

# Epilepsy Update, Part 2: Nursing Care and Evidence- Based Treatment

How to promote good health and quality of life in patients.

**OVERVIEW:** As new research has increased our understanding of epilepsy and the challenges patients with epilepsy face, the role of the nurse as an educator and advocate has grown. This article, the second in a two-part series, addresses the most important aspects of assessing and caring for patients with epilepsy—highlighting the seizure first-aid instructions that all family members of a patient with epilepsy should have; the teaching points to share with parents of young children with epilepsy; and online epilepsy resources for patients, family members, and health care professionals. The authors also discuss current medical, surgical, neurostimulatory, and dietary approaches to epilepsy treatment.

**Keywords:** epilepsy, pharmacologically refractory epilepsy, seizure, self-management, status epilepticus, treatment

Nurses play a critical role in promoting the best health outcomes for people with epilepsy by imparting information about the disease, teaching self-management skills, and discussing treatment options with patients and their families. The nurse's role, however, goes beyond that. As discussed in part 1 of this series, epilepsy presents numerous psychosocial challenges—it is a highly stigmatized, frequently misunderstood condition that may limit mobility and employment, as well as social and educational opportunities. Affected patients often have accompanying psychiatric or cognitive diagnoses and report having less self-efficacy for managing seizures and poor health-related quality of life. In addition to teaching patients and their family members about treatments, nurses must act as advocates, helping patients find

appropriate community resources, educating the public at large, and promoting positive attitudes toward people with epilepsy.

In this article, the second in a two-part series on epilepsy, we review important aspects of nursing care for patients with epilepsy, including questions to ask when assessing patients, seizure first-aid advice to offer family members, and teaching points to share with parents of young children with epilepsy. We discuss medical, surgical, neurostimulatory, and dietary approaches to epilepsy treatment and provide a list of online resources to share with patients who have epilepsy and their families.

## **NURSING CARE**

Although there is no definitive guideline that addresses comprehensive nursing care of patients with

epilepsy, by asking the right questions and giving the patient positive feedback about the ways in which she or he is managing epilepsy, nurses can identify and address the concerns and care needs of patients with epilepsy and their family members (for a list of self-management questions, see Table 1). Since assessment time may be limited, the first question to ask should be, “What is your biggest concern about your epilepsy?” The patient’s answer will then guide you in determining

- any knowledge deficits about the disease.
- the patient’s and family’s seizure treatment readiness.
- any epilepsy-related social, educational, or employment limitations.
- sexuality or reproductive concerns.
- the sufficiency of social support.
- the patient’s general mood and psychological state.

Nurses play a key role in identifying the need for further evaluation of possible psychiatric or neurocognitive conditions often diagnosed in people with epilepsy and in directing patients to the appropriate local and national resources, many of which can be found online (see *Resources*). Particularly helpful is the Epilepsy Foundation, which provides comprehensive information for patients and their families, health care providers, schools, community agencies, and first responders.

**Seizure first aid.** All people with epilepsy and their families should be taught the basics of first aid for seizures (see Table 2). Caregivers and family members can also benefit from being certified in cardiopulmonary resuscitation (CPR). Remind all patients with epilepsy that they should have a written seizure treatment plan that they carry with them at all times. Treatment plans should provide the following information:

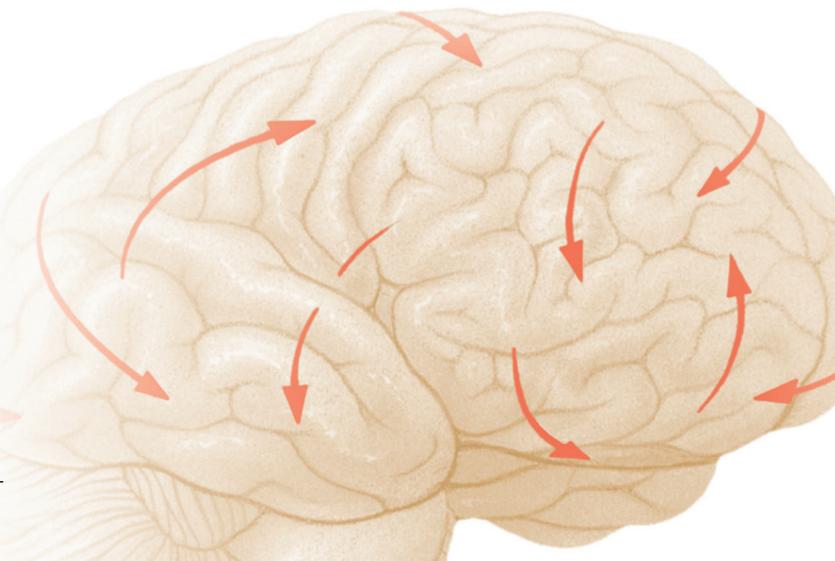
- the type of seizure the patient has had
- pertinent medical information, including whether the patient has a neurostimulator, is on an epilepsy diet, or has had epilepsy surgery
- prescribed dosage information for all maintenance and rescue antiepileptic drugs (AEDs)
- any interventions needed to address a breakthrough seizure

In addition to understanding seizure first aid, families need to be aware of the risk of sudden unexpected death in epilepsy (SUDEP) and of interventions that may be helpful in reducing the risk (see Table 3<sup>1</sup>). If a patient has a seizure while an inpatient or outpatient, nurses should follow their institution’s protocol for seizure intervention.

**Children with epilepsy.** Parents of children with epilepsy, like parents of children with any chronic disease, can find it challenging to adjust to uncertainties

in their child’s development. They benefit from receiving ongoing anticipatory guidance that promotes best health outcomes for the child and the highest quality of life for the family. Understanding that parental perceptions and concerns are often influenced by the length of time since their child’s diagnosis can help nurses develop appropriate care plans and better target patient and family education. A qualitative focus group study that examined the relationship between time since epilepsy diagnosis and prominent parental concerns sheds light on the guidance parents may require at the following stages<sup>2</sup>:

- *During the first year after diagnosis*, parents are adjusting to new medical terms and changes in routine. They may feel anxious over the unpredictability of their child’s seizures and unprepared to make decisions or solve problems related to their child’s care. Many have questions about possible causes of epilepsy and treatment effects. Providing them with a written seizure treatment plan (a template is available at [www.epilepsy.com](http://www.epilepsy.com)) will increase their ability to manage seizure activity and boost their confidence. It is also helpful for families to run periodic “seizure drills,” practicing what every family member should do if the child has a seizure. Parents may also experience heightened stress from relationship, health, sleep, work, education, and family management problems, so patient teaching should address these issues as well (see *Teaching Points for Parents of Children with Epilepsy*).
- *During the first five years following diagnosis*, parents continue to adjust to the chronicity of their child’s epilepsy and may share worries about the child’s future needs and express doubts that things will ever improve. It’s important for them to know about available resources and support during this time.



**Table 1.** Self-Management Questions and Points of Discussion in Assessing Epilepsy

• What is your biggest concern about your epilepsy?
• What information on epilepsy have you read or heard about?
• How will you handle your next seizure? Do you have a seizure treatment plan?
• Do you know what to do if you have any adverse treatment effects? Are you concerned about any current adverse effects?
• During the past month, have you been feeling down, depressed, or hopeless? How often?
• During the past month, have you felt less interest or pleasure in activities you once enjoyed? How often?
• For adults: Do you have any concerns about sexuality or reproduction?
• For women: Are you experiencing any menstrual irregularities, and do you have concerns about any sex-related health issues or pregnancy-planning questions?
• Do you have support from your family, friends, and community?
• Do you have any illness-related transportation issues?
• Do you have difficulty paying for medications or clinic visits?
• Do you have any school or employment concerns?
• What local, state, and national epilepsy resources do you find helpful?

- *After the first five years following diagnosis*, many parents feel they can handle their child's epilepsy care issues but remain uncertain about their child's future. It's important to assess the child's functioning to better help parents with future planning. For example, should they consider guardianship? Will their child be able to attend college or obtain vocational training? Many parents also demonstrate pride in having learned so much about their child's epilepsy care and express a desire to help other parents.

### PHARMACOLOGIC TREATMENT

Once epilepsy is diagnosed and intervention deemed necessary, the first-line treatment is an AED.<sup>3</sup> More than 20 AEDs are currently available, and numerous factors—including seizure type, epilepsy syndrome, cost, and such patient variables as age, sex, and comorbid conditions—must be considered when choosing which is most appropriate for the patient.

For example, divalproex (Depakote) is widely used and has a very broad spectrum of action. While it may be an excellent choice for certain forms of epilepsy, and for patients in whom the specific seizure type has not been precisely identified, it is not considered a first-line AED for young women owing to its adverse effects, which include irregular menses, fatigue, weight gain, risk of polycystic ovary syndrome, and elevated risk of teratogenicity.

Levetiracetam (Keppra), another commonly prescribed AED, is generally well tolerated, has reliable

pharmacokinetics and no significant drug–drug interactions, and is easy to titrate. Nevertheless, because it can cause irritability or mood disruption, it may be a poor choice for patients with preexisting behavioral problems or traumatic brain injury.

Topiramate (Topamax and others) is effective in controlling both seizures and migraines, but its adverse effects can include slowed cognition or word-finding difficulties, weight loss, and kidney stones. Thus, topiramate may be a poor choice for a patient who has cognitive difficulties, kidney stones, or anorexia. On the other hand, it may be an excellent choice for a patient with epilepsy who is also overweight or has migraines.

Genetics and ethnicity, too, may play a role in AED selection. For example, the life-threatening skin disorders Stevens–Johnson syndrome and toxic epidermal necrolysis are associated with the AED carbamazepine (Tegretol and others) in patients with the human leukocyte antigen allele HLA-B\*1502, especially in patients of Asian ancestry.<sup>4,5</sup>

Financial factors—such as insurance coverage and drug availability in generic form, which often makes a drug substantially less expensive than a brand-name product—may also influence choice of AED. There is controversy about the safety of switching from a brand-name AED to a generic formulation and from one generic formulation to another. Although a generic AED may deliver the same total drug as its brand-name equivalent, peak concentration times may vary.<sup>6</sup> Furthermore, generic formulations that are bioequivalent to a specific brand-name AED may not

be bioequivalent to each other.<sup>7</sup> If a generic product is prescribed, it is important that the patient ensure that the dispensing pharmacy can obtain the same generic formulation every month (that is, made by the same manufacturer) to avoid changes in the blood level of AEDs that could reduce seizure control.

The choice of first AED is commonly made in consultation with a neurologist, though some primary care providers have experience in the initial treatment of epilepsy and are up to date on available AEDs. When appropriately selected, the first AED controls seizures in approximately half of newly diagnosed patients.<sup>8,9</sup> If the first AED does not control seizures, then reasons for its lack of effectiveness must be explored (see Table 4). After one or two AED failures with good medication adherence, one of the following scenarios is likely.

- The patient has pharmacologically refractory epilepsy.
- The patient has a specific form of epilepsy that responds only to very specific AEDs.
- The events are not epileptic seizures.

In such cases, referral to an epilepsy center is recommended so that other medical, surgical, dietary, or neurostimulatory epilepsy treatments may be considered or nonepileptic causes explored.

**Status epilepticus (SE)**, as described in part 1 of this series, is a medical emergency that can occur in a person with established epilepsy or as the initial presentation of the disease. Rapid intervention is required to prevent neuronal damage, systemic complications, and death. Treatment should begin before the patient enters the hospital or ED. Those already diagnosed with epilepsy should carry a rescue medication, such as rectal diazepam (Diastat), with them at all times, in addition to a written seizure treatment plan.

The first interventions for SE include ensuring airway, breathing, and circulation. Emergency medical services or ED staff will check vital signs and blood glucose, secure IV access for rescue medication and fluid resuscitation, obtain an event history, and perform a screening neurologic examination. ED staff will, in most cases, initiate continuous electroencephalogram (EEG) monitoring and obtain a computed tomography (CT) scan of the patient's head.<sup>10</sup> They may also order a toxicology screening, lumbar puncture, and magnetic resonance imaging (MRI) of the brain if warranted by the event history or CT scan. The treatment goal is to determine the underlying cause of the seizure and stop both clinical and electrographic seizure activity. Rescue medications recommended in the consensus guidelines of the Neurocritical Care Society (NCS) include benzodiazepines (rectal diazepam, IV lorazepam (Ativan), or intramuscular midazolam), as well as phenytoin (Dilantin, Phenytek) or fosphenytoin with cardiac monitoring.<sup>10</sup> For refractory SE, the NCS guidelines also include valproate (Depacon), propofol

## RESOURCES

### Epilepsy

Centers for Disease Control and Prevention

You Are Not Alone: Resource Guide

[www.cdc.gov/epilepsy/toolkit/resource\\_guide.htm](http://www.cdc.gov/epilepsy/toolkit/resource_guide.htm)

Epilepsy Foundation

[www.epilepsy.com](http://www.epilepsy.com)

Epilepsy Resources for Patients and Families

[www.nichq.org/childrens-health/epilepsy/resources/epilepsy-resources-for-patients-and-families](http://www.nichq.org/childrens-health/epilepsy/resources/epilepsy-resources-for-patients-and-families)

Job Accommodation Network

Accommodation and Compliance Series: Employees with Epilepsy

<http://askjan.org/media/epilepsy.html>

Managing Epilepsy Well Network

[web1.sph.emory.edu/ManagingEpilepsyWell](http://web1.sph.emory.edu/ManagingEpilepsyWell)

World Health Organization

Global Campaign Against Epilepsy: Out of the Shadows

[www.who.int/mental\\_health/management/globalpilepsycampaign/en](http://www.who.int/mental_health/management/globalpilepsycampaign/en)

### Mental Health and Screening

American Academy of Pediatrics

Bright Futures

<http://brightfutures.aap.org>

Association for Behavioral and Cognitive Therapies and the Society of Clinical Child and Adolescent Psychology

Effective Child Therapy

[www.effectivechildtherapy.com](http://www.effectivechildtherapy.com)

Massachusetts General Hospital

School Psychiatry Program and Madi Resource Center

[www2.massgeneral.org/schoolpsychiatry/screeningtools\\_table.asp](http://www2.massgeneral.org/schoolpsychiatry/screeningtools_table.asp)

Nationwide Children's Hospital

Behavioral Health

[www.nationwidechildrens.org/mental-health-assessment-and-scoring-instruments](http://www.nationwidechildrens.org/mental-health-assessment-and-scoring-instruments)

NYU Langone Medical Center

Child Study Center

[www.aboutourkids.org](http://www.aboutourkids.org)

(Diprivan), phenobarbital, lacosamide (Vimpat), and levetiracetam.

### PHARMACOLOGICALLY REFRACTORY EPILEPSY

Nearly 40% of patients diagnosed with epilepsy require treatment with more than one AED, and those with refractory seizures may need to take three or more drugs in tandem.<sup>8,9,11</sup> For some of these patients,

**Table 2.** Seizure First Aid

1. Stay calm. Make sure the person's airway is clear and that her or his breathing is not impaired.
2. Prevent injury by clearing the area of any sharp or dangerous objects.
3. Time the seizure with a watch or clock. If it lasts more than five minutes, call 911.
4. Do not hold the person down if she or he moves around. There is no need to restrain a person having a seizure. Just offer supportive care.
5. Do not put anything in the person's mouth. Instead, turn patients on their side to help them breathe more easily and to prevent saliva or mucus from blocking the airway. (A person having a seizure is incapable of swallowing her or his tongue.)
6. Do not give the person water, oral medications, or food until she or he is fully alert.
7. After the seizure, place the person on her or his side. There is a small risk of postseizure vomiting before the person is fully alert. The head should be turned so that any vomit will drain out of the mouth without being inhaled. Stay with the person until she or he recovers (usually within 20 minutes).
8. When the person is alert, provide reassurance. Use simple language, be empathic and supportive, and encourage any bystanders to do the same.

Source: Epilepsy Foundation ([www.epilepsy.com](http://www.epilepsy.com)). To watch videos of seizure first aid and seizure aftercare, go to [www.epilepsy.com/epilepsy/firstaid](http://www.epilepsy.com/epilepsy/firstaid).

undergoing serial trials of various AEDs produces fewer adverse drug effects than reliance on a single AED, but it seldom results in true seizure control. In fact, the chance of seizure control diminishes with each successive trial of an AED (see Figure 1<sup>8,9</sup>). In a 20-year outcomes analysis,<sup>9</sup> conducted as a follow-up to a 14-year prospective study of children, adolescents, and adults diagnosed with epilepsy and treated with a first AED at the same epilepsy treatment center,<sup>8</sup>

about half of patients achieved seizure control with the first AED, but only about 11% of patients attained seizure control with the second drug as monotherapy, fewer than 1% did so with a third drug as monotherapy, and fewer than 3% achieved remission with a third trial of two or more AEDs.

In light of well-established data on AED success, neurologists can often identify pharmacologically refractory epilepsy in the early stages of treatment. For patients with this condition, nonpharmacologic treatments, such as surgical, neurostimulatory, and dietary treatments, are available, some of which offer patients advantages over pharmacologic choices. Comprehensive epilepsy treatment centers can not only provide such patients with a more definitive diagnosis, but they can also offer them a wide range of pharmacologic and nonpharmacologic treatment options. As with AED treatment, the choice of a specific nonpharmacologic intervention is influenced by its cost and by the patient's seizure type, epilepsy syndrome, age, sex, comorbid conditions, and insurance coverage.

### **EPILEPSY SURGERY**

Once the diagnosis of pharmacologically refractory epilepsy is established, evaluation for epilepsy surgery is indicated. The evaluation should be performed at a comprehensive epilepsy center by a multidisciplinary team that includes an experienced epilepsy surgeon. While there are many nonsurgical treatments for pharmacologically refractory seizures, in most cases surgery is the intervention most likely to stop the seizures.

In a controlled trial of 80 patients with temporal lobe epilepsy who were randomly assigned to either

**Table 3.** Interventions to Reduce Risk of Sudden Unexpected Death in Epilepsy (SUDEP)<sup>1</sup>

<ul style="list-style-type: none"><li>• Reduce the possibility of tonic-clonic seizures by providing optimum treatment and counseling about medication adherence and lifestyle interventions (regarding alcohol intake, nutrition, hydration, and sleep hygiene, for example).</li></ul>
<ul style="list-style-type: none"><li>• Medication changes should be gradual and staged; be aware of potential cardiorespiratory effects of certain antiepileptic drugs and use these drugs with caution.</li></ul>
<ul style="list-style-type: none"><li>• Persons with epilepsy should always carry a seizure intervention plan that provides instructions for first responders in the event of a breakthrough or worsening seizure.</li></ul>
<ul style="list-style-type: none"><li>• Observe patients after a seizure until they have returned to full consciousness, especially when<ul style="list-style-type: none"><li>o tonic-clonic seizures are prolonged or occur with marked cyanosis, severe bradycardia, apnea, or postictal electroencephalogram suppression.</li><li>o complex partial seizures occur with marked atonia.</li><li>o the seizure occurs in a person with a history of preexisting cardiac or respiratory impairment.</li></ul></li></ul>

## Teaching Points for Parents of Children with Epilepsy

- Epilepsy is unpredictable. Breakthrough seizures may occur despite adherence to the care plan.
- Know what to do when a breakthrough seizure occurs.
- Seek social support when necessary and take care of your personal health (by getting adequate sleep, eating well, and exercising regularly, for example).
- Do not become overprotective of your child. Understand that age-appropriate discipline will not cause a seizure and that it's necessary to set limits with a child who has epilepsy.
- It is important to include and spend time with your other children and family members.
- Connect with other parents of children with epilepsy through local resources that provide social support and services—child education and recreation or parent support groups, for example.
- Seek the information and support you need to assist with decisions about your education and career goals in light of your child's epilepsy care needs. For example, explore whether your job responsibilities and schedule can be modified so you can keep your position while accommodating your child's needs. If necessary, determine whether you can take a leave of absence from school or a job.
- You are your child's best advocate. What resources, laws, and regulations do you need to know about in order to advocate for your child in school and community settings? Learn about your federally mandated protections and explore assistance offered by advocacy groups in your state. The National Disability Rights Network ([www.ndrn.org](http://www.ndrn.org)) provides information about resources in each state.
- Review medical bills and insurance statements carefully to check for errors. Maintaining a notebook of ordered tests and their results can help you keep track of costs, as well as the scheduling of repeat or follow-up tests. Keep track of all expenses related to medical care, including costs of transportation to appointments and costs of food for prescribed diets, as some may be tax deductible. (Check with the Internal Revenue Service or a tax advisor.)

surgery or AED treatment, 58% of patients who received surgery were seizure-free at one year compared with 8% of patients assigned to AED treatment.<sup>12</sup> Surgical patients also had significantly higher quality of life scores, although the patients assigned to AED treatment had lower quality of life scores at baseline. Among patients with refractory epilepsy, temporal lobectomy is also associated with a decline in the unemployment rate,<sup>13</sup> and with significantly improved quality of life within six months of surgery.<sup>14</sup>

After an analysis of related literature published between January 1990 and June 1999, the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons, concluded that, for patients with disabling complex partial seizures, anteromesial temporal lobe resection may be more beneficial than continued AED treatment, “and the risks are at least comparable.”<sup>15</sup> Because surgery is the treatment most likely to result in cessation of seizures for such patients, surgical evaluation should take place before other nonpharmacologic treatments are attempted. While all surgery entails risk, and the thought of brain surgery may be particularly frightening, there is evidence that the risks associated with uncontrolled seizures “outweigh the risks of aggressive medical or

surgical therapy.”<sup>16</sup> Not only is sudden unexpected death 20 times more likely to occur in patients with epilepsy than in the general population, but among patients with refractory seizures receiving treatment at epilepsy referral centers, SUDEP accounts for 10% to 50% of all deaths.<sup>1</sup>

**Types of epilepsy surgery.** There are three general types of epilepsy surgery:

- *resective surgery*—removal of epileptogenic brain tissue
- *ablative surgery*—minimally invasive, image-guided laser ablation of epileptogenic brain tissue
- *disconnection surgery*—severing of specific nerve pathways along which seizures spread

Cortical resection or laser ablation is performed to stop seizure activity, whereas disconnection surgery is performed to reduce the number and occurrence of disabling seizures, and includes procedures such as corpus callosotomy and multiple subpial transections. While a cortical resection may provide freedom from seizures for a person with temporal lobe epilepsy, a palliative surgery, such as a corpus callosotomy, would be expected to halt disabling and dangerous atonic seizures in a person having several per day but would not stop other types of seizures.

**Table 4.** Common Reasons for Medication Failure

<ul style="list-style-type: none"><li>• Pharmacologically refractory epilepsy<ul style="list-style-type: none"><li>○ Approximately one-third of epilepsy cases are refractory despite appropriately chosen antiepileptic drugs (AEDs).</li></ul></li></ul>
<ul style="list-style-type: none"><li>• Imprecise epilepsy diagnosis<ul style="list-style-type: none"><li>○ Specific epilepsy syndromes respond only to a limited set of AEDs.</li></ul></li></ul>
<ul style="list-style-type: none"><li>• Nonepileptic events, including:<ul style="list-style-type: none"><li>○ psychogenic nonepileptic events</li><li>○ physiologic events, such as syncope, movement disorders, sleep disorders, or migraine</li><li>○ behavioral events</li></ul></li></ul>
<ul style="list-style-type: none"><li>• Medication nonadherence because of:<ul style="list-style-type: none"><li>○ adverse effects</li><li>○ cost</li><li>○ complexity of regimen</li><li>○ cognitive limitations or behavioral issues</li><li>○ lack of education on the condition</li><li>○ denial</li></ul></li></ul>
<ul style="list-style-type: none"><li>• Medication error, such as:<ul style="list-style-type: none"><li>○ incorrect prescription, instructions, or medication substitution</li><li>○ interaction of AED with other prescription medicines, over-the-counter medicines, or supplements</li></ul></li></ul>

All surgical procedures carry the risks of bleeding, infection, and death. With epilepsy surgery, potential postoperative neurologic deficits depend on the area of the brain that is operated on. A recent analysis of epilepsy surgery outcomes identified complications by surgical approach.<sup>17</sup> Surgeries involving the temporal lobe were associated with vomiting (7%), communicating hydrocephalus (7%), depression (5%), transient third nerve deficit (5%), postoperative hematoma (3%), meningitis (1% to 3%), chronic neurologic deficits (3%), and transient neurologic deficits (2%). For epilepsy surgery involving lobes other than the temporal lobe, identified complications included various types of hemisensory syndromes (10%), hemianopia (8%), reoperation (5%), SUDEP (5%), visual field deficit (4%), and hemiparesis (3% to 4%). For hemispherectomy, possible complications included aseptic meningitis (3% to 26%), dysphasia (13%), infection (8% to 11%), behavioral problems (9%), shunt insertion (4% to 5%), subdural hematoma (4%), hydrocephalus (1%), and death (1%). Potential complications may vary in duration, but all require intervention.

The overall outcomes of epilepsy surgery depend on several factors, including etiology, pathology, presence

of a lesion, location and type of surgery, and limitations caused by the surgery's proximity to functional regions. The ideal candidate for curative epilepsy surgery will have concordant findings (agreement) on both structural and functional presurgical evaluations. The findings will identify the onset area of seizure activity and the area in need of ablation or resection to stop the activity. On average, between 49% and 68% of patients achieve seizure freedom with surgery.<sup>15</sup> A 2005 systematic review and meta-analysis of long-term epilepsy surgery outcomes found that the median proportions of patients attaining long-term seizure freedom among those undergoing temporal lobe resection, occipital and parietal resection, frontal lobe resection, and multiple subpial resection were 66%, 46%, 27%, and 16%, respectively.<sup>18</sup> A 2010 update of this review reported that the odds of seizure freedom after epilepsy surgery were 2.5 times higher in patients whose lesions were identified by MRI or histopathology and were therefore more easily localized.<sup>19</sup> While some patients may have seizure recurrence years later, the overall success rates in appropriately selected patients with surgery are much higher than would be expected without surgery.

Epilepsy surgery, though regarded as the most important intervention for pharmacologically refractory epilepsy, is underutilized,<sup>17</sup> often owing to difficulty in obtaining an accurate diagnosis, the cost of surgery, and limited access to an epilepsy center. If, however, epilepsy surgery is not an option for a person with pharmacologically refractory epilepsy, there are other treatment considerations, including neurostimulation and epilepsy diets.

## NEUROSTIMULATION

Since epilepsy is, in many ways, a manifestation of hyperexcitability in the brain, it may seem counterintuitive to treat it with neurostimulation. Nevertheless, a strong body of evidence supports an increased role for neurostimulation in the treatment of epilepsy. There are currently two approaches to neurostimulation for epilepsy approved by the U.S. Food and Drug Administration (FDA): vagus nerve stimulation (VNS) and responsive neurostimulation (RNS).

**Vagus nerve stimulation.** The vagus nerve stimulator is a small device that is typically placed under the left clavicle. A thin lead is attached to the device and to the left vagus nerve in the lower neck (see Figure 2). The device is programmed wirelessly with a handheld computer and wand. Several parameters can be adjusted to optimize efficacy and minimize adverse effects associated with VNS, such as coughing. A handheld VNS magnet, applied for 30 to 60 seconds over the implanted device, can be used to interrupt breakthrough activity.

The rationale for VNS can be traced back decades. Early animal studies demonstrated that stimulation of

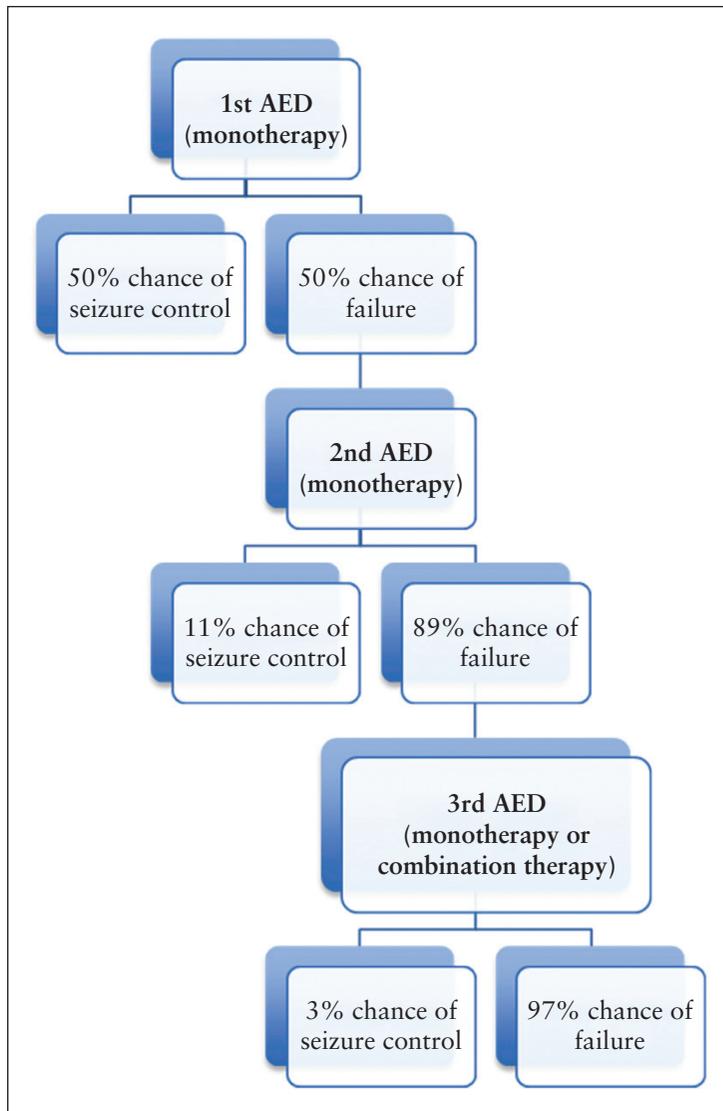
the vagus nerve could reduce “spiking” on EEGs.<sup>20</sup> Subsequently, VNS was found to reduce the frequency of seizures or shorten seizures in animal models.<sup>21</sup> It’s been hypothesized that the mechanism by which VNS exerts antiseizure effects involves changes in the release of norepinephrine in the locus coeruleus<sup>22</sup> and increased levels of the neurotransmitter gamma aminobutyric acid in the brain stem.<sup>23</sup>

The first pilot studies in humans were completed in the 1990s, and two blinded, randomized controlled trials were conducted by the Vagus Nerve Stimulation Study Group and published in 1994<sup>24</sup> and 1995.<sup>25</sup> Seizure frequency dropped by 50% or more in 38.7% of patients in the 1994 trial and in 31% of patients in the 1995 trial receiving high VNS, and in 19.4% of patients in the 1994 trial and in 13% of patients in the 1995 trial receiving low VNS.<sup>24,25</sup> In the long-term extension of these trials, the efficacy of VNS appeared to increase, and adverse effects to decrease, over time.<sup>26</sup>

The vagus nerve stimulator was approved by the FDA in 1997; since then, more than 100,000 patients worldwide have been implanted with the device.<sup>27</sup> Over the past 17 years, numerous case series have been published, all showing surprisingly consistent results. In a prospective, long-term study of 195 patients who had been enrolled in the EO5 study<sup>26</sup> and had had six or more complex partial or generalized tonic-clonic seizures, the median reduction in seizures at 12 months was 45%, with 20% of patients having more than a 75% seizure reduction and 35% having more than a 50% seizure reduction.<sup>28</sup>

More recent studies have also found that VNS efficacy improves significantly over time.<sup>29,30</sup> In a retrospective review that spanned 12 years and included 48 patients with intractable partial epilepsy treated with VNS, 29 patients (60%) responded to therapy with a reduction in seizure activity and 79% achieved a seizure reduction of more than 50% and sustained it for over two years.<sup>31</sup> No emergent systemic or central nervous system adverse effects were observed, and seizure activity continued to decrease with duration of treatment.<sup>31</sup> The continued seizure reduction seen with VNS treatment suggests that it has a cumulative effect on seizures.<sup>28</sup> However, about 3% of patients experience worsening of seizures following VNS.<sup>28</sup> Common adverse effects include voice change and cough or throat discomfort when the device stimulates the nerve (typically, for 30 seconds). Such effects are experienced primarily during the initial adjustment phase. The VNS device, however, is well tolerated by most patients and may provide such additional benefits as improved mood, better concentration, and greater alertness.

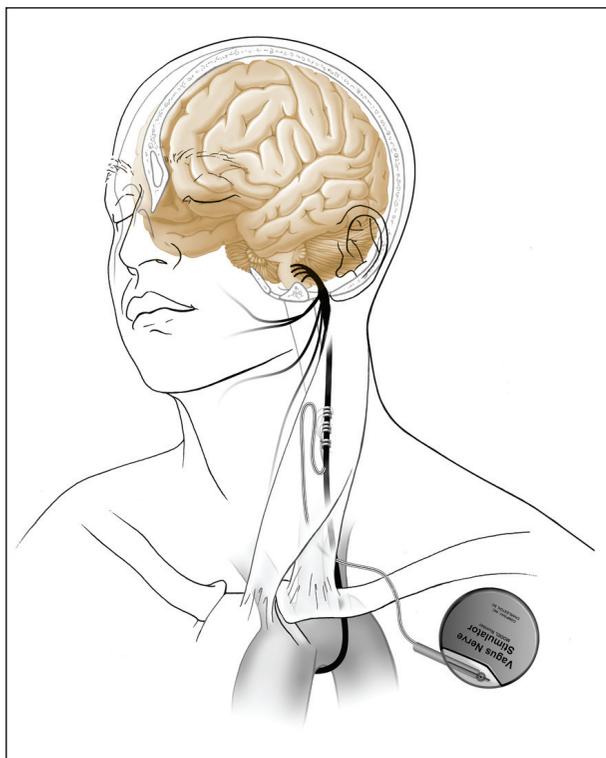
**Responsive neurostimulation** is a relatively new option for patients with partial seizures for whom the focus can be localized but not removed. Approved for use in the United States at the end of 2013, RNS uses a small microcomputer placed within the skull



**Figure 1.** Diminishing success with each subsequent antiepileptic drug (AED) trial.<sup>8,9</sup>

and electrodes placed on the brain’s surface or within the structure of the brain, in or close to the source of the seizures (see Figure 3). Electrical signals sent from the electrodes and recorded by the device can be wirelessly transmitted with a handheld wand to a laptop computer. The data are then transmitted to a secure Web site, where they can be reviewed by the treating physician. The device can also be programmed to detect the patient’s seizures; once it is doing so reliably, it can be programmed to deliver a small interfering stimulus to disrupt the seizures.

RNS is commonly used in bilateral temporal lobe epilepsy and epilepsy arising from eloquent cortex (areas involved in sensory processes, language, or movement) that cannot be removed without loss of



**Figure 2.** The vagus nerve stimulator, placed under the left clavicle, is attached to a thin lead that is also attached to the left vagus nerve in the lower neck. Illustrations by Emma Vought, MS, CMI, Department of Neurosciences, Medical University of South Carolina, Charleston.

function. While epilepsy surgery is often used to treat temporal lobe epilepsy, surgery is an option only if all seizures originate in the same temporal lobe, as removal of both temporal lobes would cause devastating memory deficits. RNS, however, is an option for patients with bitemporal epilepsy.

In a clinical trial that included 191 adults with medically intractable partial epilepsy treated with RNS, nearly one-half achieved seizure reduction of 50% or more over the course of two years, and 7.1% were seizure-free at the end of the data collection period.<sup>32</sup> RNS therapy also improved quality of life and was associated with few surgical complications, which included intracranial hemorrhage (2.1%) and infection at the point of incision or implant (5.2%). The most common adverse effects were dizziness, drowsiness, headache, abnormal thinking or confusion, and nausea and vomiting. RNS is generally well tolerated, and patients typically do not feel the stimulation.

#### DIETARY TREATMENT

The classic epilepsy diet is the ketogenic diet that is high in fat but low in carbohydrate and protein.

Typically, it calls for patients to consume four grams of fat for every one gram of carbohydrate and protein combined. Such a diet causes the body to use fat as the source of energy instead of glucose. Because the diet puts the body in a state of ketosis, ketones will be found in the blood, urine, and breath. Statistics on how widely ketogenic diets are prescribed are not readily available; but from anecdotal reports, the practice appears to be growing in popularity. For nearly a century, ketogenic and similar diets have been used throughout the world. Uncontrolled studies of children following such diets have found that they reduce seizures by about half in 50% to 60% of the children who follow them, with one-third demonstrating a 90% response rate and more than 10% becoming seizure-free.<sup>33</sup>

How the ketogenic diet works in people with epilepsy is not completely clear, but it is believed that ketosis increases cerebral energy, reduces seizures by altering excitatory and inhibitory neurotransmitters,<sup>34</sup> and may improve neuronal energy metabolism through mitochondrial involvement.<sup>33</sup> An international panel of pediatric epileptologists and dietitians prepared a consensus guideline providing evidence for the use of the ketogenic diet after two AEDs have failed and as first-line therapy for patients with glucose metabolism disorders such as glucose transporter type 1 deficiency syndrome and pyruvate dehydrogenase deficiency.<sup>35</sup> The current consensus is that, unless contraindicated, the ketogenic diet should be considered early in the treatment of patients with pharmacologically refractory epilepsy—not as a last resort.<sup>36</sup> (Contraindications for the ketogenic diet include fatty acid metabolism disorders; patients should be thoroughly screened for such disorders before adopting this diet.<sup>37</sup>) Positive outcomes have been reported for early use in epilepsy syndromes such as Dravet syndrome, infantile spasms, myoclonic–astatic epilepsy, and tuberous sclerosis.<sup>37</sup>

The ketogenic diet is usually initiated with a meeting between the patient and a specially trained dietitian on the epilepsy team, followed by prescreening laboratory studies and hospital admission for metabolic monitoring. For some patients, the diet can be initiated in the outpatient setting with appropriate epilepsy team support. Previously, the ketogenic diet was started with a period of fasting, but recent findings suggest this is not necessary.<sup>33</sup> During hospitalization, the dietitian meets with the family and teaches them the recipes and diet rules, including “sick day” plans. A printed care plan indicating that the person is on a specialized diet and should not receive intravenous infusions with glucose or other glucose products is provided to the family in case of emergency. The length of epilepsy diet treatment is at least three to six months and typically two or more years.<sup>33,35</sup> Although the diet has been

used more often in children, adults now use it also. Adverse effects can include reflux, vomiting, constipation, diarrhea, abdominal pain, kidney stones, hypoglycemia, hyperlipidemia, dehydration, and loss of bone density.<sup>37</sup> With close monitoring, these adverse effects can be reduced and treated through dietary adjustments.

understanding of people with epilepsy and their families. Using the information and resources provided in this series will enable nurses to do so.

In the quest to provide better care for patients with epilepsy, nursing priorities might include

- developing comprehensive care models that address comorbid conditions.

## Uncontrolled studies have found that ketogenic diets reduce seizures by about half in 50% to 60% of the children who follow them, with more than 10% becoming seizure-free.

The commitment of the patient and the family is paramount to the success of the ketogenic diet. It requires strict adherence and sometimes multiple dietary supplements to maintain good health. With long-term dietary maintenance, regular laboratory evaluation is required. Patients and family members must also monitor medications and personal care products (such as toothpastes and lotions) to ensure that none would cause the patient to deviate from the prescribed daily allowance of carbohydrates, potentially causing breakthrough seizure activity.

There are other epilepsy diets—such as the modified Atkins diet for epilepsy and the low glycemic index diet—that produce ketosis, but to a lesser degree than the classic ketogenic diet. These diets are less restrictive and often easier for adolescents and adults to follow. Nevertheless, such diets still require close monitoring by a multidisciplinary health care team.<sup>35</sup>

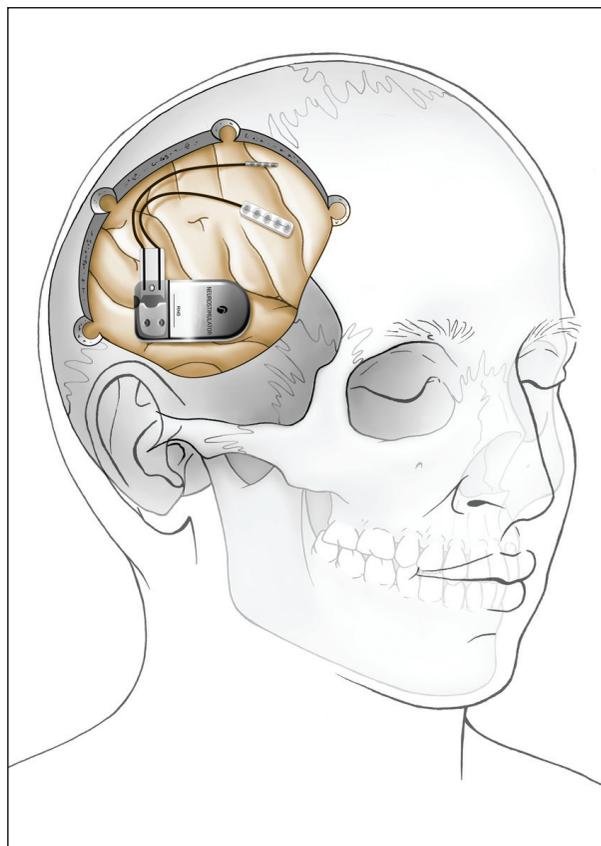
### MEDICAL MARIJUANA

The subject of marijuana as an epilepsy treatment—particularly in children—continues to be explored. For more information, visit the Web site of the Epilepsy Foundation, which features related research, data, news stories, expert discussion, and answers to frequently asked questions (go to [www.epilepsy.com/make-difference/advocacy/advocacy-priorities/epilepsy-and-medical-cannabis](http://www.epilepsy.com/make-difference/advocacy/advocacy-priorities/epilepsy-and-medical-cannabis)).

### IMPROVING EPILEPSY CARE

A 2012 Institute of Medicine (IOM) report, *Epilepsy Across the Spectrum: Promoting Health and Understanding*, emphasizes that the millions of people with epilepsy in the United States face numerous challenges in obtaining high-quality, coordinated health care and community services; overcoming social stigma; and finding support in their school or work setting.<sup>38</sup> The IOM report calls on practitioners and researchers to promote the health and

- supporting research efforts to improve seizure control and quality of life for patients with epilepsy.
- educating the public to reduce the stigma associated with epilepsy. ▼



**Figure 3.** Responsive neurostimulation uses a micro-computer that is placed within the skull and attached to electrodes on the brain's surface or within the structure of the brain near the source of the seizures.

For 81 additional continuing nursing education activities on neurologic topics, go to [www.nursingcenter.com/ce](http://www.nursingcenter.com/ce).

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## REFERENCES

- Shorvon S, Tomson T. Sudden unexpected death in epilepsy. *Lancet* 2011;378(9808):2028-38.
- Smith G, et al. Caregiving in pediatric epilepsy: results of focus groups and implications for research and practice. *Epilepsy Behav* 2014;34:34-41.
- Goldenberg MM. Overview of drugs used for epilepsy and seizures: etiology, diagnosis, and treatment. *P T* 2010;35(7):392-415.
- Chung WH, et al. Medical genetics: a marker for Stevens-Johnson syndrome. *Nature* 2004;428(6982):486.
- Lonjou C, et al. A marker for Stevens-Johnson syndrome...: ethnicity matters. *Pharmacogenomics J* 2006;6(4):265-8.
- Krauss GL, et al. Assessing bioequivalence of generic antiepilepsy drugs. *Ann Neurol* 2011;70(2):221-8.
- Karalis V, et al. Generic products of antiepileptic drugs: a perspective on bioequivalence, bioavailability, and formulation switches using Monte Carlo simulations. *CNS Drugs* 2014;28(1):69-77.
- Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med* 2000;342(5):314-9.
- Mohanraj R, Brodie MJ. Diagnosing refractory epilepsy: response to sequential treatment schedules. *Eur J Neurol* 2006;13(3):277-82.
- Brophy GM, et al. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care* 2012;17(1):3-23.
- Barker-Haliski M, et al. What are the arguments for and against rational therapy for epilepsy? *Adv Exp Med Biol* 2014;813:295-308.
- Wiebe S, et al. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med* 2001;345(5):311-8.
- Sperling MR, et al. Occupational outcome after temporal lobectomy for refractory epilepsy. *Neurology* 1995;45(5):970-7.
- Spencer SS, et al. Health-related quality of life over time since resective epilepsy surgery. *Ann Neurol* 2007;62(4):327-34.
- Engel J, Jr, et al. Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology* 2003;60(4):538-47.
- Sperling MR. The consequences of uncontrolled epilepsy. *CNS Spectr* 2004;9(2):98-101, 106-9.
- Ramey WL, et al. Current management and surgical outcomes of medically intractable epilepsy. *Clin Neurol Neurosurg* 2013;115(12):2411-8.
- Tellez-Zenteno JF, et al. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. *Brain* 2005;128(Pt 5):1188-98.
- Tellez-Zenteno JF, et al. Surgical outcomes in lesional and non-lesional epilepsy: a systematic review and meta-analysis. *Epilepsy Res* 2010;89(2-3):310-8.
- Zanchetti A, et al. The effect of vagal afferent stimulation on the EEG pattern of the cat. *Electroencephalogr Clin Neurophysiol* 1952;4(3):357-61.
- Zabara J. Inhibition of experimental seizures in canines by repetitive vagal stimulation. *Epilepsia* 1992;33(6):1005-12.
- Krahl SE, Clark KB. Vagus nerve stimulation for epilepsy: a review of central mechanisms. *Surg Neurol Int* 2012;3(Suppl 4):S255-S259.
- Ben-Menachem E, et al. Effects of vagus nerve stimulation on amino acids and other metabolites in the CSF of patients with partial seizures. *Epilepsy Res* 1995;20(3):221-7.
- Ben-Menachem E, et al. Vagus nerve stimulation for treatment of partial seizures: 1. A controlled study of effect on seizures. First International Vagus Nerve Stimulation Study Group. *Epilepsia* 1994;35(3):616-26.
- Vagus Nerve Stimulation Study Group. A randomized controlled trial of chronic vagus nerve stimulation for treatment of medically intractable seizures. *Neurology* 1995;45(2):224-30.
- Morris GL, 3rd, et al. Long-term treatment with vagus nerve stimulation in patients with refractory epilepsy. *Neurology* 1999;53(8):1731-5. <http://www.ncbi.nlm.nih.gov/pubmed/10563620>.
- Stacey WC, Litt B. Technology insight: neuroengineering and epilepsy-designing devices for seizure control. *Nat Clin Pract Neurol* 2008;4(4):190-201.
- DeGiorgio CM, et al. Prospective long-term study of vagus nerve stimulation for the treatment of refractory seizures. *Epilepsia* 2000;41(9):1195-200.
- Ardesch JJ, et al. Vagus nerve stimulation for medically refractory epilepsy: a long-term follow-up study. *Seizure* 2007;16(7):579-85.
- Labar D. Vagus nerve stimulation for 1 year in 269 patients on unchanged antiepileptic drugs. *Seizure* 2004;13(6):392-8.
- Uthman BM, et al. Effectiveness of vagus nerve stimulation in epilepsy patients: a 12-year observation. *Neurology* 2004;63(6):1124-6.
- Morrell MJ; RNS System in Epilepsy Study Group. Responsive cortical stimulation for the treatment of medically intractable partial epilepsy. *Neurology* 2011;77(13):1295-304.
- Kossoff EH, Wang HS. Dietary therapies for epilepsy. *Biomed J* 2013;36(1):2-8.
- Hartman AL, et al. The neuropharmacology of the ketogenic diet. *Pediatr Neurol* 2007;36(5):281-92.
- Kossoff EH. International consensus statement on clinical implementation of the ketogenic diet: agreement, flexibility, and controversy. *Epilepsia* 2008;49 Suppl 8:11-3.
- Wang HS, Lin KL. Ketogenic diet: an early option for epilepsy treatment, instead of a last choice only. *Biomed J* 2013;36(1):16-7.
- Kossoff EH, et al. Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. *Epilepsia* 2009;50(2):304-17.
- England MJ, et al., eds. *Epilepsy across the spectrum: promoting health and understanding*. Washington, DC: National Academies Press; 2012. <https://www.ncbi.nlm.nih.gov/books/NBK91506>.