Pediatric Seizures

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Educational Gap

The causes of seizures are many, and a number of other conditions can mimic seizures, making careful evaluation of seizurelike episodes critical. Febrile seizures are the most common type of seizure in children, and their management is usually the task of the general pediatrician. Status epilepticus constitutes an emergency situation that can have severe consequences and requires skilled therapy.

Objectives

After completing this article, readers should be able to:

1. **Identify the key elements in the evaluation of an individual who has seizures.**
2. **Know the main features of febrile seizures.**
3. **Understand the core principles in the treatment of status epilepticus.**
4. **Identify the salient clinical features of the main childhood epilepsy syndromes.**
5. **Be aware of common comorbidities in epilepsy syndromes.**
6. **Recognize the key differences between epileptic and nonepileptic seizures.**

Definition and Pathophysiology of Epilepsy

Seizures (sometimes called epileptic seizures) are the stereotypical clinical manifestations (signs and symptoms) of excessive synchronous, usually self-limited, abnormal electrical activity of neurons situated in the cerebral cortex. Epilepsy is defined as 2 or more unprovoked afebrile seizures (International League Against Epilepsy). Although both children who have normal development and children who have developmental delay can display unusual movements, the clinical signs (semiology) of epileptic seizures have specific stereotypical features.

At the cellular level, ordinarily the neurons of the cerebral cortex fire asynchronously, albeit in patterns that facilitate learning, memory, sensory input, and behavioral output of defined neural circuits. A zone of ictogenesis (an area of brain capable of generating seizures) contains millions of neurons, all of which can fire synchronously. During electroencephalography (EEG), the recording electrodes on the scalp detect the synchronous firing of at least a 1-cm^2 brain region as a spike and slow wave, the so-called epileptiform activity.

Causes of Acute Seizures and Mimics

The causes of epilepsy are varied. The most common causes of acute seizures are fevers, infections, and head injury, which are detected through history and laboratory testing. These types of seizures are referred to as symptomatic seizures. In general, patients who have focal seizures or focal neurologic signs should have neuroimaging on initial presentation.

The evaluation process begins with a careful history and description of the spells. Parents may not always recognize the symptoms of a seizure. Many epileptic seizures present as a substantial but stereotypical episode in which children demonstrate jerking of the limbs, drooling, and eye rolling, during which consciousness is clearly impaired. After this

Abbreviations

ADHD: attention-deficit/hyperactivity disorder
AED: antiepileptic drug
CAE: childhood absence epilepsy
CNS: central nervous system
EEG: electroencephalography
GTC: generalized tonic-clonic

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type of seizure, most children are confused and tired and may sleep for a prolonged period (postictal phase). However, not all seizures are easily recognized.

Signs can be subtle, with staring that resembles daydreaming or a vacant stare. During these types of seizures, children will not respond to tactile stimulation. Pertinent points in the history include the presence of clonic movements or jerks, facial movements, eye and head version, loss of bladder or bowel function, color changes, unusual noises, breathing abnormalities, heart rate changes, and other stereotypical movements. The length of each spell, the presence of a postictal phase, and how often the spell occurs should be determined.

Children often stare and do not respond to voice at times. This behavior is commonly referred to as daydreaming or mind-wandering. These benign, nonepileptic episodes may be characterized by the child quickly reorienting to the parents or caregiver, and no other signs or symptoms of a seizure are present. When a child appears to be daydreaming but has accompanying facial movements (eye rolling, blinking, or fluttering) or a pause in activity commonly referred to as behavioral arrest, one should consider the possibility of a seizure.

Episodic movements with altered consciousness suggest seizure activity when any of the following features are present: (1) no response to tactile stimulation (touch of the face or body), (2) unusual eye movements (rapid eye fluttering or fixed eye deviation), (3) unusual head movements (forced head version), (4) unusual mouth movements (chewing or lip smacking), (5) unusual facial movements (twitching of the face), (6) stereotyped hand movements (repetitive reaching), (7) unusual posturing of a limb (freezing of an arm or leg), or (8) unexpected incontinence.

The environmental setting and time of the day are also important to diagnose because nonepileptic spells may have inciting events. Nonepileptic spells during the night may be associated with sleep disorders, such as sleep apnea or sleepwalking. Nocturnal seizures may present as unexpected arousals with odd or repetitive hypermotor behavior or complex behavioral automatisms, such as lip smacking or other facial movements, stereotyped hand movements, unusual posturing, unexpected incontinence, or gelastic (laughing) spells. Nocturnal seizures are not associated with difficulty falling asleep, early morning or multiple awakenings, or prolonged periods of wakefulness without altered consciousness or other automatisms.

It is crucial to assess for other conditions that may mimic seizures, including sleep disorders, gastroesophageal reflux and other gastrointestinal disorders, and psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD). Review of the child's medications occasionally can reveal a medication that may lower the seizure threshold, although buspirone is the only psychotropic medication associated consistently with unprovoked seizures in children. Other medications used in the pediatric population, including stimulants and neuroleptics, rarely, if ever, lower the seizure threshold in an individual patient.

A family history of epilepsy is a risk factor for epilepsy in children and should be assessed. Parents should keep a seizure diary describing the spells in detail and including the time of day the spells occur, the length of the spells, and whether there was a postictal phase. Videotape recording of the spells is encouraged, especially when the event is not clearly epileptic. One should note a previous history of epilepsy; whether the child is taking antiepileptic drugs (AEDs); presence of conditions associated with electrolyte (magnesium, phosphate, or calcium) disturbances, such as diarrhea or rickets; presence of acidosis associated with hypoxia; and history of ingestion. Provoking factors, such as sleep deprivation, fevers, and illness or infections, should be noted.

A child who presents with a change in sensorium and repetitive seizures, with or without fever, should be investigated for encephalitis. Focal neurologic signs may or may not be present with encephalitis. Persistent focal neurologic signs after seizures not associated with fever should alert one to the possibility of an arterial stroke or cerebral venous sinus thrombosis. Persistent focal neurologic deficits usually warrant acute neurodiagnostic testing with computed tomography of the head with contrast.

Febrile Seizures

The most common type of seizures in the pediatric population is the febrile seizure. Febrile seizures are defined as seizures occurring in childhood after age 1 month, associated with febrile illness but not caused by infection of the central nervous system (CNS), unassociated with previous neonatal seizures or unprovoked seizures, and not meeting criteria for other acute symptomatic seizures. Febrile seizures usually occur in children ages 6 months to 5 years, with a peak age at onset of approximately 18 months. The incidence is 3% to 8% in children younger than 5 years.

There are 2 types of febrile seizures: simple and complex. Simple febrile seizures are the most common type and are characterized by (1) generalized clinical features, (2) duration less than 15 minutes, and (3) a single seizure in a 24-hour period. In contrast, complex febrile seizures

are characterized by (1) focal clinical manifestation, (2) duration longer than 15 minutes, and (3) more than one in a 24-hour period. Approximately 25% to 40% of children who have febrile seizures have a family history of febrile seizures; 9% to 22% of children have a sibling who has a history of febrile seizures.

A high incidence of sodium channel mutations is reported in patients who have febrile seizures in childhood. The most important risk factors that predispose children to having febrile seizures include peak temperature during the illness, history of febrile seizure in first-degree relatives, neurodevelopmental delays, increased exposure to human herpesvirus 6, and vaccinations with measles-mumps-rubella, diphtheria-tetanus-pertussis, and influenza vaccines. Almost 50% of the children who present with febrile seizures will not have any identified risk factors.

The main purpose of the evaluation of children who have febrile seizures is to exclude underlying CNS infections. Lumbar puncture should be considered strongly in infants younger than 12 months, those who have prolonged complex febrile seizures or febrile status epilepticus, and children who are partially treated with antibiotics. Routine EEG and neuroimaging are not indicated for simple febrile seizures. Neuroimaging is recommended in patients who have complex febrile seizures, neurologic deficit on examination, prolonged postictal state, and signs of raised intracranial pressure. Patients who have febrile status epilepticus require EEG testing.

Reassurance and counseling are essential in the management of febrile seizures. Rectal diazepam can be used in the short term in a child who has risk factors for recurrent febrile seizures, prolonged febrile seizures, or a very low threshold for febrile seizures. Daily prophylactic antiepileptic medication may reduce the recurrence of the febrile seizures but will not reduce the risk of developing epilepsy and is not recommended routinely. Recurrence of a febrile seizure usually occurs within the initial 1 to 2 years after the initial seizure. (1) This association is important to note when counseling families, given the high degree of anxiety surrounding seizures.

The risk of recurrence of a febrile seizure is approximately 60% after the initial febrile seizure. Risk factors for recurrence include younger age of onset, having an initial febrile seizure associated with a relatively low temperature, family history of febrile seizures in a first-degree relative, and brief duration between the onset of the fever and seizure. Approximately 2% to 7% of children who have a history of febrile seizures have a risk of developing epilepsy. Risk factors for developing subsequent epilepsy after febrile seizures include having a family history of epilepsy, complex febrile seizure, and neurodevelopmental abnormalities.

Approximately 40% of adults who have a history of complex febrile seizures and febrile status epilepticus in childhood develop mesial temporal lobe epilepsy. Simple febrile seizures have a benign prognosis. There is no significant association between febrile seizures and later significant cognitive developmental delay or with sudden infant death syndrome.

Treatment of Seizures

In the pediatric population, treatment with AEDs is recommended after 2 or more recurrent afebrile seizures. The characteristics of different types of seizures and drugs of choice for treating them are presented in the Table. Most children (approximately 60%) who experience a single unprovoked seizure will not have another. As indicated below, the choice of AEDs is dictated mainly by the seizure type and interictal findings on EEG. However, the other factors should be considered, including the need to control mood stability, the presence of comorbid conditions (obesity), and the simultaneous use of other medications (long-term antibiotic therapy, such as with macrolides).

The Food and Drug Administration has approved a number of drugs, including levetiracetam and oxcarbamazepine, for use as therapy in pediatric seizures. Levetiracetam can be used to treat partial or generalized seizures, whereas oxcarbamazepine is indicated for partial seizures. Initial doses of levetiracetam (20 mg/kg daily; range, 20-60 mg/kg daily) and oxcarbamazepine (10 mg/kg daily; range, 10-40 mg/kg daily) can be increased every week to a higher dose. Other AEDs are discussed below and include valproic acid, used to treat juvenile myoclonic epilepsy; ethosuximide-lamotrigine, used to treat childhood absence epilepsy (CAE); and carbamazepine-gabapentin, used to treat benign rolandic epilepsy.

Fast-metabolizing individuals between 6 and 60 months of age can be identified by measuring trough AED levels before the initial morning dose. Oxcarbamazepine and carbamazepine levels can be elevated by macrolide antibiotics. Levetiracetam can exacerbate known neurobehavioral symptoms. A total of 100 mg/d of vitamin B_6 can mitigate this problem. Complete blood cell counts and serum sodium levels are monitored in patients taking oxcarbamazepine because this drug can depress the white blood cell counts and sodium levels.

When doses of AEDs are missed, the medication should be taken at the next opportunity (after the realization that the dose was missed). When patients are seen

Table. **Characteristics of Distinct Seizure Phenotypes**

Seizure Type	Interictal EEG Features	Treatment of Choice
Partial complex	Focal epileptiform or focal slowing	Oxcarbamazepine, levetiracetam
Generalized		
Tonic-clonic	Generalized epileptiform activity	Lamotrigine, valproic acid topiramate
Absence	3-Hz generalized spike wave	Ethosuximide, valproic acid, lamotrigine
Atypical absence	≤2.5-Hz generalized spike wave	Valproic acid
Myoclonic tonic or atonic	4- to 6-Hz spike/polyspike and 1.5- to 2.5-Hz generalized spike wave	Valproic acid, levetiracetam Lamotrigine, topiramate, clobazam, rufinamide, felbamate

in the emergency department with frequent seizures after missing doses, levetiracetam can be reloaded intravenously at 20 to 30 mg/kg per dose.

In general, AED therapy is continued for at least 2 years of seizure freedom. AEDs should be weaned gradually for months when possible. The risk of seizure recurrence (approximately 90%) is highest in the 2 years after therapy discontinuation, with most recurrences in the first year.

Children who have the highest risk of seizure recurrence are those having (1) a history in the distant past of a disorder, such as viral encephalitis, that is known to cause seizures; (2) abnormal EEG findings (epileptiform discharges or focal slowing); (3) nocturnal seizures; (4) a history of febrile seizures; and (5) a history of Todd paresis. (2)

Pediatric patients who have active epilepsy should not participate in contact sports that can cause head injury, such as football, and should never swim unsupervised or alone or ride a bicycle without a helmet. In addition, every family should be educated about seizure first aid, when rescue medications should be administered, and when to go to the emergency department for increased seizure frequency.

Uncontrolled seizures put patients at risk for significant morbidity and mortality. For instance, the risk of death is elevated 8-fold for children who have autism who also have epilepsy. Sudden unexplained death in epilepsy can occur in patients who have uncontrolled seizures. Current standard of care in these patients includes conversations about the deadly consequences of seizures, the implication on prognosis, and the impact on quality of life.

Treatment of Status Epilepticus

Status epilepticus is defined commonly as repeated seizures without a return to consciousness lasting longer than 30 minutes. Most types of epileptic seizures can be manifested as status epilepticus. The 2 major types of status epilepticus, generalized convulsive status epilepticus (major motor seizures and recurrent generalized tonic-clonic [GTC] convulsions) and nonconvulsive status epilepticus (recurrent nonconvulsive seizures, which include absence status, partial complex status, and simple partial status), are recognized clinically.

Convulsive status epilepticus is the most common emergency associated with neurologic disease because brain damage and death can result from the systemic consequences of repeated GTC seizures. Most persons who experience GTC status epilepticus have localized cerebral disturbances as a cause and therefore have secondary generalized partial seizures.

Repeated cerebral epileptic activity can disrupt brain structures or otherwise cause permanent neurologic or intellectual deficits. Common causes of status epilepticus include CNS infections, toxins, ingestions (including AED ingestion), and drug withdrawal, such as from opiates or benzodiazepines. The most common cause of benzodiazepine withdrawal seizures is abrupt discontinuation of clonazepam use in patients undergoing long-term therapy for seizures or anxiety.

Therapy must be directed at suppressing all ictal (electrical seizure) activity on EEG. Ictal EEG activity can show the following progression: (1) discrete seizures, (2) merging of seizures with waxing and waning of amplitude and frequency in variable locations, (3) continuous ictal activity, (4) continuous ictal activity intermixed with periods of isoelectric EEG, and (5) a periodic lateralized or generalized epileptic discharge pattern.

Frequent repetitive GTC seizures create a life-threatening systemic condition of hyperpyrexia, failure of cerebrovascular autoregulation, acidosis, and severe hypoxia, causing hypotension, hypoperfusion of the brain, pulmonary edema, electrolyte disturbances, and eventual circulatory collapse. Even after cessation of status epilepticus and

correction of systemic abnormalities, sepsis from aspiration pneumonia can be a late but life-threatening complication.

Treatment of status epilepticus consists of correction of glucose, electrolyte, magnesium, and calcium disturbances; control of blood pressure and oxygenation; and the administration of benzodiazepines and a series of routine anticonvulsants. At home, caregivers and parents can administer rectal diazepam, which is absorbed rapidly through blood vessels, while they call 911 to summon emergency medical personnel.

Intravenous lorazepam (0.1 mg/kg per dose) usually is administered first in treating status epilepticus. If the seizures do not break, a second dose of intravenous lorazepam (0.1 mg./kg per dose) is followed by fosphenytoin (20 mg/kg per dose). Next, a loading dose of phenobarbital (20 mg/kg per dose) is considered if seizures continue. Intubation is a consideration if respiratory depression is observed with either benzodiazepines or phenobarbital. Seizures that are refractory to the treatments described may necessitate the use of inhaled gases or, more commonly, pentobarbital-induced medical coma. During status epilepticus, transport to a facility skilled in dealing with pediatric status epilepticus, pediatric intensive care monitoring, and continuous video EEG monitoring is essential.

Partial Complex Epilepsy

The most common type of seizure during childhood, a partial seizure, is described in 2 categories. Simple partial seizures are those in which the initial clinical signs and EEG signatures begin focally in one area of the brain without impairment of consciousness. Simple partial seizures show focal neurologic signs, such as focal jerking of one hand or arm, sensory change or pain in one limb, or a unilateral contraction of the face.

Partial complex seizures (psychomotor seizures) are the more common of the 2 types of partial seizures that manifest as focal neurologic signs with impairment of consciousness. Commonly, for instance, in temporal lobe epilepsy, patients may experience a gustatory sensation, rising epigastric feeling, or some other aura followed by behavioral arrest. The child does not respond, often staring off, then becomes lethargic. Sometimes children develop jerking movements of limbs contralateral to the seizure focus.

Secondary generalization of partial complex seizures occurs when seizures spread to the opposite hemisphere and are manifest clinically as GTC seizures. Thus, when obtaining a clinical history in a patient who has had GTC seizures, it is important to consider partial epilepsy. The interictal epileptiform activity (between seizures) is unilateral, focal, or multifocal epileptiform discharges. The ictal manifestations on EEG usually include evolving focal sharp waves or spike and slow wave discharges. Levetiracetam or oxcarbazepine often are used as first-line monotherapy for the treatment of pediatric partial seizures.

As children become older, epileptiform discharges on EEG are more frequent in the frontal or centrofrontal regions. Adolescents can have multifocal epilepsy, in which the predominant seizure type is a partial complex seizure. However, most seizures in the adolescent are generalized seizures. GTC seizures are the most common type of generalized seizures.

The seizure may have a prodrome in which a change in behavior is seen. However, most seizures begin without warning when the patient falls to the floor and cries out, the eyes roll toward the back of the head, and the limbs exhibit a rhythmic, tonic-clonic-tonic pattern of jerking. The individual may lose bowel or bladder function at the end of the seizure (ictal phase). Cyanosis can develop but usually is transient.

GTC seizures are typical of frontal lobe epilepsy, which occurs in adolescents. The EEG correlate is a buildup of low-voltage fast activity, which evolves into high-amplitude spike/polyspike or polyspike and wave discharges. Patients typically are sleepy or confused for a period after the seizure (postictal phase).

Many broad-spectrum AEDs, including levetiracetam, lamotrigine, topiramate, valproic acid, and zonisamide, are used in the treatment of GTC seizures.

Idiopathic Generalized Epilepsies

The second most common type of epilepsy, CAE, accounts for 8% of epilepsy cases in school-age children and has an estimated incidence of 7 in 100,000 children ages 1 to 15 years. The incidence peaks at age 5 years, and girls constitute 60% to 70% of those who have CAE. Absence seizures are characterized by lapses in consciousness in which one can see a motionless stare, usually lasting 10 to 15 seconds. During this brief event, eyelids may droop, flutter, or briefly roll backwards. The children usually resume their full activity after the seizure or may be briefly confused (<30 seconds).

Absence seizures can be associated with other activity, including automatisms, brief clonic movements of arms or eyelids, or loss of postural tone. The onset of absence seizures is associated with an EEG pattern of regular, bilaterally frontal-predominant generalized 3-Hz spike and

wave discharges, which begin and end suddenly in the setting of a normal EEG background.

With either absence or GTC seizures, children can have fragments of interictal discharges, which include bilaterally frontal-predominant generalized spike and slow wave discharges. In the clinical trial study of CAE, treatment with ethosuximide, valproic acid, and lamotrigine had the greatest efficacy. (3) Ethosuximide, which causes gastric upset, is taken in capsules or liquid at a dose of 20 mg/kg daily divided twice a day. Lamotrigine had the least efficacy but the best adverse effect profile in the trial. With its black box warning regarding the risk of rash and Stevens-Johnson syndrome, lamotrigine should be administered cautiously, with dose changes every 10 to 14 days, until reaching a dose of 5 mg/kg daily divided twice a daily. Valproic acid is discussed below. In general, most children who have CAE have remission of absence seizures by ages 12 to 16 years. Comorbidities are common and include subtle cognitive deficits, linguistic difficulties, and psychiatric disorders, particularly ADHD and anxiety.

Atypical absence seizures are lapses in consciousness in which the patient can manifest a motionless stare, but these spells are associated more with motor signs, particularly changes in tone, and can be more apparent than typical absence seizures. These seizures can have focal or lateralizing signs. The onset and cessation of these seizures are less clear, and the duration is longer, typically 15 to 60 seconds, with variable postictal confusion. These children are more likely to have absence status epilepticus.

The clinical onset is associated with similar generalized spike-wave discharges but usually at a frequency of less than 2.5 Hz. Although atypical absence seizures can be seen in the setting of Lennox-Gastaut syndrome, these seizures are not common in this population. These seizures and typical childhood absence seizures often are responsive to valproic acid. Valproic acid usually is given at 10 to 15 mg/kg daily divided twice daily and should be avoided in children younger than 2 years. Maintenance doses usually are 25 to 30 mg/kg daily. Because of its ability to depress platelet counts and elevate liver function test results and pancreatic enzyme levels, routine blood monitoring of valproic acid levels, blood cell counts, and liver and pancreas function tests is recommended.

Juvenile myoclonic epilepsy is an epileptic syndrome of the idiopathic generalized epilepsy type of CAE, which begins at approximately ages 5 to 15 years. This epilepsy is defined by (1) myoclonic jerks on awakening, (2) GTC seizures in 90% of patients, and (3) development of absence seizures in one-third of all patients. Myoclonic seizures (epileptic myoclonus) are relatively rare outside the syndrome of juvenile myoclonic epilepsy and usually are seen in the most profoundly affected epilepsy patients, such as those who have Lennox-Gastaut syndrome. The broader term *myoclonus* refers to quick, involuntary muscle jerks that involve any part of the neuroaxis. Myoclonic seizures can be differentiated both by semiology and neurophysiologically from movement disorders, hyperreflexia, and rare cases of spasticity. Myoclonic seizures usually are bilateral generalized jerks (although they can be unifocal, multifocal, or unilateral), which are either sporadic or rhythmic in nature.

Commonly, myoclonic seizures are rapid, rhythmic, bilateral synchronous jerks (2-8 Hz) of the upper extremities with occasional lower-extremity or whole body involvement. The ictal EEG is characterized by generalized 4- to 6-Hz polyspike and slow wave discharges associated with the quick jerks. Most neuroimaging does not detect abnormalities in classic juvenile myoclonic epilepsy. Seizures usually are controlled easily with valproic acid (20-40 mg/kg daily divided twice daily) or levetiracetam (20-40 mg/kg daily divided twice daily).

Symptomatic Generalized Epilepsies

Tonic and atonic seizures are more common than, but not necessarily always associated with, Lennox-Gastaut syndrome. Those AEDs with Food and Drug Administration indications for Lennox-Gastaut syndrome, including lamotrigine, topiramate, rufinamide, clobazam, and felbamate, are all effective for seizures that collectively are causes of drops attacks (tonic, atonic, and myoclonic seizures).

Tonic seizures are more common in childhood and represent a continuum of the atonic-tonic seizures. These seizures are characterized by tonic spasms of the face or chest and trunk, with tonic flexion of the upper extremities and flexion or extension of the lower extremities. Along with impairment of consciousness, patients can have papillary dilation, tachycardia, apnea or cyanosis, and urinary incontinence, followed by a period of postictal confusion. Ictal EEG is low-amplitude, very fast activity.

Atonic seizures (usually called drop attacks) consist of a sudden loss of postural tone. In some patients, the drop attacks are preceded by one or more clonic jerks. In mild forms, the child may have a brief head drop (forward flexion of head and neck). In severe forms, the patient's whole body may drop to the floor and, if refractory to medications, may require a seizure helmet. The atonic seizure usually lasts only a few seconds and has little to no postictal period. The ictal EEG of an atonic seizure exhibits either generalized polyspike and wave discharges

or a sudden electrodecrement (suppression) of the EEG. Because synchronization of discharges between hemispheres is important for these seizure types to develop, a corpus callosotomy can be an effective surgical treatment to abolish these seizures.

Benign Rolandic Epilepsy

Benign rolandic epilepsy, also referred to as benign childhood epilepsy with centrotemporal spikes, is the most common type of partial epilepsy in childhood, with onset usually between the ages of 5 and 10 years. On the basis of its neuroanatomical location, most of these seizures involve unilateral facial sensory-motor and oropharyngogutteral symptoms, hypersalivation, and speech arrest. This partial seizure is the hallmark of benign rolandic epilepsy. The child is awake, fully aware but unable to speak, drooling, and experiencing unilateral face and arm twitching. GTC seizures also occur, and approximately 75% of children have these seizures only during sleep and have 5 or fewer seizures in their lifetime. Seizures can happen during the day and with more frequency in some patients.

Most child neurologists will prescribe medications only after 3 or more seizures, and, even then, the interval between seizures plus parental concern and anxiety are considered when initiating treatment with AEDs. Almost all of these seizures usually remit by age 16 years. However, approximately 20% have a medication-resistant epilepsy with several seizures or clusters of seizures during the day.

The hallmark of the EEG is biphasic, focal centrotemporal spikes and slow waves. The centrotemporal spikes are a clinical biomarker, with a strong genetic influence and linked clinical phenotype. Some patients who have centrotemporal spikes have a chromosome 11p13 autosomal dominant inheritance pattern with variants of the *ELP4* gene, a gene important in cortical maturation. Half of the children who demonstrate centrotemporal spikes might not show any clinical presentation of this EEG trait. According to 2006 International League Against Epilepsy guidelines, no AED has level A or level B evidence for efficacy and effectiveness. Carbamazepine, levetiracetam, valproic acid, phenobarbital, phenytoin, and clonazepam have equivalent efficacy in this syndrome. If AEDs are prescribed, they may be slowly tapered in patients who are seizure free for 2 years or more. Most seizures remit by age 16 years.

Infantile Spasms

Infantile spasms (West syndrome) are a specific type of seizure occurring in infancy that often is classified as an epileptic encephalopathy. This condition is considered among the most severe developmental epilepsies of infancy and childhood. With more than 200 known causes, infantile spasms has a diverse set of causes, including hypoxic ischemic encephalopathy; tuberous sclerosis; brain malformations; central nervous system infections, including TORCH (toxoplasmosis, other [syphilis, varicella-zoster, parvovirus B19], rubella, cytomegalovirus, herpes) infections and encephalitis with herpes simplex virus; metabolic disorders; and genetic causes, such as Down syndrome.

Gene mutations that affect synapse development, ion transport, protein phosphorylation, gene transcription, and other cellular functions are novel genetic causes associated with infantile spasms.

The clinical presentation of infants ages 3 to 9 months includes spasmlike seizures that involve flexion, extension, or mixed flexion-extension of the arms, legs, and trunk. The spasms occur in clusters associated with electrodecremental response on EEG. The background or interictal EEG is chaotic, with a characteristic pattern called hypsarrhythmia.

High-dose adrenocorticotropic hormone therapy (150 IU/m^2 body surface area per day) for 2 weeks, followed by a taper, is considered by the American Academy of Neurology and the Child Neurology Society to be the treatment of choice for infantile spasms. Adrenocorticotropic hormone therapy remains the gold standard for the termination of spasms and resolution of hypsarrhythmia on EEG. Both goals are considered important to maximize neurodevelopmental outcome. Thus, it is considered important to identify and begin therapy as soon as possible in patients who are having infantile spasms.

Vigabatrin (100-150 mg/kg daily divided twice daily) usually is the treatment of choice for children who have tuberous sclerosis who have infantile spasms. Treatment with vigabatrin typically is for 6 months, during which time formal eye examinations should be monitored for retinal toxic effects. The overall neurologic outcome is poor in patients who have symptomatic causes of infantile spasms, whereas those who have cryptogenic infantile spasms can have better outcomes. Children who have Down syndrome, however, respond well to treatment of infantile spasms. Recurrence of other seizure types after treatment of infantile spasms is common. Patients who experience cessation of infantile spasms should be considered for long-term AED therapy for at least 1 year after treatment.

Cognitive and Behavioral Issues in Epilepsy

Many epileptic syndromes, such as benign rolandic epilepsy and CAE, demonstrate that pediatric epilepsies

can have significant potential comorbidities that involve behavior and cognition. (4) Recent studies in children who have new-onset epilepsy suggest that the mechanisms responsible for seizures in childhood rather than the epilepsy itself may be responsible for cognitive difficulties. Children who have new-onset seizures have a higher occurrence of depressive disorders (22.6%), anxiety disorder (35.8%), and ADHD (26.4%) compared with controls ($P<.01$), but no difference was found in children who have focal vs generalized seizures. In 45% of the children who have epilepsy, psychiatric comorbidity antedated epilepsy. (5)

In a similar group of patients who have new-onset seizures, ADHD, inattentive type, was seen in 31% of patients vs 6% of controls ($P<.001$). The onset of ADHD antedated the diagnosis of epilepsy in 82% of patients, with 65% of patients having been referred for educational support services. Again, no difference was seen in generalized vs focal epilepsy.

Data on cognitive ability, language skills, and presence of psychopathology in 69 children who have CAE and 103 age- and sex-matched healthy children suggested a similar theme. Patients and their parents had semistructured psychiatric interviews, cognitive evaluation, and language testing. Twenty-five percent and 43% of the children who had absence epilepsy had subtle cognitive and linguistic deficits, respectively. Interestingly, a surprising 61% of children who have absence epilepsy satisfied *Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition)* criteria for a psychiatric illness, particularly ADHD and anxiety. Parents reported significant scores on the Child Behavioral Checklist in the areas of attention, somatic symptoms, and social and thought problems. (3)

The relation of these symptoms to the overall duration and frequency of absence seizures and to AED treatments suggests that the electrographic signature of 3-Hz spike and wave, even after disappearance of clinical seizures with AED treatment, may herald continuing neuronal dysfunction in multiple cortical-thalamic circuits.

Pediatric Pseudoseizures

Psychogenic nonepileptic seizures, also referred to as pseudoseizures, are relatively rare in the pediatric populations. (6) The prevalence is rare in adults (2-30 per 100,000 population), without similar data existing for pediatric populations. Approximately 5% of all events seen in the pediatric epilepsy monitoring of a children's hospital are psychogenic nonepileptic seizures. Most of these episodes occur in patients who have no history of epilepsy (67%), although one-third may occur in children who have epilepsy.

Psychogenic nonepileptic seizures are paroxysmal events that often resemble epileptic seizures but are psychological in origin. The major causes are stressors, usually associated with family, school, or friends. Less than 5% are due to physical or sexual abuse, but nonetheless it is important to screen for this important potential cause.

In younger patients, prolonged unresponsiveness with subtle motor changes tends to be the norm without any electrical changes on the EEG. Overall, children who have nonepileptic seizures typically are older, in the age range of 11 to 14 years. The mean duration of nonepileptic seizures (≥3-4 minutes) is much longer than the typical pediatric epileptic seizure duration of 1 to 2 minutes. Tremors, either synchronous or asynchronous, in the upper extremity are the most common motor signs. Tremors confined to one limb are observed commonly in the setting of at least some responsiveness.

Unresponsiveness with expression of mostly negative emotion (weeping, crying, painful facial expression, or fear) or laughing was observed more in the older patients. More complex motor movements, often asynchronous and involving multiple limbs, often are associated with disturbed consciousness. Memories of these events and a short apparent postevent period with quick return to normal activity should increase the suspicion of a nonepileptic seizure.

Treatment of nonepileptic seizure begins immediately after video EEG monitoring with a consultation with a child psychiatrist. Before the consultation, a conversation with the child's caregivers regarding the nature of the spells and video EEG findings is of paramount importance. Nonepileptic seizures do not have an organic cause but require a search for psychogenic factors. The loss of consciousness that can occur during nonepileptic seizures is puzzling but should be discussed with the family.

Typical conversations center around the reactions of the body, comparing nonepileptic seizures to other stress reactions. It is important to point out that although the cause is psychological in origin, the condition is no less important and also very amenable to treatment if instituted promptly. It is important to emphasize to parents that undergoing further unnecessary medical diagnostic testing only delays treatment and should be avoided.

Treatment of psychological factors with medications for anxiety or depression with or without cognitive behavioral therapy usually results in a lessening and then complete disappearance of the nonepileptic seizures.

Suicidal and homicidal thoughts or delusions should be treated aggressively in conjunction with a child psychiatrist. Success with these treatment modalities is high in children up to age 18 years, with more than 80% of patients experiencing significant reductions or cessation of their nonepileptic seizures.

Summary

- On the basis of strong evidence, treatment is highly dependent on the seizure semiology results, electroencephalography (EEG) findings, and origin.
- On the basis of moderate evidence and consensus, vigorous use of video EEG recordings and home video cameras should be used to delineate the epileptic syndromes.
- On the basis of strong evidence, pediatric epilepsy syndromes have common comorbidities. As a consensus, some pediatric epilepsy centers consider referral to a neuropsychologist to be first-line care in these patients.
- On the basis of strong evidence and consensus, antiepileptic drug therapy has its own complications and should be discontinued after an appropriate treatment course.
- On the basis of moderate evidence and consensus, uncontrolled seizures put patients at risk for significant morbidity and mortality.

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Parent Resources From the AAP at HealthyChildren.org

The reader is likely to find material relevant to this article to share with parents by visiting these links:

- http://www.healthychildren.org/English/health-issues/injuries-emergencies/Pages/Seizures.aspx
- http://www.healthychildren.org/English/health-issues/conditions/head-neck-nervous-system/Pages/Difference-Between-Seizure-and-Convulsion.aspx
- http://www.healthychildren.org/English/health-issues/conditions/head-neck-nervous-system/Pages/Seizures-Convulsions-and-Epilepsy.aspx

PIR Quiz

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1. A 2-year-old has febrile seizures. Which of the following factors will increase her risk of subsequently developing epilepsy?
   - A. An initial febrile seizure with a relatively low temperature.
   - B. Brief duration between onset of the fever and seizure.
   - C. Complex febrile seizure.
   - D. Family history of febrile seizures in a first-degree relative.
   - E. Younger age at onset of febrile seizures.

2. Treatment with antiepileptic drugs is recommended after 2 or more recurrent afebrile seizures. A common question from parents in response to this treatment parameter is, "What percentage of children who experience a single unprovoked seizure will not have another?"
   - A. 10%.
   - B. 20%.
   - C. 40%.
   - D. 60%.
   - E. 80%.

3. An 8-year-old child with a long history of recurrent generalized tonic-clonic seizures develops generalized convulsive status epilepticus. Which of the following is the first treatment of choice on encountering trained medical personnel?
   - A. Diazepam.
   - B. Fosphenytoin.
   - C. Lorazepam.
   - D. Pentobarbital.
   - E. Phenobarbital.

4. A 7-year-old boy develops spells that consist of a unilateral contraction of the left side of his face without impairment of consciousness or speech arrest. Which of the following is the most likely diagnosis?
   - A. Absence seizures.
   - B. Benign rolandic epilepsy.
   - C. Juvenile myoclonic epilepsy.
   - D. Psychomotor seizures.
   - E. Simple partial seizures.

5. Generalized tonic-clonic seizures in adolescents are typical of which epileptic region of the brain?
   - A. Centrofrontal lobe region.
   - B. Corpus callosum region.
   - C. Frontal lobe region.
   - D. Parietal lobe region.
   - E. Temporal lobe region.

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