Epilepsy is one of the most common neurologic disorders. The term epilepsy refers to a collection of signs and symptoms that can have a variety of underlying etiologies that cause seizures—the principal symptom of epilepsy. A seizure is caused by an excessive discharge of cortical neurons; the location and pattern of the spread of activity determine the clinical manifestations. Recurrent seizures are the hallmark of epilepsy; however, their etiology may be genetic, secondary to insult or injury to the brain (eg, from trauma, infection, fever, metabolic disturbances, or drug effects), or idiopathic. Epilepsy can be classified according to seizure type or syndrome, and such classifications can be based upon a number of factors including seizure type, natural history, electroencephalogram (EEG), etiology, and response to anticonvulsants. Clinical signs and symptoms useful in classifying seizures include changes in behavior.

Challenges in Seizure Management: Wrong Diagnosis, Wrong Drug, Wrong Dose?
Ronald P. Lesser, MD

ABSTRACT

PURPOSE: To review the management of patients with epilepsy, particularly those who experience seizures refractory to traditional pharmacologic therapy.

EPIDEMIOLOGY: Epilepsy affects approximately 2.5 million Americans. As many as two thirds of individuals can be successfully managed with medication; the remainder may experience recurrent episodes due to inappropriate therapy or misdiagnosis.

REVIEW SUMMARY: Epilepsy ranks among the most common neurologic diseases, and individuals with uncontrolled epilepsy bear the financial burden of costly medical treatments and lost work, as well as a tremendous psychosocial burden of a disorder that is often feared. This condition prevents individuals from performing essential functions in society and can be associated with serious injuries and death. Although the majority of patients can be successfully managed with medication, the remainder may experience recurring episodes because of inappropriately selected therapies. This review highlights common areas of misdiagnosis (such as psychogenic nonepileptic seizures), discusses various pharmacologic options (including the benefits of and management of monotherapy), and discusses epilepsy surgery.

TYPE OF AVAILABLE EVIDENCE: Randomized controlled trials, prospective studies, textbooks.

GRADE OF AVAILABLE EVIDENCE: Good.

CONCLUSION: The first step in helping individuals with refractory seizures is to exclude other clinical entities that mimic epilepsy. Complex multidrug regimens often can be avoided if monotherapy with the correct medication is prescribed at an adequate dose. Polypharmacy can be responsible for noncompliance because of impractical medication schedules and adverse effects. Nonpharmacologic modalities such as behavioral modification, counseling, and ketogenic diet are useful for many epileptic patients. If the patient continues to have seizures despite efforts to optimize therapy, surgery should be considered.

ior, motor activity, sensorium (auras), level of consciousness, or autonomic nervous system activity.

**HISTORY AND EPIDEMIOLOGY**

Many of the ancients believed that seizures were caused by demons. One recommended treatment in ancient Greece was to sleep in a temple overnight in the hopes that the god Asclepius would come to you in your dreams and cure you. Hippocrates, however, suggested a treatment of medicines and special diet. The ancient Romans believed epilepsy was contagious and ostracized those who were afflicted. In Europe during the Middle Ages and Renaissance periods, individuals with the “falling sickness” might have sought cures from patron saints such as Valentine or might have been considered to possess mystic properties or powers. During the last 2 centuries, individuals with epilepsy have at times been confined to mental institutions, prohibited from marrying, or forced to undergo sterilization. In the United States as recently as the early 1970s, immigration laws prohibited individuals with epilepsy from entering the country.

Ten percent of the US population has experienced at least a single seizure in their lifetime. About 4% could be diagnosed with epilepsy (ie, they have experienced 2 or more seizures). The World Health Organization estimates that 50 million people worldwide are affected. Childhood is one of the peak periods for the onset of epilepsy. Men are slightly more prone than women to epilepsy, as are those of Hispanic and African American descent. There seems to be a higher prevalence of epilepsy among those of lower socioeconomic status (perhaps because the disorder limits their earning power) and among those with conditions such as mental retardation and cerebral palsy. The lifelong cost for each year’s newly diagnosed patients (about 181,000 cases) has been estimated to reach approximately $11.1 billion, with an annual total cost (direct and indirect) estimated at $12.5 billion. Buck et al reported that of 300 patients who had experienced at least 1 seizure in the prior year, 24% reported head injuries, 16% reported burns, 14% were at risk for drowning because they had experienced a seizure while bathing or swimming, 10% experienced dental trauma, and another 6% reported fractures. Furthermore, anticonvulsant medication use in pregnant women may have teratogenic side effects and may impair growth and development in children.

Apart from the obvious physical risks associated with uncontrolled seizures, epilepsy is associated with significant psychosocial consequences. For example, individuals with epilepsy often are not permitted to drive because of the risk of experiencing a seizure while operating a vehicle.

**PHARMACOLOGIC CONTROL OF EPILEPSY**

The seizures of about two thirds to three fourths of patients can be controlled with medication. Annegers et al evaluated patients diagnosed with epilepsy in Rochester, Minnesota, between 1935 and 1974. After 1 year of treatment with appropriate medications, 42% of patients were seizure free; after 10 years, the remission rate rose to 65%; after 15 years, 76% of patients were seizure free; and at 20 years postdiagnosis, the overall seizure remission rate was 70%. The authors found that the prognosis for remission of epilepsy was poorer in patients with associated neurologic dysfunction identified from birth and for those with adult-onset and partial-complex seizures; conversely, prognosis was better for patients with idiopathic seizures as well as for those who were diagnosed with generalized seizures before the age of 10 years. Of those whose seizures were not controlled, about two thirds experienced partial seizures (seizures that begin in a localized part of the brain), and the remaining one third experienced generalized seizures (seizures that appear to begin throughout the brain without clear evidence of a localized point of origin).

When anticonvulsant therapy fails, 1 of 3 situations is at work: the patient either has been given the wrong diagnosis, the wrong drug, or the wrong dose.

**WHEN DRUGS DON’T WORK—QUESTIONS TO ASK**

First, ask if there is an underlying cause for the seizures. Seizures may be caused by acute systemic conditions or head trauma. If these are present, the underlying condition should be treated. Possible underlying conditions include metabolic imbalances (such as hypoglycemia, hyponatremia, or hypocalcemia); infections (including meningitis or encephalitis); substance abuse; exposure to toxins; and other neurologic conditions, including stroke, cerebral malformations, and brain tumors. Control of the underlying condition under some circumstances can result in complete seizure control. In other cases, anticonvulsant drugs must be continued.

**NONEPILEPTIC VS EPILEPTIC SEIZURES**

Nonepileptic events at times can mimic epileptic seizures. These include vasovagal syncope; orthostatic hypotension; migraine; cardiac diseases; sleep disturbances (such as narcolepsy); movement disorders; and a host of psychiatric conditions that include hyperventilation syndrome, anxiety states, and psychogenic nonepileptic seizures (often called pseudoseizures or psychogenic seizures). If any of these are present, the response to anticonvulsant therapy would be expected to be poor, since the episodes are not caused by epilepsy. Thus, the first and foremost task in the successful management of a patient’s epilepsy is to establish whether the patient actually has the disorder.

Patients with epilepsy may experience more than 1
type of seizure. A semiologic classification system developed in 1998 classifies seizures according to behavioral or symptomatic criteria, including sensory symptoms (eg, auras), level of consciousness, autonomic signs, and motor phenomena (eg, tonic or tonic-clonic movements). This method of classification allows diagnosis of seizure type to be made strictly on historic data. Other methods of diagnosis also are useful. The EEG is an important tool for classifying seizures. Standard EEG, however, is limited by the fact that it is unlikely to record a seizure in the brief time the sample is taken. Sleep deprivation increases the chance of making the diagnosis, as do repeat tracings or prolonged monitoring, including prolonged ambulatory monitoring (similar to the Holter monitor for cardiac arrhythmias); however, the standard today for diagnosing epilepsy is the performance of video EEG monitoring. With prolonged recording, it is possible both to view the actual event and to review the EEG changes in the brain at the time of the event. This usually makes it possible to distinguish epileptic events from nonepileptic events.

Once it has been determined that epilepsy is indeed the cause of a patient’s seizures, one must then determine the type of epilepsy, since different medications target different types of seizures. For example, petit mal or absence seizures are very different from complex partial seizures and yet the 2 are sometimes confused (Table). Petit mal seizures are generalized seizures, which affect the entire cortex at seizure onset, whereas complex partial seizures (sometimes referred to as psychomotor or temporal lobe seizures) begin in a restrict-

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>PNES</th>
<th>CPS</th>
<th>Petit Mal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warning (“aura”)</td>
<td>May or may not occur</td>
<td>May or may not occur</td>
<td>Does not occur</td>
</tr>
<tr>
<td>Onset of loss of responsiveness</td>
<td>Gradual or abrupt</td>
<td>Can be abrupt or preceded by warning</td>
<td>Abrupt</td>
</tr>
<tr>
<td>Symptoms/signs at onset</td>
<td>Variable, including sensory symptoms; palpitations; headache; dyspnea; and unusual odors, tastes, or sensations. There may be unilateral motor or sensory changes.</td>
<td>Variable, including unusual odors, tastes, or sensations. There may be unilateral motor or sensory changes.</td>
<td>Typically none prior to loss of consciousness and onset of staring.</td>
</tr>
<tr>
<td>Motor behaviors during event</td>
<td>Variable, including thrashing; trembling; stiffening; semiautomatic activities; motionlessness; or staring.</td>
<td>Automatisms common but may be motionless.</td>
<td>Often motionless, staring</td>
</tr>
<tr>
<td>Vocalizations during event</td>
<td>Crying; yelling; screaming; or sobbing. There may be more complex dramatic, tragic, obscene, or mystical utterances.</td>
<td>A variety of utterances may occur. If seizure generalizes, cry may occur at onset of generalized seizure and grunting may accompany motor signs of generalized seizures.</td>
<td>Typically none</td>
</tr>
<tr>
<td>Injury</td>
<td>May occur</td>
<td>May occur</td>
<td>Typically does not occur</td>
</tr>
<tr>
<td>Urination and defecation</td>
<td>Both are reported</td>
<td>Both are reported</td>
<td>Unusual</td>
</tr>
<tr>
<td>Duration</td>
<td>Longest: often longer than 2 minutes</td>
<td>Typically 1 to 2 minutes</td>
<td>Typically less than 1 minute; may last seconds. The longer the episode, the more likely it will resemble a CPS</td>
</tr>
<tr>
<td>Age of onset</td>
<td>Any age</td>
<td>Typically second decade or later</td>
<td>Typically first or second decade</td>
</tr>
<tr>
<td>EEG during periods of unresponsiveness</td>
<td>Normal</td>
<td>Abnormal—typically focal epileptiform discharges</td>
<td>Abnormal—typically generalized 3-per-second spike and slow wave discharges</td>
</tr>
</tbody>
</table>

ed region of the cortex, sometimes called the seizure focus or epileptogenic region, which generally is in the temporal or frontal lobe. Most common in childhood, petit mal epilepsy has a unique EEG pattern that suggests a unique pathophysiology. Clinically, absence seizures are marked by a brief interruption in motor and mental activity, often without change in muscle tone or posture. These attacks generally last fewer than 30 seconds; the individual may appear to be staring into space for this period. Petit mal seizures are sometimes accompanied by movements of the face and/or automatisms (eg, lip smacking or fumbling motions with the fingers), but these are neither as dramatic nor as long lasting as are the complex partial seizures usually seen in adolescents or adults. There is neither a prodrome nor postictal state with true petit pal seizures, and the individual usually has no recall of what occurred during the seizure.

By contrast, complex partial seizures are associated with partial to complete impairment of awareness and may be associated with various psychic symptoms, including memory flashbacks (déjà vu sensations), dreamlike states, sensations of fear, or hallucinations of various types. As with absence seizures, the stricken individual may stare blankly and may exhibit automatisms; however, with complex partial seizures there are more likely to be auras or postictal states marked by confusion, headache, or other signs and symptoms. The EEG in patients with complex partial seizures shows focal epileptiform discharges, which are quite different from the generalized discharges that occur in cases of petit mal epilepsy.

**Psychogenic Nonepileptic Seizures**

One other important type of “mistaken identity” includes psychogenic nonepileptic seizures (PNES), or seizures that result from psychologic disturbance rather than from the abnormal electrical discharges in the brain that cause epilepsy (Table). In epilepsy referral centers, about 20% of patients are found to have PNES.9 PNES is more commonly seen in women (70% of cases) than in men. The underlying psychiatric mechanism varies; conversion reactions are present in some but not all patients with PNES. Sexual or physical abuse has been found to be present in some, but again, not all patients.10

Although the prevalence of PNES is nearly as high as that of multiple sclerosis or trigeminal neuralgia (2 to 33 per 100 000),10 misdiagnosis is not only common, but can persist for decades, which suggests that physicians often do not maintain a high enough index of suspicion for the disorder. Reuber et al studied 313 consecutive patients with PNES and found that, on average, patients were accurately diagnosed 7.2 years after the onset of PNES (SD = 9.3 years). Relatively younger age, EEG findings thought to be interictal epileptiform potentials, and treatment with anticonvulsant medications have been associated with longer delays—of up to 50 years in some cases—because once a patient has begun antiepileptic drug (AED) therapy, it is assumed that he or she has epilepsy.11 Patients in such cases are exposed to inappropriate pharmacotherapy and its associated adverse reactions; moreover, they are deprived of the psychiatric therapy they require. It is particularly important to be aware that EEGs are frequently misinterpreted12; EEGs thought to have interictal epileptiform potentials may actually be normal.

Video EEG monitoring interpreted by an experienced epileptologist allows for a definitive diagnosis in the majority of cases of PNES.9 Nonetheless, once the diagnosis is recognized, only about 30% of patients respond well to psychiatric treatment13,14; younger patients and those who have suffered from their episodes for shorter periods of time tend to have the best prognoses.10,11 It is important to note that 10% to 30% of patients with PNES also have epilepsy—these individuals require AED therapy as well as treatment for PNES. By contrast, some patients who had been thought to have PNES are found to actually have epilepsy during video EEG monitoring.

**Anticonvulsant Failure: The Wrong Drugs, the Wrong Dosages?**

Studies reveal that 96% of patients with epilepsy take multiple anticonvulsant drugs that sometimes require a complex dosing schedule; this, in turn, can complicate compliance.15 The literature also shows that if appropriate medication is selected, control of seizures often can be achieved with a single drug.

**Monotherapy—Finding the Appropriate Dose**

The idea that monotherapy can be used successfully to treat seizures is not a new concept,16,17 but its value was confirmed in a study by Kwan and Brodie, who evaluated 525 unselected, untreated, previously undiagnosed patients with epilepsy. These patients were started on AED therapy and followed for 5 years. Sixty-one percent of patients were seizure free with single-drug therapy: 47% with the first drug selected, 13% when a second drug was substituted, and 1% after a switch to a third type of monotherapy.18,19 Moderate daily anticonvulsant doses were often effective with the following therapies: carbamazepine ≤800 mg/day, valproate ≤1500 mg/day, or lamotrigine ≤300 mg/day. The most common dose range was 400 to 600 mg for carbamazepine, 600 to 1000 mg for valproate, and 125 to 200 mg for lamotrigine.20

Some patients do not respond to the above doses of medication, and for these individuals, higher doses are often needed. One way to determine the appropriate...
maximal dose is to check anticonvulsant blood levels, but this must be done carefully. For example, some years ago, a study showed that unbound carbamazepine and phenytoin levels might better reflect clinical effects in the case of medications that are highly protein bound, because only the unbound fraction penetrates into the brain. Unbound levels ranged from 0.14 to 3.3 mcg/mL for carbamazepine and 1.9 to 3.6 mcg/mL for phenytoin, with toxicity occurring with free phenytoin levels >3 mcg/mL.17 In a more recent study, Christensen et al concluded that optimal response to topiramate occurred at plasma concentrations above 2 mcg/mL, with toxicity occurring at concentrations above 10.5 mcg/mL.21 Further studies like these are needed.

Pending such studies, a key point to understand is that so-called “normal” plasma concentrations of anticonvulsants, as listed on laboratory slips, are often not based on formal studies, and there are only limited data correlating laboratory values with either anticonvulsant efficacy or toxicity. It is better to titrate patients on a case-by-case basis to the medication dose that controls their seizures without producing side effects. Blood levels can be useful as a guide, but many patients require levels outside of the ranges printed on the laboratory slips in order to achieve seizure control. There may be a variety of reasons for the wide variation in optimal doses for patients; relevant factors include drug absorption, mechanism of drug action, receptor properties of brain cells, and protein binding.

**MONOTHERAPY VS POLYPHARMACY**

A study conducted by Schmidt of 30 patients with intractable complex partial seizures supports the notion that polypharmacy often creates no advantage over monotherapy. In this long-term prospective study of adults who failed to respond to the maximum dose of carbamazepine, phenytoin, phenobarbital, or primidone as their first drug, a second drug was added in escalating doses as necessary until clinical toxicity occurred. The drug that seemed to be the most promising given the patient’s past history was selected as the additional drug and included either carbamazepine, clobazam, clonazepam, phenobarbital, phenytoin, primidone, or valproic acid. Of the 30 patients evaluated, 5 experienced >75% reduction in seizure activity (although only 2 were seizure free), 6 had <50% reduction in seizures, 12 noticed no change, and 7 patients reported increased numbers of seizures. In 3 patients, the frequency of seizures increased by more than 100% after adding a second medication.22 Two-drug therapy may result in improved seizure control in a minority of patients, but not in most. Unfortunately, there are only limited data available in regards to when 2-drug therapy is likely to improve seizure control. There is little or no evidence that the use of 3 drugs further improves seizure control. In addition, polypharmacy increases the likelihood of side effects. In one study, the incidence of adverse reactions rose from 20% with monotherapy to 45% with the addition of 2 or more medications.23

For these reasons, whenever possible, no more than 2 anticonvulsant drugs should be used at the same time. When a single drug is effective, it should be maintained since it simplifies treatment, decreases the likelihood of side effects and/or interactions with other drugs, improves compliance, and lowers costs for the patient. If a patient is already on more than 1 AED and a trial of monotherapy seems appropriate, it is important to withdraw the other drug slowly, sometimes over several months. This author prefers to first eliminate sedative drugs (eg, phenobarbital, benzodiazepines), in part to eliminate sedative effects. In addition, many clinicians feel that medication withdrawal seizures can be more frequent with use of at least some sedative drugs, such as phenobarbital, although this was not confirmed in a study.24 It is known that when a patient takes a medication at a given dose, it takes 5 to 7 half-lives for that drug to reach steady state in blood levels.25 For that reason, as a rule of thumb, this author waits at least 5 to 7 half-lives of a drug between each change of dose—at times longer—to decrease the possibility of withdrawal seizures and to reduce the likelihood of other withdrawal effects.

It also is important to recognize that different forms of the same drug may be absorbed differently. A variation in the formulation of the drug given by the pharmacy from month to month can result in decreased anticonvulsant drug levels and seizures or, at increased levels, toxicity. To avoid these problems, it is best for the patient to take the same formulation of the medication from month to month.26

**FINDING THE APPROPRIATE DRUG**

Marson et al performed a series of meta-analyses of randomized placebo-controlled trials in which the newer anticonvulsants (ie, gabapentin, lamotrigine, tiagabine, topiramate, vigabatrin, and zonisamide) were used as supplemental therapy in patients with refractory partial epilepsy. In the studies reviewed, the efficacy and tolerability of these drugs had been compared to placebo or to one another. Twenty-nine trials (n = 4091 patients) were examined. The researchers found that all of the AEDs studied were more effective than placebo. When drugs were cross-compared, confidence intervals overlapped and there was no conclusive evidence of differences in efficacy or tolerability, although trends suggested that some differences might be present.27,28

A panel of experts, the Therapeutics and Technology Assessment Subcommittee and Quality
As prescribed. However, in one study, when patients were prescribed medication 3 or 4 times per day, compliance decreased to 64% and 35%, respectively. The frequency of dosing depends on a number of factors. The faster the drug is metabolized, the more often it needs to be taken. The slower the absorption, the less often it may need to be taken. On the other hand, if a drug is taken less often, a higher dose may be needed. In this case, each dose is given each time, and if a particular total daily dose is needed, the drug may have to be taken more often each day.

**Drug Interactions**

Drug interactions can occur whenever the patient is taking medication for other problems, and that medication is not limited to prescription drugs. Patients should be asked about herbal remedies they may be taking that can alter the metabolism of AEDs. Additionally, the patient’s age may affect how his/her body responds to an anticonvulsant medication. In the elderly, the fraction of active drug unbound to protein may be higher and, if so, increased amounts of drug may enter the brain. For this reason, elderly patients often need lower doses than do younger patients. Whether a patient is younger or older, starting a drug at a low dose and slowly titrating upward is the best way to avoid adverse effects and can help to determine the optimal dose.

**Withdrawal of Medication**

Medication does not control seizures in all patients, but it can help some become seizure free. For these patients, it is important to determine when medication may safely be withdrawn. Shinnar et al studied 88 children in whom antiepileptic medications were discontinued after they had not experienced an episode in 2 to 4 years. They followed these patients for a mean of 22 months (6 months to 5 years) and found that 75% could be successfully taken off their medicines without seizure recurrence. The authors reported that a history of complex partial seizures, younger age of onset, and certain characteristic patterns on EEG carried a more favorable prognosis. This study suggested that, in many cases, it would be possible to predict reasonably well which children could safely stop therapy.

A prospective study followed 1013 adults for 2 years. Of these, 510 were randomized to be slowly tapered off their medicines, and 59% remained seizure free after medications were slowly discontinued, compared with 78% who continued to be seizure free while remaining on medication. In the latter group, longer periods of seizure control resulted in lower risk of
seizure recurrence; use of multiple drugs and history of tonic-clonic seizures increased the risk of recurrence. Of the 409 patients whose seizures recurred following withdrawal of therapy, 95% had been seizure free for at least 1 year at 3 years postseizure recurrence, and 90% were seizure free for 2 years at 5 years postseizure recurrence. Risk of seizure recurrence was greater if the duration of the seizure-free interval was shorter, if the patient had experienced seizures during treatment, or if the patient experienced partial seizures at seizure recurrence. Patients who restarted or increased treatment at seizure recurrence increased the probability of further periods of 1- or 2-year remission by about 30%.

The Quality Standards Subcommittee of the American Academy of Neurology reviewed the literature and concluded that in both children and adults, the likelihood of continued remission after medication withdrawal was greater for patients who had been seizure free for 2 to 5 years, had a single type of partial or generalized seizure, had a normal neurologic examination and normal intelligence, and had an EEG that normalized with treatment.

**Surgery—A Last Resort?**

When individuals with refractory epilepsy do not respond to pharmacologic therapies, surgery should be considered. Surgery carries risks, including those associated with anesthesia, the physical risks associated with the procedure, and the risk that the surgery will be unsuccessful. However, the decision to forgo surgery also carries risks, including continued uncontrolled seizures, the risks of injury or death, and psychosocial risks, such as limitations on driving or occupation.

To select appropriate surgical candidates, a thorough review of the patient’s history and a series of key diagnostic tests, including EEG, magnetic resonance imaging (MRI), computed tomography, positron emission tomography (PET), and video EEG monitoring are essential (Figure). PET scans are needed in some patients. Video EEG monitoring is probably the most important single test because it allows the clinician to observe the manifestations of the seizures and to correlate these with the EEG in order to localize where the seizures originate and exclude the possibility of nonepileptic seizures. MRI is also important in helping to assess the presence of structural lesions, because they might give clues regarding the site of seizure onset.

In 1997, McLachlan et al conducted a prospective study that followed surgically vs medically treated patients with temporal lobe epilepsy. Seventy-two patients underwent temporal lobectomy with continuing medical management, and 21 patients with the same diagnosis had medical management alone. At 24 months, 88% of patients who had undergone surgery reported a 90% to 100% reduction in seizure activity. This occurred in 8% of patients treated with medication alone.

Wiebe et al performed a randomized controlled study that compared epilepsy surgery (40 patients) to continued treatment with anticonvulsants (40 patients). At the end of 1 year, 58% of the surgery group was seizure free, compared with only 8% of those taking medicine alone. An accompanying editorial concluded that these results strongly support the value of epilepsy surgery in patients with intractable epilepsy. Temporal lobectomy is not necessarily a cure; about one third of patients experience seizure recurrence if anticonvulsants are discontinued after surgery, nevertheless, many patients will be able to take less medication to maintain seizure control.

Patients who undergo resections outside of the temporal lobe have a lower success rate. With anterior temporal lobectomy, approximately 70% of patients are seizure free, 20% show improvement, and 10% show no improvement. With extratemporal resections, approximately 45% become seizure free, 35% show improvement, and 20% show no improvement.

After hemispherectomy, 70% to 80% are seizure free. (These patients typically have widespread areas of potential epileptogenesis in 1 hemisphere, resulting in hemiparesis and hemisensory loss.) Despite the extensive resection, intellectual function often improves after surgery; however, there are potential serious complications with this procedure, which include subarachnoid bleeding, hemosiderosis, blockage of cerebral spinal fluid, and hydrocephalus.
Key Points: Pharmacologic Management of Seizures

- Confirm that the patient has epilepsy!
- First control underlying conditions that may be causing seizures (e.g., metabolic imbalances—hypoglycemia, hyponatremia, or hypocalcemia; infections—meningitis or encephalitis; substance abuse; exposure to toxins; stroke; cerebral malformations; brain tumors)
- Select the appropriate drug based on seizure type and patient history
- Treat with 1 drug, rather than multiple drugs, if possible
- Choose a regimen that requires fewer doses per day to improve compliance
- Keep the drug formulation the same each month

Callosotomy

Corpus callosotomy is a procedure whereby the large fiber bundle that connects the 2 sides of the brain is severed. This procedure is most effective for atonic-tonic seizures (“falling seizures”), generalized tonic-clonic seizures, and multifocal or generalized seizure discharges, and at times has been used for specific syndromes, such as Lennox-Gastaut syndrome. Though this procedure is palliative and not curative, seizure frequency is reduced by an average of 70% to 80% after partial callosotomy and 80% to 90% after complete callosotomy. Generalized tonic-clonic seizures, and seizures manifested by falling are particularly likely to decrease in frequency. On the other hand, focal seizures may actually become more severe and cognition may worsen afterwards; therefore, appropriate patient selection is vital to this procedure’s success.

Vagal Nerve Stimulation

The vagal nerve stimulator is a small electrical device that is placed in the chest and connects to the vagus in the neck. It stimulates this nerve according to a predetermined intermittent program and also may be patient- or family-triggered via a magnet in response to epilepsy prodromes, such as auras, or in response to seizures. It is unclear by what mechanism the vagal nerve stimulator functions to suppress a seizure from occurring, or how it results in seizure termination when the magnet is used; however, its use results in improved seizure control in a number of patients. Adverse reactions are generally mild, but may include hoarseness, throat discomfort, or dyspnea. About 10,000 patients have had a vagal nerve stimulator implanted. Of these, about one third have experienced a >50% reduction in seizures, although only a few become seizure free; one third experience a 30% to 50% reduction in seizures; and one third, a <30% reduction. In a study of 454 patients of whom 440 yielded assessable data, median seizure reductions compared with baseline were 35% at 1 year, 44.3% at 2 years, and 44.1% at 3 years. A ≥50% reduction postimplantation occurred in 36.8% of patients at 1 year, in 43.2% at 2 years, and in 42.7% at 3 years. Median seizure reductions compared with baseline were 35% at 1 year. Although vagal nerve stimulation is generally not a cure, with only a small fraction of patients (1% to 2%) becoming seizure free, many find the vagal nerve stimulator to be a valuable therapy. In this study, continuation rate was 72.1% at 3 years.

Conclusion

Epilepsy is a clinical syndrome characterized by uncontrolled electrical activity in the brain that is manifested as seizures. It affects millions of people worldwide and may severely affect the daily lives, safety, and health of those affected, especially if their seizures are not easily controlled. Anticonvulsant therapy failure or medication side effects may occur because of misdiagnosis, selection of the wrong drug, or use of the wrong dose. Excluding other clinical entities that mimic epilepsy (via video EEG monitoring) is the first step in helping individuals with refractory seizures. Syncope and psychogenic episodes rank among those most commonly confused with epilepsy, and failure to recognize them may cause a delay in the true diagnosis of many years, during which time patients are subjected to the costs and adverse effects of inappropriate medications. Complex multidrug regimens can be avoided if monotherapy with the correct medication is employed at an adequate dose. Polypharmacy often is responsible for noncompliance due to impractical medication schedules and adverse effects. If the patient continues to have seizures despite efforts to optimize therapy, surgery should be considered.

REFERENCES


