pregnancy. Breastfeeding women taking tiagabine should monitor their infants for adverse events.</td>
<td>May interact with enzyme-inducing anti-epileptic medications</td>
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<td>Topiramate (Topamax, Qudexy XR, Trokendi XR)</td>
<td>1996</td>
<td>Mono-therapy for partial-onset and primary generalized tonic-clonic seizures in patients 10 years of age and older; as add-on therapy for partial seizures in adults and pediatric patients 2-16 years of ages; as add-on therapy in primary generalized tonic-clonic seizures in adults and pediatric patients 2-16 years of age; and for treatment of seizures associated with Lennox Gastaut syndrome in patients 2 years of age and older</td>
<td>Has several mechanisms of action and good efficacy but can decrease appetite and lead to renal stones and glaucoma</td>
<td>Periodic renal ultrasounds are needed to rule out kidney stones, as well as vision monitoring for glaucoma.</td>
<td>Side effects include cognitive dulling (word-finding difficulties and memory disturbances), somnolence, dizziness, ataxia, nervousness, and fatigue, which tend to be worse while titrating and reduce over time. There is an increased rate of congenital malformations when used during pregnancy, and high concentrations are found in breast milk if taken at doses &gt;200 mg/day.</td>
<td>Drug interactions are minimal, although phenytoin and carbamazepine may increase topiramate levels.</td>
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Medications for the Treatment of Epilepsy* (continued)

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<tr>
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<tr>
<td>Valproate (Depakote, Depakene, Stavzor)</td>
<td>1983</td>
<td>Mono-therapy and add-on therapy for partial seizures and simple and complex absence seizures; add-on therapy for multiple seizure types</td>
<td>Offers good efficacy and mood stabilizer effects, but has many side effects and contraindications</td>
<td>Blood levels, platelets, and liver function should be monitored. Patients experiencing abdominal pain should be checked for pancreatitis.</td>
<td>Severe but rare adverse events include pancreatitis, liver dysfunction, and low platelets. More common side effects are weight gain, nausea, vomiting, diarrhea, anorexia, abdominal pain, tremors, dizziness, agitation, hair thinning or loss, and osteomalacia. When used in pregnancy, there is an increased risk of major congenital malformations, delayed intellectual development in the child, craniofacial abnormalities, and neuronal tube defects. Pregnant women on valproate must have folic acid supplementation. Breastfeeding is not contraindicated. Cannot be used in mitochondrial disease.</td>
<td>Interacts with ethosuximide, primidone, and phenytoin, increasing their levels; use with felbamate increases the level of valproate; use with carbamazepine may decrease the level of valproate</td>
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<tr>
<td>Vigabatrin (Sabril)</td>
<td>2009</td>
<td>Mono-therapy for infantile spasms and add-on therapy for refractory complex partial seizures</td>
<td>Main advantage is superior effectiveness as treatment for two severe types of seizures: infantile spasms and refractory partial seizures. Disadvantages include that it may worsen myoclonic and absence epilepsy.</td>
<td>Risk Evaluation and Mitigation Strategy (REMS) program existed to monitor vision needs; vision checks are necessary every 3 months.</td>
<td>Adverse effects include visual field loss, rare cognitive issues, MRI changes in deep gray and white matter (usually transient and asymptomatic), weight gain, fatigue, somnolence, irritability, behavioral changes, psychosis, depression, ataxia, and hyperactivity and agitation in children. Animal studies have shown intrauterine growth retardation, minor congenital malformations, and delays in skeletal development when used during pregnancy. It is secreted in breast milk in low quantities.</td>
<td>May decrease phenytoin levels</td>
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<td>Zonisamide (Zonegran)</td>
<td>2000</td>
<td>Add-on treatment of partial seizures; also widely used for treatment of generalized seizures, seizures associated with Lennox-Gastaut syndrome, and infantile spasms</td>
<td>Advantages include once-daily dosing and a lack of interaction with other antiepileptic drugs.</td>
<td>Patients should be watched for sedation and cognitive impairment.</td>
<td>Adverse effects include cognitive side effects, risk of kidney stones, and rash (rare). More common side effects include ataxia, dizziness, nausea, fatigue, somnolence, agitation, irritability, and anorexia. These seem to be dose related and do not occur if the medication is increased slowly. There are limited data about its use in pregnancy, but there seems to be no higher risk than with other antiepileptic medications. Use in pregnancy is indicated only if potential benefits outweigh risks. Zonisamide is extensively secreted in breast milk, but there are limited data about its effects on infants, so infants should be closely monitored for sedation or irritability. It should not be used in people with allergies to sulfa drugs.</td>
<td>When used with topiramate, increases the risk of renal stones</td>
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<tr>
<td>Cannabidiol (Epidiolex)</td>
<td>2018</td>
<td>Seizures associated with Lennox-Gastaut syndrome and Dravet syndrome</td>
<td>Advantage is that it is effective for hard to control seizures in two pediatric epileptic encephalopathies with a unique mechanism of action. Can be given via gastrostomy tube. Disadvantage is possible side effect of drowsiness and liver abnormalities. It must be given either with or without food and is only available in a liquid.</td>
<td>Liver function should be checked before initiating therapy and periodically thereafter. Dose can be increased weekly.</td>
<td>Adverse effects include drowsiness, somnolence, rash, decreased appetite and hyperactivity. Cannot be given if the person is allergic to sesame or strawberries.</td>
<td>Use with clobazam can increase somnolence; use with valproic acid can cause liver transaminase elevations</td>
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* This table is intended only as a guide; likewise, Internet sources should not be considered definitive. Patients should verify all medication-related information with their health care provider.
What is a ketogenic diet?

A ketogenic diet is a high-fat, low-carbohydrate eating plan used to treat certain forms of epilepsy that are resistant to medical treatment. It was first created at the Mayo Clinic in Rochester, MN, in 1921 but was used more widely by Johns Hopkins Hospital in Baltimore, MD. The diet produces high levels of ketones (byproducts of the dietary fat used for energy). A high ketone level in the blood can reduce the frequency of epileptic seizures. Following the diet requires carefully measuring foods and maintaining a strict ratio of fat to protein plus carbohydrate eaten.

Variations of the classic ketogenic diet provide more flexible eating. These include the medium-chain triglyceride (MCT) ketogenic diet, the low-glycemic diet, and a modified Atkins diet. Fats are classified by their chemical structure. Usual dietary fats are long-chain triglycerides. People following the MCT diet derive more than half of their calories from MCT oils (man-made through the processing of coconut and palm oils). MCT fats are a more efficient source of ketone bodies because they enter the liver (where ketone bodies are produced) more efficiently than other fats. This allows patients to eat more carbohydrate and protein as ketone levels are elevated. A low-glycemic diet also affords greater carbohydrate intake by emphasizing those carbohydrate foods that keep blood glucose at an even level. The modified Atkins diet limits carbohydrate to about 10 grams per day but does not limit protein, which makes meal preparation easier.
CONCLUSION

For children and adults with intractable epilepsy, there are a number of viable options, which, even if they do not alleviate all seizures, may at least decrease the frequency of seizure activity, leading to improved development and quality of life. Families and patients are often rightfully concerned about possible adverse effects of more invasive treatments. It is important to discuss all treatment options, including those that may at first seem drastic, with your health care providers. These options include surgery, a ketogenic diet, and a large arsenal of medications.

If epilepsy surgery is indicated in your case, it is important to remember that it is safe, well tolerated, and should be performed as soon as possible after a person is identified as a surgical candidate. It is important that the patient and family work with a team from a Comprehensive Epilepsy Center to ensure the best outcomes.


Steven M. Wolf, MD, Patricia Engel McGoldrick, NP, MSN, MPA, have worked together to care for people with epilepsy since 2000.

Patricia Engel McGoldrick, NP, MSN, MPA, was born and raised in New York and lives in New York with her husband and three children. She has a master’s degree in Public Administration from New York University and a master of science degree in Nursing from Columbia University.

She is a nurse practitioner in partnership with Dr. Wolf. She is also Co-Director of the Tuberous Sclerosis Program at Mount Sinai and the Associate Director of the Developmental Disability Center at Mount Sinai West, while her primary responsibility is to the Comprehensive Pediatric Epilepsy Center at Mount Sinai Health System. She is adjunct faculty at Columbia University School of Nursing.

Ms. McGoldrick and Dr. Wolf have co-authored numerous articles and small books, the best known of which are Parents’ Guide: When the Seizures Don’t Stop...Why—and What to Do Next and A Parent’s Guide: When Seizures Are Not the Only Problem—Learning and Developmental Issues. These have been distributed free of charge throughout the United States since 2005 as part of an epilepsy awareness educational initiative.

Steven M. Wolf, MD, was born and raised in New York and lives in New York City with his wife and two children. He is a graduate of the 6-year medical program at Rensselaer Polytechnic Institute and Albany Medical College and served his pediatric and neurology residency and epilepsy fellowship at Montefiore Medical Center, Albert Einstein College of Medicine.

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