

Advances in managing epilepsy

Even with newer medications and surgical options, the goal of optimal patient management remains the same: seizure free without side effects.

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More than 2.5 million people in the United States and over 50 million worldwide suffer from epilepsy. In the United States, more than 300,000 people with epilepsy are younger than 14 and more than 500,000 are older than 65. Each year, 150,000 people in the United States are newly diagnosed as having epilepsy with the cumulative lifetime incidence approaching 3%.¹ Although most people with epilepsy become seizure free with appropriate therapy, 30% to 40% of patients will continue to have seizures despite the use of antiepileptic drugs (AEDs) either alone or in combination.²

While the basic, underlying risk of developing epilepsy is about 1%, individuals in certain populations are at higher risk. It is estimated that epilepsy can be expected to develop in

- 10% of children with mental retardation
- 10% of children with cerebral palsy
- 50% of children with both disabilities
- 10% of patients with Alzheimer's disease
- 7% of ischemic stroke patients
- 15% of hemorrhagic cortical stroke patients
- 8.7% of children of mothers with epilepsy
- 2.4% of children of fathers with epilepsy
- 33% of people who have had a single, unprovoked seizure.^{1,3}

Characterizing seizures

Epilepsy is a chronic neurologic condition characterized by recurrent, unprovoked seizures and is classified as idiopathic or symptomatic. Idiopathic epilepsy may be genetic in origin, and the patient has no other signs of neurologic disease or mental deficiency. Symptomatic or cryptogenic epilepsy results from a known condition, such as stroke, head injury, poisoning, Lennox-Gastaut syndrome, or cerebral palsy.⁴

Certain areas of the brain are likely to be involved in seizure activity. The motor cortex, which is responsible for body movement, and the temporal lobes, including the hippocampus, which is involved in memory, are particularly sensitive to biochemical changes such as decreased oxygen level, metabolic imbalances, and infection that provoke abnormal brain cell activity.

Seizures are classified as partial and generalized (see Table 1, page 30). Partial-onset seizures involve only a portion of the brain at onset and can be further divided into two types:

- Simple partial, in which consciousness is not impaired

Article at a glance

- Epilepsy is a chronic neurologic condition characterized by recurrent, unprovoked seizures.
- The goal of optimal epilepsy management is seizure free without side effects.
- Primary care physicians play a major role in caring for patients with epilepsy.
- The mainstay of epilepsy treatment is antiepileptic drugs (AEDs).
- AED selection is primarily based on clinical efficacy, safety, tolerability, drug interaction profile, and ease of use, but affordability needs to be considered as well.
- Despite a lack of head-to-head trials in the United States, second-generation AEDs (gabapentin, lamotrigine, and oxcarbazepine) have been compared with carbamazepine as monotherapy and have been found to have better tolerability but with no difference in efficacy.
- Depression, anxiety, and attention-deficit hyperactivity disorder are common comorbidities of epilepsy.

TABLE 1
Types of seizures

Simple (awareness retained)

Motor symptoms: Jerking, muscle rigidity, spasms, head turning

Sensory symptoms: Unusual sensations affecting vision, hearing, smell, taste, or touch

Autonomic symptoms: Stomach sensation

Psychological symptoms: Memory or emotional disturbances (déjà vu, fear)

Complex (awareness impaired)

Automatisms such as lip smacking, chewing, fidgeting, walking, and other repetitive, stereotyped movements

Partial seizures that become generalized

Begins as partial (simple or complex) and evolves into grand mal seizure (unconsciousness, convulsions, muscle rigidity)

- Complex partial, in which consciousness is impaired.

Both types can spread, resulting in secondarily generalized tonic-clonic seizures. About 70% of adult patients with epilepsy have some type of partial-onset seizures, and approximately 50% of these have both partial seizures and generalized tonic-clonic seizures. In general, these latter seizures are easier to control (followed by complex partial seizures and then simple partial seizures) because seizure medications are typically more effective in blocking seizure spread than in preventing initiation.

Generalized seizures are those in which the first clinical changes indicate that both hemispheres are initially involved. Consciousness usually is impaired during generalized seizures, although some myoclonic seizures may be so brief that impairment of consciousness cannot be assessed.

Causes and risk factors

Many abnormalities of the nervous system can result in seizure activity. Seizures can also occur in the normal nervous system when its metabolic balance is disturbed (see Table 2, page 31). Certain genetic and environmental factors may be involved, including head trauma, brain tumor,

stroke, medication, and infections. About 35% of all cases of epilepsy have no clearly definable cause.²

Treatment

Only 15% to 20% of patients with new-onset epilepsy are initially seen by a neurologist, with primary care clinicians providing approximately 40% of the long-term management of epilepsy patients with or without initial consultation with a specialist.⁵ Thus, primary care clinicians play a vital role in the treatment of patients with epilepsy with ongoing seizures. Many patients who have a single seizure or recurrent seizures can be safely and appropriately cared for by a primary care physician, although it may be best to coordinate initial care with a neurologist and/or an epileptologist (see the algorithm, “Evaluation and management of seizures,” page 32).

Once the initial evaluation is complete, the mainstay of epilepsy treatment is AEDs. Prior to 1993, the choice of an anticonvulsant was limited to 5 medications—primidone, phenytoin, carbamazepine, phenobarbital, and valproate. While these medications continue to be widely used, they continue to be problematic because of the narrow therapeutic window of dosing, frequent dose-dependent CNS side effects, and rare but severe idiosyncratic end-organ toxicities.

Since 1993, 8 AEDs have been approved by the FDA (see Table 3, page 33). While several of the newer drugs are approved for monotherapy, only one—oxcarbazepine—is approved for initial monotherapy. Although there are subtle differ-

Drugs mentioned in this article

Carbamazepine (Epitol, Tegretol, Carbatrol)	Phenytoin (Dilantin, Phenytek)
Felbamate (Felbatol)	Primidone (Mysoline)
Gabapentin (Neurontin)	Tiagabine (Gabitril)
Lamotrigine (Lamictal)	Topiramate (Topamax)
Levetiracetam (Keppra)	Valproate (Depakote)
Oxcarbazepine (Trileptal)	Zonisamide (Zonegran)
Phenobarbital	

TABLE 2

Causes of epilepsy**Genetic factors****Head trauma****Stroke****Metabolic disturbances**

Electrolyte imbalance

Kidney failure with uremia or changes that occur with kidney dialysis

Hypoglycemia or hyperglycemia

Hypoxia

Liver failure and elevation of associated toxins

Infection

Infections of the nervous system (including meningitis, encephalitis, HIV and related infections)

Neurodegenerative disease

Alzheimer's disease

Prion-related disorders

Creutzfeld-Jakob disease

Degenerative diseases of childhood

Phenylketonuria

Tay-Sachs disease

Neurocutaneous syndromes

Neurofibromatosis

Sturge-Weber syndrome

Tuberous sclerosis

Febrile seizures**Medications, drugs, and alcohol**

Overdose of and abrupt withdrawal from some prescription drugs

Chronic recreational drug use (cocaine, heroin, amphetamines, phencyclidine [PCP])

Alcohol withdrawal

Poisoning from carbon monoxide, lead, and other heavy metals

Other substances include the following:

Antipsychotic medications (chlorpromazine, haloperidol, clozapine)

Aminophylline

High doses of penicillin

Lithium

Tricyclic antidepressants

Brain tumors

Malignant and benign

ences in the FDA-approved indications for each of these agents, all have demonstrated efficacy as adjunctive treatment of partial seizures with or without secondary generalization. None of the new agents has a formal indication for the treatment of absence (brief loss of consciousness) and other forms of primarily generalized epilepsy, although topiramate is indicated for the treatment of generalized tonic-clonic seizures.^{6,7}

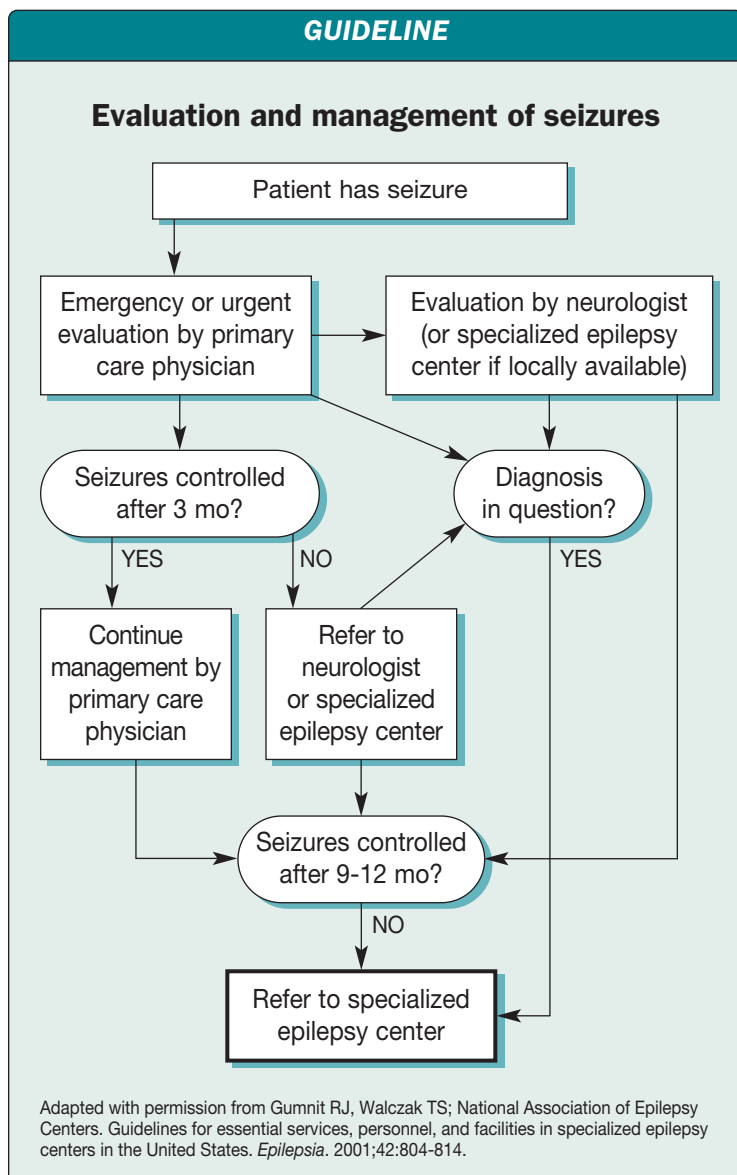
AEDs are selected first and foremost according to clinical efficacy, then safety, tolerability, drug interaction profile, and ease of use. Cost is a major factor in the underserved population. Most neurologists agree that monotherapy is currently the best pharmacotherapeutic option and is mandatory when first starting AED treatment. There is evidence to suggest that in people newly diagnosed with epilepsy, only a relatively small percentage of patients who do not achieve seizure control with monotherapy will do so with polytherapy. One study showed that of the 64% of patients who were newly diagnosed and who subsequently became seizure free, 61% were

seizure free on monotherapy, and 3% were seizure free on a 2-drug regimen.²

An appropriate drug for the seizure type and epilepsy syndrome with low adverse event risk and expected best efficacy should be selected, using accepted dosing guidelines and appropriate titrating to response. If monotherapy is poorly tolerated or ineffective, the strategy is to switch to another drug. If the first drug has partial efficacy and is well tolerated, it is worth trying another drug in combination. Add-on therapy appears to be more effective when started immediately after first-drug failure, rather than waiting until a second drug has also failed. Special issues for young women with epilepsy include contraception, pregnancy planning, teratogenicity, parenting, and breastfeeding.

Specific treatment concerns

Despite a much better understanding of, and an increased ability to predict drug-drug interactions, serious drug interactions still occur. More than 30% of all new seizures occur in the elderly;



because this population may be taking other medications, the addition of an AED can have profound effect on these other therapies.

Carbamazepine, oxcarbazepine, phenobarbital, primadone, and phenytoin (and topiramate to some extent) all enhance cytochrome P-450 microsomal oxidative enzyme activity, thereby increasing steroid hormone clearance. In women, these particular AEDs can cause significant alterations of sex hormones and decrease the efficacy of oral contraceptives. In children and adults, these AEDs may result in long-term endocrine effects, including bone loss and lipid, thyroid, and sex hormone abnormalities. Adults

taking AEDs are at increased risk for osteopenia and osteoporosis because of abnormalities of bone metabolism associated with AEDs and may require calcium and vitamin D supplementation. Physicians should counsel these patients about good bone health practices. Evaluation of bone health by measuring bone mineral density (BMD) is advisable after 5 years of AED treatment or before treatment in postmenopausal women.⁸

For most patients, antiepileptic monotherapy is less likely to cause unwanted side effects and more likely to control seizures. Other advantages of monotherapy include lower costs, ease of compliance, and decreased possibility of drug interactions. The older AEDs are known to have a problem with interactions among both other anticonvulsants and other therapeutic classes.⁹

Despite the array of new drugs, seizure control may not be achievable for all patients. From 60% to 70% of newly diagnosed patients will achieve remission once treatment with AEDs is initiated. The remainder—about 30% of patients—will continue to have recurrent seizures despite treatment.¹⁰

Disappointingly, these figures have remained largely static. Direct comparisons between newer and established AEDs show, that for partial seizures, there is little or no difference in efficacy between all the available drugs.¹¹

Are the new AEDs better?

One of the major differences between the older and the newer AEDs is the potential of the older drugs for significant interactions with other medications. Many of the drug-drug interactions involving the older AEDs are reciprocal, that is both drugs affect each other. In contrast, the newer AEDs have either no or limited drug inter-

TABLE 3
Second-generation antiepileptic drugs

Drug	Indication	Dosage
Felbamate	Adjunctive or monotherapy in adults with severe seizures; in children with Lennox-Gastaut syndrome when seizures are not controlled; use now largely restricted to patients with Lennox-Gastaut syndrome for whom benefits outweigh significant risk of fatal aplastic anemia and liver failure	Initiate at with 1200 mg/d (adults); 15-45 mg/kg/d (children)
Gabapentin	Adjunctive therapy for partial seizures with or without secondary generalization	Initiate at 300 mg/d; increase to 900-1800 mg/d (children >12 y)
Lamotrigine	Adjunctive therapy for partial seizures with or without secondary generalization; withdrawal to monotherapy	Initiate at 50 mg/d; increase to 300-500 mg/d; with valproic acid, start with 25 mg every other day; increase to 150 mg/d (children >16 y)
Levetiracetam	Adjunctive therapy for partial onset seizures in adults; pediatric indication filed with the FDA in January 2005	Initiate at 500 mg/d bid; increase in increments of 1000 mg/d every 2 wk to a maximum of 3000 mg/d
Oxcarbazepine	Adjunctive and monotherapy for partial seizures in adults; adjunctive treatment for partial seizures in children 4-16 y	In adults, initiate adjunctive therapy at 300-600 mg/d in 2 divided doses; dosage can be increased after 1 wk. Initiate monotherapy at 600-1200 mg/d in 2 doses. Higher dosages may be necessary when used as polytherapy in patients with refractory seizures. MHD levels of 10-30 mcg/mL are usually attained. Reduce dosage by half for patients with renal insufficiency. In children, initiate at 8-10 mg/kg/d in 2 divided doses. Children <8 y may need a higher dose relative to weight than older children. Increase dosage slowly to minimize side effects, with a target dosage of 10-50 mg/kg/d.
Tiagabine	Adjunctive therapy in adults and children 12 years and older for partial seizures	Initiate at 4 mg/d; increase by 4 mg at week 2, then 4-8 mg at weekly intervals up to 32 mg/d (children); up to 56 mg/d (adults)
Topiramate	Adjunctive therapy for partial onset of generalized seizures	Initiate at 50 mg/d; increase to 50-400 mg/d (children >16 y)
Zonisamide	Adjunctive therapy for partial seizures in adults	Initiate at 100 mg/d; increase to 200 mg/d at 2 wk for 2 wk, then 300 mg/d and 400 mg/d

Key: MHD, minimum hemolytic dose.

action potential, which allows increased ease of use and perhaps greater safety, especially for patients taking multiple medications.¹²

There is some question as to whether the new AEDs are superior to their older counterparts. While there have been no head-to-head trials comparing the newer drugs with the older ones,

gabapentin, lamotrigine, and oxcarbazepine have been compared with carbamazepine as monotherapy and have been found to have better tolerability, but with no difference in efficacy.^{13,14}

In 2004, the American Academy of Neurology (ANA) issued an evidence-based assessment of the efficacy, tolerability, and safety of 7 of the new

TABLE 4
Health and safety concerns
for patients with seizures

Driving restrictions (vary from state to state)
Avoidance of seizure precipitants
Alcohol
Recreational drugs
Sleep deprivation
Severe stress
Personal safety
Avoid operating heavy equipment
Avoid open heights (climbing ladders, onto roofs)
No swimming or bathing without a friend or family member nearby
Practice bicycle safety (helmets)

AEDs (gabapentin, lamotrigine, topiramate, tigabine, oxcarbazepine, levetiracetam, and zonisamide).¹⁵ The ANA practice parameter states that gabapentin, lamotrigine, topiramate, and oxcarbazepine have efficacy as monotherapy in newly diagnosed adolescents and adults with either partial or mixed seizure disorders. There is also evidence that lamotrigine is effective for newly diagnosed absence seizures in children.¹⁵

Because there are insufficient data for target concentration ranges for the newer AEDs, routine therapeutic drug monitoring is not required unless the patient is responding in an unexpected manner. Most of the new AEDs have not demonstrated significant interaction with other hepatically metabolized medications or potentially life-threatening adverse effects. However, they are 3 to 4 times more expensive than their older counterparts and have shown no evidence of being more effective.

Selecting an AED

Selection of either an older or newer AED for first-line therapy requires careful consideration, an individualized evaluation, and should be based on the following:

- Select an AED based on seizure type and epilepsy syndrome.
- For focal-onset seizures, select an AED based

on pharmacokinetics, side effect profile, dosing frequency, and cost since all available AEDs are efficacious.

- Start one AED at a time.
- If feasible, start AEDs at a low dosage and increase gradually. However, an initial therapeutic level of an anticonvulsant such as phenytoin becomes mandatory if the patient is susceptible to recurrent seizure activity. An alternative anticonvulsant can be substituted over time if clinically indicated. The dose escalation recommended in the labeling for AEDs may be well tolerated by otherwise healthy patients, but a slower dose escalation is usually necessary for patients on concomitant AEDs or psychoactive drugs or for those who have concomitant illnesses.
- Increase the dosage until either it is effective or side effects occur to define the maximum tolerated dose before deciding that it is ineffective.¹⁶

While drug therapy is the mainstay of epilepsy treatment, it is only one part of patient management. Patients also need information about their conditions and to be reminded about the practical issues related to their safety and well-being (see Table 4). The requirements for licensed drivers to report a seizure condition varies from state to state. A summary of state driving laws can be found at the Epilepsy Foundation Web site (<http://www.epilepsyfoundation.org>).

When to refer

When adequate seizure control is obtained, no further neurologic consultation is necessary. However, if seizures persist and cannot be brought under control within 3 months, a neurologist or epileptologist should be consulted.¹⁷ Once the seizures are fully controlled, care can be transferred back to the primary care physician. Should the initial diagnosis of epilepsy be in question, early referral to an epilepsy center is appropriate as evidence suggests that early, accurate diagnosis followed by optimal medical therapy may decrease seizure recurrence, reduce the number of drug trials, and minimize the impact of seizures.¹⁸ If 2 drugs have failed as monotherapy, the patient should also be referred to a neu-

Comorbidities of epilepsy

Depression is the most common comorbid condition that affects people with epilepsy, and it occurs 3- to 10-fold more often in those with uncontrolled epilepsy than in the general population.¹ Depression affects up to 55% of patients with recurrent epilepsy and up to 9% of those with well-controlled seizures, although estimates vary according to the patient population studied, disease severity, and methodology used.² Furthermore, the clinical presentation of mood disorders in patients with epilepsy often differs from that in nonepileptic patients and does not always concur with standard diagnostic criteria. This may lead to underrecognition or to varying estimates of their prevalence.

Anxiety is another common comorbid disorder in epilepsy. Despite its frequent occurrence in this patient group, the relationship between anxiety and epilepsy has been less thoroughly investigated than other psychiatric conditions. Estimates of its incidence in patients with epilepsy are crude and range from 3% to 50%, although incidences of up to 66% have been identified. Like other psychiatric disorders, anxiety can occur prodromally,

ictally, or postictally as an adverse consequence of antiepileptic drugs, or it may be an unrelated disorder.³

Other psychiatric comorbid conditions include psychoses and attention-deficit hyperactivity disorder (ADHD). Psychotic disorders affect 6% to 10% of patients with epilepsy.² The mechanisms of these disorders, although poorly understood, seem to be related to epileptic conditions, since their recurrence is linked to exacerbation of seizures. Children with epilepsy commonly show behavioral symptoms of inattention and hyperactivity, and some of these children have ADHD. Estimates of ADHD prevalence in children with epilepsy vary, although studies using standardized diagnostic criteria have documented ADHD in 14% to 40% of children, compared with 5% in otherwise normal school-aged children.⁴

1. Attarian H, Vahle V, Carter J, et al. Depression in epilepsy and intractability of seizures. *Epilepsy Behav.* 2003;4:298-301.
2. Gilliam F, Kanner AM. Treatment of depressive disorders in epilepsy patients. *Epilepsy Behav.* 2002; 3(5S):2-9.
3. Bazil CW. Comprehensive care of the epilepsy patient: control, comorbidity and cost. *Epilepsia.* 2004;45:3-12.
4. Dunn AW, Austin JK, Hareslak J, Ambrosius WT. ADHD and epilepsy in childhood. *Dev Med Child Neurol.* 2003;45:50-54.

orologist or epileptologist. Such patients may be candidates for brain surgery; if this is not feasible, polytherapy or vagus nerve stimulation (VNS) can then be considered.

Referrals may also be required for women who become pregnant, as anesthesia requirements during delivery may have to be carefully titrated, and for patients with comorbidities such as depression, anxiety, or attention-deficit hyperactivity disorder (see "Comorbidities of epilepsy").

Nonpharmacologic management

Surgery is an option for a small number of patients whose epilepsy cannot be controlled with medication. A good candidate for surgery has seizures that always begin in the same cerebral location, assuming that the tissue can be resected without creating deficits. Neurosurgeons generally avoid performing surgery in areas of the brain responsible for speech, hearing, and other important functions. Surgical options include

Lobectomy (lesionectomy) removes a small part of the brain where seizures originate. It is appropriate only for partial seizures.

Multiple subpial transection involves a series of small incisions are made that impede the spread of nerve activity. This procedure may be used when seizures originate in a part of the brain that cannot be removed.

Corpus callosotomy is used to treat uncontrolled generalized tonic-clonic seizures, complex partial seizures with drop attacks, and other generalized seizures. In this procedure, the surgeon severs the nerve fibers that connect the hemispheres of the brain to each other. Reduced seizure activity usually continues on one side.

Hemispherectomy is a last resort in children with severe brain damage on one side and seizures that do not respond to medication. It involves removing the entire affected side of the brain. The remaining hemisphere develops language and motor areas for both sides of the body. With

TABLE 5

Epilepsy treatment strategies for patients and physicians

Patients can . . .

- Take responsibility and control over their disease
- Stay informed
- Keep a seizure diary
- Monitor medication reactions
- Attend support groups or counseling
- Use medication-taking reminder systems (pillbox, alarm wristwatch, medication cues)

Physicians can . . .

- Establish a good relationship with the patient (spend adequate time with the patient and family)
- Schedule frequent visits
- Offer evening office hours for patients who work during the day
- Have the pharmacist send prescription reminders
- Refer patients to counseling and patient support groups
- Provide education about epilepsy and medications
- Provide written instructions
- Tailor the medication regimen to each patient
- Reinforce the need and value of treatment
- Use simple regimens

intense rehabilitation, many patients will lead functional lives.

Devices for epilepsy

In VNS, a small, pacemaker-sized device is implanted near the collarbone and attached to the vagus nerve. It delivers small bursts of electrical energy to the nerve, and therefore the brain at regular, preprogrammed intervals. Each device is programmed for the individual patient, and the patient or a caregiver has the ability to initiate or abort stimulation with the use of a handheld magnet.

It is thought that by stimulating the vagus nerve, electrical energy is discharged upward into a wide area of the brain, disrupting the abnormal brain activity responsible for seizures.¹⁹ A second theory suggests that stimulating the vagus nerve causes the release of special brain chemicals that decrease seizure activity. In some patients, seizure

frequency is reduced. Most patients remain on antiepileptic medication but may be able to reduce the dosage. Since 1997, VNS has been approved by the FDA for use as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with partial onset seizures that are refractory to antiepileptic medications.

In deep brain stimulation (DBS), electrodes are implanted into the brain, usually the thalamus, hippocampus, or temporal lobe. The equipment includes a pulse generator similar to a pacemaker, which is implanted under the chest as well as a tiny electrode and connecting wire. The implanted electrode stimulates the specific structures deep in the brain and may actually disrupt the circuits that generate seizures. Some clinical trials are looking at the effect of placing the electrode into the hippocampus. The investigators seek to determine whether the generator can detect a seizure at its onset and then deliver a stimulation in response, which could then teach the neurostimulator the patient seizure-onset pattern. Because the electrodes are placed directly into the brain, DBS is more risky than VNS. Currently, DBS is FDA approved only for Parkinson's disease and essential tremor.

Diet, lifestyle, and alternative interventions

A ketogenic diet is used in children who do not respond to standard therapy or cannot tolerate the side effects produced by AEDs. The diet is a high-fat, low-carbohydrate diet that fundamentally changes the body's metabolism from using glucose as a primary energy source to using ketones. A recent review of the results from numerous studies of the ketogenic diet found that over half of children with seizures unresponsive to AEDs have a 50% or greater decrease in seizure frequency with the ketogenic diet.²⁰

The ketogenic diet is most effective in children 10 and younger. Compliance, which is essential for controlling seizures, is difficult to maintain. The regimen often is initiated with a 12- to 24-hour fasting period. Every meal includes exact

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amounts of fats, proteins, carbohydrates, and beverages, and only those foods listed for the diet can be eaten. Snacking is discouraged and sugars are not allowed. Vitamin A and mineral supplementation must be given.

The diet should be undertaken only with close medical supervision. Children must be monitored for growth and nutritional deficiencies. Common complications include poor growth and poor weight gain, hypercholesterolemia, and constipation.

Yoga, acupuncture, aromatherapy, biofeedback, behavior psychotherapy, and meditation may improve the quality of life for patients with epilepsy. Patients who practice interventions that promote sleep and reduce stress may be able to abort seizure activity.

Fostering patient adherence

Persons with epilepsy sometimes miss taking their medication, with many reporting that missed medication had caused problems for themselves or their families. Reasons for noncompliance include complex medication regimens, limited access to medications, adverse effects, or feeling it was not important to take medication. Demographically, teenagers and adults younger than 60 are least likely to comply.²¹

Compliance is enhanced when clinicians work in partnership with the patient. Education, including information about drug half-lives and their importance in maintaining adequate drug levels may help, together with simple dosing schedule cues (pills placed near a toothbrush to facilitate the morning and evening dosage) and compliance reinforcement by the physician. Table 5 lists patient and physician strategies to improve as well as to identify and eliminate barriers to compliance (page 36). □

This consensus article was written by Jill Shuman in consultation with Drs Karceski, Kelley, and Schachter.

Dr Kelley discloses that he is on the speakers' bureau for Pfizer. Dr Schachter discloses that he is a consultant for and on the speakers' bureau for Pfizer and UCB Pharma. Dr Karceski discloses that he on the speakers' bureau for GlaxoSmithKline, Novartis, Eisai, and Cyberonics.

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REFERENCES

1. Epilepsy Foundation. Statistics, 2004. Available at: <http://www.epilepsy-foundation.org/answerplace/statistics.cfm>. Accessed January 26, 2005.
2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med*. 2000;342:314-319.
3. Jansen AC, Andermann E, Andermann F. Biparental inheritance in idiopathic generalized epilepsy. *Epilepsia*. 2003;44:1250-1254.
4. Blume WT, Luder HO, Mizrahi E, et al. Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. *Epilepsia*. 2001;42:1212-1218.
5. Willmore L. Care of adults with epilepsy in the United States. *Neurology*. 1997;48(6 suppl 8):S39-S43.
6. LaRoche S, Helmets S. The new antiepileptic drugs. *JAMA*. 2004;293:605-614.
7. Cole AJ. Initial individualized selection of long-term anticonvulsant drugs by neurologists. *Neurology*. 2004;63(suppl 4):1-2.
8. Pack AM, Morrell MH. Epilepsy and bone health in adults. *Epilepsy Behav*. 2004;5(suppl 2):S24-S29.
9. Vazques B. Monotherapy in epilepsy: role of the newer antiepileptic drugs. *Arch Neurol*. 2004;61:1361-1366.
10. Schmidt D, Gram L. Monotherapy versus polytherapy in epilepsy: a reappraisal. *CNS Drugs*. 1995;3:194-208.
11. Sandler JWAS. Some aspects of prognosis in the epilepsies: a review. *Epilepsia*. 1993;34:1007-1016.
12. Anderson G. Pharmacogenetics and enzyme induction/inhibition properties of antiepileptic drugs. *Neurology*. 2004;63(suppl 4):3-8.
13. Houtkooper MA, Lammertsma A, Meje JWA, et al. Oxcarbazepine: a possible alternative to carbamazepine? *Epilepsia*. 1987;28:693-698.
14. Dam M, Ekberg R, Loyning Y, et al. A double-blind study comparing oxcarbazepine and carbamazepine in patients with newly diagnosed, previously untreated epilepsy. *Epilepsy Res*. 1989;3:70-76.
15. French JA, Kanner AM, Bautista J, et al. Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004;62:1261-1273.
16. Tatum WO, Galvez R, Benbadis R, et al. New antiepileptic drugs: into the new millennium. *Arch Fam Med*. 2000;10:1135-1141.
17. Scheuer ML, Pedley TA. The evaluation and treatment of seizures. *N Engl J Med*. 1990;323:1468-1474.
18. Ross S, Estok RP, Chopra SS, et al. Management of patients with newly diagnosed epilepsy: a systematic literature review. *Am Fam Physician*. 2004;70:824,827-828.
19. Schachter SC, Wheless JW. The evolving place of vagus nerve stimulation therapy. *Neurology*. 2002;59(6 suppl 4):S1-2.
20. Jarrar RG, Buchhalter JR. Therapeutics in pediatric epilepsy, Part 1: the new antiepileptic drugs and the ketogenic diet. *Mayo Clin Proc*. 2003;78:359-370.
21. Buck D, Jacoby A, Baker GA, et al. Factors influencing compliance with antiepileptic drug regimes. *Seizure*. 1997;6:87-93.