REVIEW ARTICLE

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Counseling and Management of the Risks of Living With Epilepsy

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ABSTRACT

PURPOSE OF REVIEW: For patients living with epilepsy, quality of life is determined not only by seizure control but by mood, antiepileptic drug adverse effects, relationships, and access to education, employment, and transportation. This article reviews some of the most commonly encountered concerns associated with epilepsy, including mood disorders, driving, injuries, mortality, bone health, genetic burden, and impact on relationships.

RECENT FINDINGS: People with epilepsy are at increased risk for anxiety, depression, and suicide. Depression is underrecognized in patients with epilepsy, but effective validated screening tools are available for use. Mortality rates for people with epilepsy are 2 times higher than those of the general population, but much of this is attributable to underlying conditions rather than seizures. Sudden unexpected death in epilepsy (SUDEP) occurs in an estimated 1:1000 adults with epilepsy per year, and the risk can be reduced by improved observation and seizure control. An increased risk of injury, including fractures, is also present in patients with epilepsy. Reduced bone health leading to increased fracture risk is an important negative consequence of long-term use of antiepileptic medication. Seizures while driving can also cause accidents and injury. Despite the importance of driving for people with epilepsy, physicians are underperforming in providing counsel about driving.

SUMMARY: Optimal care of the patient with epilepsy includes addressing risks to emotional health, physical health including fractures and SUDEP, social health, and an independent lifestyle. Identification of and treatments to reduce these risks can do more to improve quality of life than a narrow clinical focus on seizure control alone.

INTRODUCTION

Medical care of epilepsy is often focused on reducing the frequency and severity of seizures and managing antiepileptic drugs (AEDs). However, quality of life for people living with epilepsy is determined by many factors beyond seizure control, as stressed in a 2012 Institute of Medicine report on epilepsy and public health.[1] Comprehensive care of the person with epilepsy

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CASE 9-1

A 32-year-old woman with a history of focal epilepsy presented for a follow-up visit with concerns about her antiepileptic medication. She had been diagnosed with temporal lobe epilepsy 6 months prior after having several episodes of transient expressive aphasia, one of which progressed to loss of awareness with unresponsiveness and oral automatisms. At that time, she was started on lamotrigine titrated to 100 mg 2 times a day and had subsequently been seizure free.

At her follow-up appointment, she reported significant daytime fatigue and lack of energy despite routinely getting 10 hours of sleep at night. At work she struggled to maintain her mental focus and complete her assignments on time. She admitted to ongoing worries about having another seizure in public and had cut back her social activities and work-related travel significantly. She was previously training for a half marathon with her husband, but she no longer exercised because of loss of interest and low energy. She reported that these issues were negatively impacting her relationship with her husband. She suspected the fatigue and cognitive issues were caused by the lamotrigine and wondered if she should try a different medication.

Her serum lamotrigine level was in the low therapeutic range. She scored 15 on the Neurological Disorders Depression Inventory for Epilepsy, suggesting the possibility of major depression, although her score on the Adverse Events Profile was only 22, driven mostly by higher scores for the items in the Mood/Emotion domain of the Adverse Events Profile. After reviewing her situation, her neurologist advised that these symptoms were more likely to reflect depression rather than an antiepileptic drug side effect. She agreed to a trial of citalopram, a selective serotonin reuptake inhibitor (SSRI), at 20 mg/d and continuation of her dose of lamotrigine. After 3 months of treatment, her symptoms significantly improved.

COMMENT

This case illustrates the challenges in recognizing depression and anxiety in patients with epilepsy. Patients with epilepsy and their medical providers may struggle to distinguish the effects of a mood disorder from medication side effects. Use of a depression screening tool validated for the epilepsy population, together with systematic screening for adverse events with the Adverse Events Profile, can be an effective means of identifying mood disorders in the outpatient clinic. A study involving 20 epileptologists who utilized the Neurological Disorders Depression Inventory for Epilepsy and the Adverse Events Profile systematically in their clinics before patient visits demonstrated that use of these tools improved both the number of discussions about these important aspects of daily living with epilepsy, as well as increasing patient-physician agreement about these issues after clinic visits.[13]

therefore optimally addresses the impact of the diagnosis on other areas of daily living including mood, AED adverse effects, safety, driving, education, employment, and independence. In current vernacular, this may be described as a focus on *living well* or *wellness* rather than a focus on the disease. *Wellness* incorporates not only seizure management but also overall physical, spiritual, mental, and social health as well as lifestyle factors such as occupation, finances, and housing. The adverse impact of epilepsy beyond seizures can be measured as a financial cost to society. In the United States alone, the total cost related to epilepsy in 1995 was $12.5 billion, 85% of which was the indirect cost.[2] For individuals with epilepsy, these costs are real and measurable: missed days of work and school, underemployment, unemployment, social isolation, strains on relationships, and the emotional and financial burden of care placed on family. Costs, direct and indirect, are higher in people with refractory epilepsy.[2]

Addressing wellness and the risks associated with epilepsy is not a "one size fits all" endeavor. People with epilepsy experience widely varying types, timing, frequency, and severity of their seizures. Further, epileptic seizures by their nature are often unpredictable and sporadic. The challenge is how to best balance restrictions on activity designed to maintain health and safety during seizures with the sometimes-competing goal of maintaining a full and active lifestyle during periods of seizure freedom. This review aims to help medical care providers impart accurate information about the risks associated with seizures while still empowering people with epilepsy to achieve optimal quality of life.

KEY POINT

- **Depression risk is increased 2 to 3 times in people with epilepsy. People with epilepsy are twice as likely to report suicidal thoughts and up to 3 times more likely to die of suicide compared to the general population.**

EMOTIONAL HEALTH: MOOD DISORDERS, DEPRESSION, AND ANXIETY

People with epilepsy are at increased risk for psychiatric disorders including depression, anxiety, and attention deficit disorder.[3–5] Meta-analyses of population-based studies indicates a pooled lifetime prevalence of 23% for depression and 20% for anxiety in people with epilepsy, representing a twofold to threefold increased lifetime risk.[4,5] Rates are even higher in people with intractable epilepsy.[6] Furthermore, people with epilepsy are twice as likely to report suicidal thoughts and up to 3 times more likely to die of suicide compared to the general population.[7–9]

Mood disorders and anxiety are significant determinates of quality of life for children and adults with epilepsy.[10] Depression can occur at any time or any age in people with epilepsy and may precede the onset of seizures.[11] Furthermore, increased depression severity is associated with an increased likelihood of uncontrolled seizures and has been correlated with lower adherence to AED therapy.[11,12] The relationship between epilepsy and mood is complex and likely reflects shared biological and neurochemical pathways related to etiology, seizures, and medication as well as psychosocial factors.[10]

Despite the potentially serious implications for quality of life, depression in epilepsy is underrecognized.[10] One reason for this may be the challenge of distinguishing the physical symptoms of depression such as fatigue, altered sleep, and cognitive slowing from the adverse side effects of AEDs, as illustrated in **CASE 9-1**. Patients and family members may also attribute depression to a "normal" response to the limitations from seizures and thus not seek care. Furthermore, depression in people with epilepsy may present in atypical ways or may fluctuate in temporal relation to seizure activity.[10] Recognition can be improved through use of brief screening tools for depression that have been validated for people with epilepsy and are available for free, public use: the

Neurological Disorders Depression Inventory for Epilepsy, the Patient Health Questionnaire-9, and the Patient Health Questionnaire-2.[14] These tools intentionally focus less on physical symptoms of depression that could overlap with adverse AED side effects.[14] Of course, screening tools are not a replacement for a more detailed evaluation by a physician but can help identify depression as a concern requiring further attention.

Distinguishing the symptoms of a mood disorder from the common problem of AED adverse effects in a person with epilepsy is a related challenge for the epilepsy clinician. Fortunately, a readily available tool, the Liverpool Adverse Events Profile, can assist with discriminating adverse effects from AED treatment, and use of this tool has been shown to improve clinicians' ability to effectively screen for side effects of treatment to make therapeutic changes in AEDs that may benefit patients' quality of life.[15]

Mood disorders in people with epilepsy are also undertreated.[10] As many as 70% of people with depression seen in epilepsy clinics are not receiving

TABLE 9-1 Studies of Treatment of Depression in Patients With Epilepsy

Intervention	Study Sample	Outcome
Amitriptyline versus nomifensine versus placebo[19]	n = 42, ages 18-60	Equivalent improvement in Hamilton Depression Rating Scale score for both active treatments and placebo at 6 weeks, nomifensine more effective than amitriptyline at 12 weeks
Venlafaxine versus no treatment[20]	n = 64, ages 7-60	Improved Hamilton Depression Rating Scale score at 8 weeks with active treatment
Paroxetine versus doxepin[21]	n = 67, ages 14-62	Improved Hamilton Depression Rating Scale score in both groups at 8 weeks; lower side effects with paroxetine
Cognitive-behavioral therapy versus selective serotonin reuptake inhibitor (SSRI)[22]	n = 15, adults with temporal lobe epilepsy	Improved Beck Depression Inventory score in both groups at 12 weeks
Cognitive-behavioral therapy versus control[23]	n = 37, age 60 and older, community dwelling	Geriatric Depression Scale score improved in both groups, no difference in treatment versus control after 6-week intervention
PEARLS randomized trial: Home-based collaborative care intervention including psychiatric consultation, versus treatment as usual[24]	n = 80, age 18 and older	Improved Hopkins Symptom Checklist-20 score at 6, 12, and 18 months versus control
Cognitive-behavioral therapy versus control[25]	n = 45, ages 18-65	Improved Neurological Disorders Depression Inventory for Epilepsy score after 9 weeks active treatment; no difference seen at 3-months posttreatment
Project UPLIFT: Web/telephone-delivered cognitive-behavioral therapy–based mindfulness program versus treatment as usual[26]	n = 128, adults	Decreased incidence of new or relapsed major depressive episodes and Beck Depression Inventory score at 10 weeks in treatment group

PEARLS = Program to Encourage Active, Rewarding Lives; UPLIFT = Using Practice and Learning to Increase Favorable Thoughts.

treatment for the mood disorder.[16] One often cited barrier to pharmacologic treatment is fear that antidepressant medications exacerbate seizures.[10] In fact, this fear appears largely unfounded and is not supported by meta-analysis of trials submitted to the US Food and Drug Administration (FDA).[16] One exception is bupropion, which has been shown to increase the risk of seizures and is generally contraindicated in patients with epilepsy.[17,18]

Another barrier may be the lack of high-quality evidence to guide treatment decisions specific to depression in patients with epilepsy. Few randomized controlled trials have been conducted on the treatment of depression in epilepsy (**TABLE 9-1**).[19–26] Class III and IV evidence supports the effectiveness of citalopram, mirtazapine, reboxetine (not available in the United States), and sertraline.[27–30] Consensus expert recommendation is to use a selective serotonin reuptake inhibitor (SSRI) as first-line therapy.[10,31] Psychotherapy and counseling are also appropriate interventions, either alone or in combination with pharmacologic treatment.[31] Cognitive-behavioral therapy–based treatments, in particular, administered directly or via telecommunication programs, have evidence as effective interventions for depression in epilepsy (**TABLE 9-1**).[22–26] Referral to a psychiatrist is often appropriate, particularly for depression that is moderate to severe or that does not respond to first-line interventions.

Choice of AED therapy can also impact mood for better or worse. Expert consensus recommendations for treatment of mild depression in people with epilepsy include use of an AED with mood-stabilizing properties such as lamotrigine or valproate, as well as avoidance of medications with an increased likelihood for adverse emotional side effects.[10] Lamotrigine was shown in two randomized, double-blind trials to improve mood in participants with epilepsy after 7 to 8 weeks of treatment.[32]

In 2008 the FDA issued a safety alert for increased risk of suicidal behavior and suicidal ideation with AEDs as a class, leading to a change in drug labeling.[33] This was based on a meta-analysis of placebo-controlled AED trials for any indication (25% epilepsy, 27% psychiatric, 48% other, including pain) showing an odds ratio of 1.8 (1.24 to 2.66) for suicidal behavior or ideation in individuals exposed to AEDs.[33] This analysis was limited by having been based on studies that were not designed to assess psychiatric outcomes, studies with short observation times, and studies that often excluded subjects with a significant psychiatric history. Previously released expert consensus recommendations for treatment of mild depression in patients with epilepsy had recommended use of an AED with mood-stabilizing properties such as lamotrigine, valproate, or carbamazepine and avoidance of those AEDs with an increased likelihood for adverse mood side effects, reflecting the long-established clinical observations that impact on mood varied by AED.[10] A 2010 case-control study from the United Kingdom Practice Research Database did find increased risk of suicidal behavior in users of newer AEDs with a "high potential to cause depression" (levetiracetam, tiagabine, topiramate, vigabatrin) as compared to "low potential" AEDs (lamotrigine, gabapentin, pregabalin, oxcarbazepine).[34] When the impact of individual drugs was analyzed, only current use of levetiracetam was associated with increased risk of suicidal thoughts and behavior.[35] Providers should be aware of the potential impact of a given AED to influence depression and anxiety when making therapeutic decisions for epilepsy. The author of this article has found that discussing these issues, including the FDA warning, when prescribing a new AED is beneficial to reducing patient concerns and may help improve medication compliance.

KEY POINTS

- **Depression in patients with epilepsy is underrecognized and undertreated.**
- **The often-cited fear that a selective serotonin reuptake inhibitor will worsen seizure control is not supported by evidence and should not be a barrier to treatment of depression in the patient with epilepsy.**

IMPACT OF LIFESTYLE: FOCUS ON DRIVING

In a survey of people with epilepsy, driving was rated as their number one concern impacting quality of life.[34] Ability to drive can influence ability to work, maintain relationships, and to live independently. It is not difficult to conceive that a seizure with loss of awareness while driving could have catastrophic consequences; however, a recent systematic review found insufficient evidence to conclude that people with epilepsy are at greater risk for motor vehicle crashes.[36]

One challenge in ascertainment of risk is that single-vehicle crashes without major injury may not be reported to law enforcement agencies or to health care providers. Self-reporting surveys provided to drivers with epilepsy have the potential to capture the frequency of such events. One such survey in Canada found no difference in the rates of motor vehicle crashes in drivers with and without epilepsy.[37] A self-reporting survey of adults with epilepsy living in Arizona and New Jersey found 5% to 11% reported having a crash related to a seizure.[38] Studies on publicly reported crashes also paint an inconsistent picture of the true risk of driving with epilepsy. A recent study from Maryland evaluating crash reports for 254 patients with epilepsy approved to drive by the Maryland Motor Vehicle Administration found only two seizure-related crashes in 7 years, suggesting a very low risk for drivers meeting local legal licensing requirements.[39] In contrast, a Canadian population-based study of motor vehicle crashes leading to medical care found an increased risk for drivers with epilepsy (odds ratio 1.62, 95% confidence interval 0.95–2.76).[40]

Driving is also highly regulated for people with epilepsy compared to other medical conditions that could impact driving, although epilepsy may not represent the condition of greatest threat to on-the-road safety. A study of fatal US car crashes found that 0.2% were related to epilepsy as compared to 4% related to cardiovascular disease and 30% related to alcohol.[41,42] The risk of crashes for drivers with epilepsy should also be placed in perspective to other categories of drivers. For example, in the United States, the fatal crash rate per 100,000 population is estimated at 8.6 for those with epilepsy as compared to 28.1 in all drivers younger than 25 years of age.[41] Regardless of absolute risk, every state has laws regulating driving for people with seizures. Specific requirements and processes vary between states.[43] Driving privileges in the United States are primarily determined by the patient's duration of seizure freedom. The optimal duration of seizure freedom is not established, and standards typically range between 3 and 12 months.[43] An analysis of motor vehicle crash reports in Arizona before and after the required seizure-free interval was changed from 12 to 3 months found no significant change in the rate of seizure-related crashes and a decrease in the number of such crashes resulting in fatality.[44] In a 2007 position statement, the American Academy of Neurology (AAN) endorsed a 3-month seizure-free period.[45] Some state laws also consider modification of driving restrictions based on special circumstances such as a consistent prolonged aura, seizures that are exclusively nocturnal, seizures provoked by a prescribed medication change, or seizure symptomatology that is unlikely to impact safe driving; these exceptions are supported in the AAN position statement.[43,45]

Patients with epilepsy require accurate information about driving if they are to be protected from physical and legal harm. Physicians are generally poor at counseling patients with epilepsy regarding driving laws.[38,46] In one survey, one-third to one-half of adults with epilepsy stated they had never been counseled by a medical provider about driving.[38] Chart review of a single US tertiary care hospital found that among people seen by an emergency department provider for a seizure or syncope, less than 10% were documented to have received counseling on driving.[46] Providers may be challenged to balance advocating for the needs of an individual patient with promoting the safety of the individual and the public, a dilemma that is illustrated in CASE 9-2. Physicians are strongly encouraged to know their relevant state driving laws and to follow them. This includes completing necessary forms as required by the Department of Motor Vehicles and reporting as mandated by law in selected states (TABLE 9-2). For medicolegal reasons, it is also important to document counseling of the patient regarding driving and the reasons for individual driving recommendations. Refer to the article "Driving and Epilepsy: Ethical, Legal, and Health Care Policy Challenges" by Joseph S. Kass, MD, JD, FAAN, and Rachel V. Rose, JD, MBA,[47] in this issue of *Continuum* for further information about the medicolegal issues for the provider with regard to driving and epilepsy.

PHYSICAL HEALTH

People with epilepsy are at increased risk of accidents and injuries,[48] which, to a large degree, is directly attributable to seizures causing immediate harm.[45] Adverse effects of AEDs on motor coordination and alertness and comorbid cognitive or physical disabilities can also contribute. Seizures often cause injuries due to falls. Additional risk factors for seizure-related injury include uncontrolled epilepsy, seizures with altered awareness, medication noncompliance, and seizures occurring when a person is alone. Generalized tonic-clonic seizures can result in shoulder dislocation, vertebral compression fractures, and tongue lacerations. Seizures with altered awareness of the environmental dangers can lead to burns, drowning, and motor vehicle crashes. Most seizure-related injuries are mild to moderate in severity and commonly include lacerations, fractures, dental injuries, concussions, and burns.[49] Severe injuries such as subdural hematoma or death due to drowning do occur, but infrequently.[49]

Among many suggested strategies to reduce injury risk, the most important intervention is improved seizure control. Other methods to reduce injuries are summarized in TABLE 9-3. Risk prevention strategies should be individualized and include consideration of epilepsy-related factors such as seizure type, frequency, timing (sleep versus awake), and triggers. It is further important to consider the age, independence, and cultural and social norms of the patient and family. For example, recommending a parent sleep with a young child with frequent nocturnal convulsions might be an acceptable and reasonable safety precaution but is an unnecessary and unacceptable recommendation if the patient is a college-age young adult with rare seizures living in the family home. Excessive safety precautions may also discourage people with epilepsy from participating in activities that are part of a healthy lifestyle, such as physical exercise, and may keep the patient from achieving independence.

Fractures are of particular concern in patients with epilepsy. The rate of fractures in both children and adults with epilepsy is estimated to be 2 to 6 times higher than in the general population.[50–52] Fractures are partially attributable to falls, but use of an AED also plays a role. Fracture risk increases with duration of AED exposure.[51,53] By one estimate, for every decade of AED use, risk of any fracture increased by 40% and risk of seizure-related fracture increased by 60%.[53] Women on AEDs are at higher risk for both falls and fractures as

KEY POINTS

- People living with epilepsy rated their ability to drive as the most important factor determining quality of life.
- Physicians are underperforming in counseling patients with epilepsy about driving.
- Fracture risk is 2 to 6 times higher in people with epilepsy than in the general population, and fracture risk increases with duration of antiepileptic drug therapy.

CASE 9-2

A 21-year-old man with juvenile myoclonic epilepsy presented for an outpatient visit after a seizure-related motor vehicle crash. He had been diagnosed with juvenile myoclonic epilepsy at age 15 and was initially seizure free on valproic acid. During college he had several episodes of morning myoclonus provoked by binge alcohol use and sleep deprivation. He related that in the last 3 months he had experienced three generalized tonic-clonic seizures triggered by alcohol use and minimal sleep. He had often stayed up late because of schoolwork and socializing. In addition, he admitted to frequently missing doses of his medication.

The most recent seizure occurred while driving to a 7:00 AM college class and resulted in major damage to the vehicle but no personal injury. His serum valproate level was found to be subtherapeutic in the emergency department, where he had been transported after the collision.

At the current presentation, he brought a letter from the Department of Motor Vehicles requesting a medical report from his physician regarding his fitness to drive. He stressed the importance of his being able to drive to get to school and work. The neurologist explained that according to the state law where this patient resided, he must be seizure free for a period of at least 90 days before he can legally operate a motor vehicle.

The patient and neurologist reviewed the importance of compliance with the law both for his safety and the safety of the general public. They discussed strategies to improve seizure control including medication compliance, improved sleep schedule, and avoidance of alcohol. In addition, the neurologist communicated with the patient's university, requesting accommodation with class sessions starting later in the day. She explained that if he was seizure free in 3 months and was compliant with medication and lifestyle changes, that she would work with him at that time to file an updated medical report for the Department of Motor Vehicles. The neurologist documented in the electronic medical record the recommendations and counseling that were provided regarding driving status.

COMMENT

This case illustrates the provider's roles in caring for the driver with epilepsy and exemplifies how responsibilities toward the patient and public may sometimes be in conflict. In the context of the doctor-patient relationship, the provider has an obligation to optimize seizure control and the patient's quality of life. As a patient advocate, the physician should promote the patient's independence, including facilitating attendance at school and work, but also promote personal safety. Finally, the physician has an obligation to maintain public safety and has a responsibility and liability under the law, including a duty to accurately inform and counsel the patient about relevant driving laws and to file required reports to government agencies. The physician can also help protect herself from liability by carefully documenting these steps in the medical record.

compared to men.[51,53,54] In appropriately selected cases in which seizure freedom is likely without medication, timely discontinuation of chronic AED therapy may help lower future fracture risk. In addition to concern about impact of chronic AED use on bone, people with epilepsy commonly have concerns about the adverse effects of AEDs on employment, education, sex life, driving, emotion, and cognitive function.[55]

The association between AED use and fracture is largely attributed to adverse drug effects on bone density and quality.[54,56] One of the most commonly cited explanations for this relationship is alteration of vitamin D metabolism by induction of hepatic cytochrome P450 enzymes, resulting in reduced calcium absorption. Supporting this theory, a large cohort study of more than 60,000 people with epilepsy on active treatment found the rate of fractures was significantly higher in those taking hepatic enzyme–inducing AEDs compared to non–enzyme-inducing AEDs.[54] However, other studies have shown increased rates of bone density loss and fracture compared to the general population in people who used either enzyme-inducing AEDs or non–enzyme-inducing AEDs.[51,56,57] In a tertiary epilepsy center, more than half of patients on hepatic enzyme–inducing AEDs and one-third on non–enzyme-inducing AEDs had vitamin D deficiency.[58] Published evidence evaluating the level of risk to bone health associated with an individual AED is very limited, particularly for newer-generation agents.[56]

Presently, no evidence-based guidelines address prevention, screening, or treatment of low bone density in people with epilepsy. One prospective treatment trial was conducted in men on chronic AED therapy and compared use of calcium and vitamin D supplementation alone or in combination with risedronate.[59] Calcium and vitamin D alone were effective in improving bone mineral density but less so than with the addition of risedronate. The group treated with risedronate also had a lower rate of vertebral fracture.[59] Common practice is to recommend calcium and vitamin D supplementation to patients taking AEDs as a simple, low-cost intervention for prevention and potential treatment of AED-related bone disease, with higher doses of vitamin D (such as 2000 IU per day) recommended for those taking enzyme-inducing AEDs. Measurement of serum vitamin D levels and parathyroid hormone can be considered, but again there is no consensus about when or how often. Additionally, no consensus or evidence indicates when and in whom to consider screening with bone mineral density analysis. Given the complexity of

States Requiring Mandatory Reporting of People With Seizures to the Motor Vehicle Administration

TABLE 9-2

- California
- Delaware
- Nevada
- New Jersey
- Oregon
- Pennsylvania

diagnostic and management decisions, involvement of an endocrinologist may be considered.

Mortality is also increased for people with epilepsy. Population-based studies have found standardized mortality ratios of 1.6 to 3.0 for adults with epilepsy and 6.4 to 7.5 for the subgroup with childhood-onset epilepsy.[60] Mortality is often related to medical conditions, of which seizures are symptomatic. A 30-year population-based study of childhood-onset epilepsy in Olmsted County, Minnesota, found that death was primarily caused by complications of disease underlying epilepsy or from causes unrelated to epilepsy.[61] Mortality due to a seizure was rare and similar to that expected in the general population.[61] In children and adults, death can occur from seizure-related injuries and accidents, including drowning, falls, and motor vehicle crashes.[60] As noted earlier, the risk of suicide is also increased in people with epilepsy.[7–9] Noncompliance with prescribed AED therapy has been linked to increased risk of mortality.[62]

The most common cause of mortality directly associated with a seizure is sudden unexpected death in epilepsy (SUDEP).[63] SUDEP is a sudden, unexpected, nontraumatic, nondrowning death in a person with epilepsy where autopsy reveals no other anatomic or toxicologic cause of death. Most occurrences of SUDEP are unwitnessed, but victims are often reported to have had a known or suspected generalized tonic-clonic seizure shortly prior to death. Based on a recent evidence-based review, the incidence of SUDEP in childhood is 0.22/1000 patient-years (95% confidence interval 0.16–0.31) and in adults is 1.2/1000 patient-years (95% confidence interval 0.64–2.32).[64] This corresponds to 1:4500 children with epilepsy in 1 year and 1:1000 adults with epilepsy in 1 year. Several risk factors for SUDEP have been identified (TABLE 9-4).[64] The strongest association is with uncontrolled generalized tonic-clonic seizures. Having one to two convulsions per year carries a fivefold increased risk for SUDEP, and three or more convulsions per year carries a 15-fold increased risk.[65]

Physicians do not necessarily agree on how, when, and with whom to discuss SUDEP. Chart review indicates that documentation of SUDEP discussion by providers is rare.[66] Reasons cited by providers to avoid this discussion include the

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TABLE 9-3

Selected Strategies to Reduce Risk of Seizure-related Injury

- Wear a helmet when biking or horseback riding
- No unsupervised swimming
- Use a shower rather than a bathtub
- Adjust the temperature on the hot water heater to lower the risk of scalding
- Use a microwave versus a stovetop
- Avoid locking the bathroom or bedroom door
- Place bed mattress on the floor
- Use an epilepsy safety pillow (designed to reduce risk of suffocation if lying face down)
- Use soft or padded furniture
- Avoid high ladders
- Follow driving regulations for people with epilepsy
- Take medication as prescribed

generally low risk and the potential to cause unnecessary anxiety and stress.[67] In a survey of families who had experienced SUDEP, only 18% recalled being informed about SUDEP, but 72% wished they had received this information from their physician.[68] Only 10% preferred no counseling.[68] In surveys of adults with epilepsy and parents of children with epilepsy, the majority of respondents indicated they want this information from their neurologist.[69,70] In 2017, the AAN issued a practice guideline on SUDEP, which includes recommendations about how to counsel patients and families.[64] Risk of SUDEP can be reduced through nocturnal supervision, either direct or via a listening device, and through improved medication compliance.[64] As with other safety restrictions, recommendations should take into consideration the specifics of the individual's epilepsy as well as social and cultural norms.

SOCIAL HEALTH: RELATIONSHIPS AND GENETIC BURDEN

Epilepsy can negatively impact relationships with family, caregivers, friends, schoolmates, and coworkers. In a survey of more than 1000 people with epilepsy living in the community, the diagnosis was reported to negatively affect relationships with others in 32%, relationship with spouses or partners in 28%, and relationship between patients and their children in 25%[55]; 21% of patients reported that epilepsy negatively affected their sex lives.[55] Men and women with epilepsy are less likely to be married and less likely to have children regardless of marital status.[71–73] The lower birth rate for people with epilepsy likely reflects both social and biological factors. Potential barriers include financial restrictions due to underemployment, social isolation, adverse effects of seizures and AEDs on sexual desire and reproductive endocrine function, and concerns about AED use during pregnancy causing birth defects. Some may also worry about epilepsy heredity.

Surveys of adults with epilepsy in both the United States and Korea showed that patients perceive the risk of passing on epilepsy to a child as much higher than the actual risk, and that this concern contributed to decisions to have fewer children.[74,75] A population-based study in Olmsted County, Minnesota, found that first-degree relatives of people with epilepsy have a threefold increased risk of having seizures.[76] Epilepsy is, of course, not a single disease and encompasses many etiologies ranging from those with little to no genetic risk to catastrophic genetic disorders with serious implications for family planning. Even among

Risk Factors for Sudden Unexpected Death in Epilepsy[a]

TABLE 9-4

Factor	Strength of Evidence
Presence of generalized tonic-clonic seizures (present versus not present)	Moderate
Frequency of generalized tonic-clonic seizures >3 per year	High
Uncontrolled seizures	Moderate
Failure to adjust medication for treatment-refractory seizures	Moderate

[a] Modified with permission from Harden C, et al, Neurology.[64] © 2017 American Academy of Neurology.

hereditary forms of epilepsy, inheritance is often complex and multifactorial. The task of appropriately counseling individuals who seek to know the risk of passing on epilepsy to a child can thus be highly complex. Genetic testing for epilepsy diagnosis is reviewed in the article "Evaluation of Seizure Etiology From Routine Testing to Genetic Evaluation" by Stephan U. Schuele, MD, MPH, FAAN,[77] in this issue of *Continuum*. For some individuals and their families, genetic testing can provide important information about etiology, treatment, and prognosis and thus improve overall life quality. However, genetic testing can also have negative financial, emotional, and social consequences. The International League Against Epilepsy endorsed guidelines on genetic testing in 2010 that address these concerns.[78] Before proceeding with a genetic investigation, clinicians should consider the test accuracy, clinical validity, clinical utility, and utility to the individual with epilepsy and must be prepared to provide counsel on the implications of both a positive and negative result.[79] The task of counseling and test selection can be daunting to many neurologists, and referral to a geneticist or epileptologist with expertise in this area may be warranted.

KEY POINTS

- Evidence-based or expert consensus recommendations on prevention, screening, and treatment of bone disease and fractures in people with epilepsy are lacking. Medical providers must rely on common sense or strategies used in the general population.
- Mortality in patients with epilepsy is primarily attributable to underlying medical disorders, rather than to seizure-related injury or sudden unexpected death in epilepsy.
- Uncontrolled generalized tonic-clonic seizures are an important risk factor for sudden unexpected death in epilepsy.
- The majority of people with epilepsy want to be informed by their physician about sudden unexpected death in epilepsy.
- People with epilepsy tend to overestimate the risk of passing on epilepsy to a child, which may falsely influence decisions about having children.

CONCLUSION

The repercussions of epilepsy can extend well beyond the isolated moments of time in which seizures occur. Negative implications for emotional, physical, and social health can significantly adversely affect the quality of life and "wellness" of the person with epilepsy, as well as that of their family, and has a high cost to society. Physicians are committed to promoting the health of patients under their care and should advocate for their well-being and independence, but to do so successfully, providers must be well versed in the risks of epilepsy beyond seizures to improve detection, treatment, and provide appropriate counsel. For many areas including depression treatment, SUDEP, bone health, and fractures, additional investigation and evidence to guide management is greatly needed.

USEFUL WEBSITES

CENTERS FOR DISEASE CONTROL AND PREVENTION MANAGING EPILEPSY WELL NETWORK
The Managing Epilepsy Well Network website has information for providers and patients about several self-management interventions including PEARLS (Program to Encourage Active, Rewarding Lives) and Project UPLIFT (Using Practice and Learning to Increase Favorable Thoughts).
cdc.gov/epilepsy/research/MEW-network.htm

EPILEPSY FOUNDATION STATE DRIVING LAWS DATABASE
A searchable database of state driving laws for epilepsy.
epilepsy.com/driving-laws

WEBEASE (EPILEPSY, AWARENESS, SUPPORT, AND EDUCATION)
WebEase (Epilepsy, Awareness, Support, and Education) is a free online self-management program for adults with epilepsy designed to help set and achieve goals.
webease.org/

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