

Recognition and Management of Pediatric Seizures

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Epilepsy, sometimes also referred to as a seizure disorder, is one of the three most common neurologic disorders (with headaches and school problems) seen in a pediatric practice setting. Despite rapid advances in new medications and technology, such as video EEG monitoring and epilepsy surgery, there are a limited number of pediatric neurologists and epileptologists. Therefore, it is essential that pediatricians be well-versed in the recognition, management and outcome of pediatric seizures. This article provides an overview of seizure assessment and management in the pediatric setting, including seizure classification, differentiation between seizures and nonepileptic events, initial seizure work-up, commonly used anti-epileptic medications, seizures associated with neurocutaneous disorders, infantile spasms, febrile seizures, sudden death in epilepsy, and common comorbidities in pediatric seizure.

TERMINOLOGY

A seizure is a paroxysmal clinical event of the central nervous system, characterized by an abnormal electrical discharge and associated with a change in the usual functioning. A seizure occurs when there is a sudden imbalance between the excitatory and inhibitory inputs to a network of neurons in the cerebral cortex, so that there is overall excessive excitability.

Epilepsy is a chronic disorder characterized by recurrent unprovoked seizures. The diagnosis of epilepsy is made

when a child has two or more unprovoked seizures — that is, seizures not associated with triggers such as sleep deprivation, infection, trauma, intake of alcohol or the use of illicit drugs. Population-based studies have demonstrated a cumulative lifetime risk of having at least one seizure to be about 10%.^[REFERENCE] There is a higher incidence of seizures in both the elderly and the very young, with many epileptic syndromes presenting in childhood.

Epilepsy affects 0.5% to 1% of children up to age 16.¹ In children with developmental disabilities, the incidence of epilepsy increases by 30% to 50%.² Mortality is increased in people with epilepsy, but increased risk in childhood occurs primarily in children with associated neurologic abnormalities or intractable epilepsy. Epilepsy has a variety of causes, both genetic and acquired. The majority of new-onset epilepsy in children is idiopathic.

SEIZURE CLASSIFICATION

The classification of the seizure is critical for diagnosis and management. Seizures are classified on the basis of clinical event and electroencephalographic abnormalities (Sidebar 1, see page xxx). Seizures can be grouped into two broad categories, partial (focal) or generalized. Other events also may at first appear to be seizures.

Partial (Focal) Seizures

Partial (focal) seizures arise from a discrete area of the cortex of the brain.

Partial seizures can be either complex (impaired consciousness) or simple (no impairment of consciousness.) Complex partial seizures rarely begin with just tonic-clonic movements but typically start with some degree of impairment of consciousness and are then followed by automatic uncontrolled behaviors called automatisms. Automatisms may consist of unusual or typical body movements without purpose, such as lip smacking, gesturing, or repeating words or phrases.

Simple partial seizures can present as simple hand twitching or a focal sensation of a limb. They manifest clinically according to the part of the brain that is affected — motor, sensory, visual, auditory, olfactory, gustatory, or affective. Simple or complex partial seizures can rapidly generalize (spread) to involve the entire brain, so that it may be unclear clinically that the seizure actually began as a partial (focal) seizure onset, thus making accurate diagnosis and treatment complicated.

Generalized Seizures

Generalized seizures arise from the whole brain — that is, there is no one specific “seizure focus” that shows where the seizure begins on electroencephalogram (EEG). Generalized seizures can be characterized by either myoclonic (rapid jerk of body or limbs), atonic (loss of tone, drop attack), tonic (rigidity or stiffness), tonic-clonic (jerking with stiffness), or absence (staring spells) events. These seizure types also

may be a manifestation of one of the epileptic syndromes of infancy and childhood.

Other Events Masquerading as Seizures

It is sometimes difficult, especially in small children and infants, to determine whether a paroxysmal event is a seizure or a nonepileptic event. Examples of nonepileptic events include syncopal episodes, reflux, cardiac events, breath-holding, hyperreflexia, tics, self-stimulatory behaviors, psychogenic events, and dystonia. Particularly if the child is an infant or toddler, clues to the diagnosis may come from an eyewitness's

recounting of the event. For example, in breath-holding spells, the child cries, holds his or her breath, becomes cyanotic, and loses consciousness. There may be subsequent postural changes or convulsive or jerking movements. In infantile syncope, there is always a triggering factor, such as a bump on the head or a fright, after which the child becomes pale and loses consciousness secondary to decreased cardiac output (vasovagal response).

Other events that may seem to be seizure activity include tics, Tourette's syndrome, gastrointestinal reflux, dystonia, and self-stimulatory behaviors (autistic stereotypies). These are summarized in Table 1 (see page xxx).

any other prescribed or illicit medications, and increased stress, all of which may lower the seizure threshold.

The parents should be questioned about whether similar events have occurred in the past and whether the child has ever exhibited staring spells or episodes of confusion, jerking or twitching, or drop attacks. Question carefully, also, about sleep — does the child wake frequently, is he or she a sleepwalker, and is he or she not getting enough sleep? Seizures may occur during sleep and be unnoticed by the family and, again, lack of sleep can lower the seizure threshold. Family history is also important, so the clinician must ask about seizures and epilepsy as well as genetic diseases and whether any family members have ever had similar events.

CME EDUCATIONAL OBJECTIVES

1. Describe a plan for the evaluation of pediatric seizures.
2. Identify common neurocutaneous syndromes associated with seizure disorders in pediatric patients.
3. Diagnose and manage infantile spasms.

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[DISCLOSURES NEEDED]

THE FIRST ENCOUNTER

When a child presents to the office or emergency department for the first time after an unexplained paroxysmal event, the first goal is to stabilize the patient. After the child has been stabilized, the physician must determine if a seizure has occurred, and if so, if it is the child's first episode. Typically, the determination of whether or not a seizure has occurred is based upon the history.

The history should include a detailed description of the event. This is often difficult to ascertain because the witness may not be present in the exam room, since the event may have occurred at school, at a friend's home or with a babysitter. It is not uncommon to find that witness's memories of the event focus on the child's respiratory status and color or the lack thereof, as well as the child's lack of responsiveness. They often do not remember the sequence of events. It is important, therefore, to question them more than once, particularly regarding the onset of the event. Questions should include those listed in Sidebar 2 (see page xxx). Precipitating events must be taken into consideration and include sleep deprivation, use of over-the-counter cough and cold medications, use of

EVALUATION

The next goal is to determine the cause of the seizure. A full physical examination should be completed, with special attention paid to the skin (checking for neurocutaneous findings,) cranial nerves, reflexes, and cerebellar signs. The American Academy of Neurology Practice Parameter for evaluation of a first nonfebrile seizure in children states that, in the emergency department, the following tests should be performed.³

Laboratory tests should be based on individual historic or clinical findings and are not necessary in all cases. Tests may include serum sodium, glucose, magnesium, calcium, a complete blood count, and urine toxicology

Computed tomography (CT) should be done in a child of any age who presents with a focal neurological deficit or who has not returned to baseline within several hours after the seizure

Lumbar puncture need not be performed in a child with a first nonfebrile seizure and should be used only if there is concern regarding possible meningitis or encephalitis

Electrocardiogram (ECG) should be

performed if any cardiac symptoms are evident.

If the child presents to the office and initial evaluation was previously done in the emergency department, the following tests are recommended:

Electroencephalogram (EEG)

Magnetic resonance imaging (MRI) of the brain should be performed on any child with a significant motor or cognitive impairment of unknown etiology, abnormalities on neurological examination, a seizure of partial (focal) onset, age younger than 1, or EEG results that do not represent a benign partial epilepsy of childhood or primary generalized epilepsy (these include benign Rolandic epilepsy and childhood absence epilepsy).

If the child is known to have epilepsy, CT should be performed if the seizure is different from the usual seizures or there are new focal findings on the examination. In addition, serum levels of any anti-epileptic medications should be obtained (Table 2, see page xxx), and parents and child should be questioned to uncover any missed medication dosages.

Neurologists will use the results of the EEG to help determine if medications are required. In most instances, this can be a routine EEG (awake and drowsy recording). Starting at about age 10 or in anyone where the seizures arise out of sleep, it is prudent to order a sleep-deprived EEG, so that the child falls asleep during the test. Sleep is a very disinhibited state, thus EEG abnormalities are seen more frequently. However, there has been some recent controversy regarding whether or not sleep-deprived EEGs actually increase the yield of epileptiform abnormalities.

The MRI of the brain is the preferred imaging exam for a patient with seizure and is used to look for structural abnormalities, tumors, and vascular abnormalities. Young children or those with

SIDEBAR 1.

Classification of Seizures

Partial (focal, local) Seizures

- Simple partial seizures (consciousness maintained)
 - With motor signs
 - With autonomic symptoms and signs
 - With somatosensory or special sensory symptoms
- Complex partial seizures (consciousness impaired)
 - Partial seizures evolving to secondary generalized tonic-clonic seizures

Generalized Seizures (convulsive and nonconvulsive)

- Absence (consciousness impaired)
- Atypical absence (marked change in tone, not rapid in onset or cessation)
- Myoclonic seizures
- Clonic seizures
- Tonic seizures
- Atonic seizures (drop attacks)

Unclassified Epileptic Seizures

- Seizures that cannot be classified because of inadequate or incomplete data

behavioral issues may need to be sedated for the MRI. Table 3 (see page xxx) provides a list of all radiologic testing options in new-onset seizures.

SPECIAL CONSIDERATIONS

Febrile Seizures

A febrile seizure is defined as a “seizure in association with a febrile illness in the absence of CNS infection or acute electrolyte imbalance in a child older than 6 months of age without prior afebrile seizures.”⁴ Important things to remember are that a fever may not be present at time of seizure, febrile seizures can occur in any child, and febrile seizures are most common between ages 6 months and 6 years. The peak incidence of febrile seizures is age 18 months, and onset after age 7 is very uncommon.

A simple febrile seizure is an isolated brief generalized seizure, while a complex febrile seizure occurs when the seizure is prolonged (greater than 10 or 15 minutes) or there are multiple seizures within same febrile illness. Risk factors for febrile seizures include a first- or

second-degree relative with a history of febrile seizures, a neonatal nursery stay of more than 30 days, a developmental delay, and attendance at day care.⁵

When a child presents with a febrile seizure, acute management mandates that serious conditions, including meningitis, encephalitis, electrolyte imbalances, and other acute neurologic illnesses, are sought first. The American Academy of Pediatric guidelines suggest a lumbar puncture be strongly considered in children younger than 12 without an obvious source of the fever, children with a first complex febrile seizure, children with persistent lethargy, or children recently receiving antibiotics.⁶ An MRI or CT scan is not necessary for simple febrile seizures, and an EEG is of limited value with a simple febrile seizure. An EEG can be considered if the seizure was complex, there is a family history of epilepsy, or there are pre-existing developmental abnormalities.

In terms of prognosis, about 33% of all children with first febrile seizure will experience a second, and 10% will have

TABLE 1.

Classification of Pediatric Paroxysmal Events

Event	Disorder	Age	Information
Shuddering events – brief	Shuddering attacks	Infancy	Often with feeding
Jitteriness	Tremors	Neonates	Can be suppressed by holding limb, induced by movement
Periods of apnea, tonic extension, stiffening	Gastroesophageal reflux	Infancy	Child may also exhibit feeding problems such as spitting up
Exaggerated startle, apnea	Hyperreflexia	Infancy	Excessive startle (with touch or loud noises)
Breath-holding	Cyanosis or pallor, loss of consciousness, brief convulsion	Infancy, toddlerhood	Precipitating events
Repetitive movements or stiffening of legs	Self-stimulatory behaviors – stereotyped, purposeless	Infancy, toddlerhood	Often pattern of occurrence
Myoclonus/sleep myoclonus	Focal repetitive and rhythmic jerks that are multifocal and lightning fast	Any age	Associated with cerebral palsy
Psychogenic Pseudoseizures	Nonrhythmic posturing and clonic activity with no post-ictal period	School-age through adolescence	Precipitating factors include depression, abuse, school problems
Staring spells	Noted only by teachers or in certain situations	Toddlerhood through adolescence	Boredom, distractibility, associated with school problems, anxiety, language delays
Muscle contractions	Tics – intermittent, repeated, stereotyped – occur in infrequent to almost continuous manner	School age through adolescence	Vocal or motor
Syncope	Sudden faints	Often precipitating event	May be vasovagal
Visual symptoms	Migraines	Scotomas, visual loss	
Dystonia	Sustained muscle contractions that may cause twisting or repetitive movements		Painful postures or positions
Chorea	Irregular, rapid, uncontrolled, involuntary excessive movement that seems to flow randomly from one part of the body to another		

three or more.^[REFERENCE] Because the peak age of occurrence is 18 months, children who have febrile seizures at a younger age are more likely to have recurrences. There is an increased risk of febrile seizures with a positive family history of febrile seizures.⁷ Parents and caregivers should be instructed in fever prophylaxis, including the use of acetaminophen every 4 hours and ibuprofen every 6 hours. However, there is limited evidence that these measures prevent the

febrile seizure.

Neurocutaneous Syndromes

Neurocutaneous syndromes are a group of disorders in which skin lesions are associated with central nervous system abnormalities. Epilepsy is a feature of many of these disorders, most commonly tuberous sclerosis and Sturge-Weber syndrome.

Tuberous sclerosis (Figure 1, see page xxx) is the most common of the

neurocutaneous syndromes, occurring in approximately 5 in 100,000 births. It consists of a triad of seizures, learning disorder, and facial angiomas. Two gene loci have been documented; TSC1 is located at 9q34, and codes for the protein hamartin while TSC2, located at 16p13,³ codes for the protein tuberin. Sporadic TSC2 mutations are associated with the more severe clinical phenotype and present earlier in life with seizures and frequently with infantile spasms, mental

retardation, subependymal nodules and cortical tubers, and more severe renal involvement.⁷ Epilepsy occurs in approximately 78% to 96% of patients with tuberous sclerosis.^{8,9}

Epilepsy occurs in approximately 80% of children with Sturge-Weber syndrome, a sporadically occurring syndrome in which facial capillary angiomas are associated with leptomeningeal angiomas. A port-wine birthmark usually involves the trigeminal nerve and is associated with brain calcifications on the ipsilateral side (Figure 2, see page xxx). Approximately 85% of seizures begin before the second year of life.^{5,8} The seizures are focal, usually ipsilateral to the birthmark, often difficult to treat, and with a high incidence of status epilepticus. There is also a high incidence of mental retardation and associated progressive cortical atrophy. Treatment for the seizures usually begins with standard antiepileptics, but early resective surgery is advocated by some to preserve cognitive function.⁷

Neurofibromatosis type 1 (Figure 3, see page xxx) is a syndrome associated with multiple café-au-lait spots, neurofibromas, axillary freckling, Lisch nodules, and abnormalities on the brain MRI. NF-1 is an autosomal dominant disorder with a locus mapped to 17q11.² Children with NF-1 frequently are found to have learning disabilities, gliomas, bony dysplasias, attentional issues, and abnormalities on brain MRI, but the incidence of seizures is relatively rare. Approximately 3% to 12% of children with NF have seizures, and an additional 1.5% have infantile spasms.⁷

Infantile Spasms

Pediatricians frequently are the first to evaluate children with spasms. Parents usually present with complaints of unusual startles or jerking movements on awakening and falling asleep. Infantile spasms are perhaps one of the most devastating of the epilepsy syndromes

SIDEBAR 2.

Questions to Ask When Taking A Seizure History

- What was the age at onset?
- Is there a family history of seizures and similar events?
- What is the child's developmental history?
- Were there precipitating events? (Illness, trauma, toxicity, sleep deprivation, use of over the counter medications, etc.)
- What is the seizure etiology?
- Is there an aura? Visual, auditory, or other?
- Are there staring spells? Memory issues?
- What is the behavior before the seizure? After? During? Mood changes?
- Are there vocalizations? How are they characterized? Cry or gasp? Slurred speech? Garbled speech?
- Are there motor events during the seizure? Does the head turn? If so, is this early in the event or late? Do the eyes deviate? If so, to which side? Is there jerking, stiffening, repetitive purposeless movements? Are the movements generalized or focal?
- Is there a change in breathing? Is there cyanosis?
- Are there autonomic changes? Is there pupillary constriction or dilatation? Are there changes in respiratory or heart rate? Is there pallor? Is there loss of ability to speak or understand?
- Is there confusion, lethargy, sleepiness, incontinence, drooling, nausea, or vomiting during or after the event?
- What symptoms follow the event?
- Is there amnesia for the event? Is there confusion?
- Is there transient focal weakness? Is there paralysis?
- Did the child drop or fall to the ground?
- Was there generalized shaking or was it just one side or one part of the body?
- How long did the event last?
- Did the child exhibit chewing or any other kind of automatic behaviors?
- At what time of the day did the event occur?
- Had the child been sleeping? If so, how long after the child fell asleep did the event occur?

and may be missed at first. Onset tends to be between ages 4 and 7 months, and the spasms are characterized by a sudden contraction of flexor or extensor muscle groups of the head, trunk or extremities. Estimated prevalence is 1 in 2,000 to 6,000 live births, with most occurring in children with tuberous sclerosis, hypoxic-ischemic injury, congenital infectious diseases, inborn errors of metabolism, malformations of cortical development, genetic syndromes and chromosomal abnormalities. In a small percentage, the spasms are idiopathic.¹⁵

Clinically, the seizures may present as brief spasms with head drops and ex-

tensions of the upper extremities. Often, they are followed by a cry, and they may occur in clusters, many times daily. Presentation may be subtle and can also be confused with benign seizure disorders. Therefore, it is imperative that the pediatrician is aware of the child's developmental progress; it is more common for children with infantile spasms to demonstrate developmental delays either before or after the onset of spasms.¹⁶ The EEG diagnostic for infantile spasms and may show either a hypsarrythmia pattern (generalized disorganization) or a burst-suppression pattern.

The gold standard for treatment of

TABLE 2.

Indications, Dosing, and Side Effects of Anti-epileptic Medications

Medication (Brand Names)	FDA Indications	Other Common Uses	Starting Dose	Maintenance Dose	Dosage Schedule	
Carbamazepine (Tegretol, Tegretol XR, Carbatrol)	Simple and complex partial seizures	Behavioral issues	10 to 20 mg/kg/day	20 to 30 mg/kg/day	Two or three times per day	
Valproic acid (Depakote, Depakote ER, Depakene)	Partial and generalized seizures	Headache prevention, behavioral issues	10 to 15 mg/kg/day	60 mg/kg/day	Three times per day; daily or twice per day for extended release	
Lamotrigine (Lamictil)	Lennox-Gastaut, partial and generalized seizures; bipolar disorder	--	1 to 5 mg/kg/day	200 to 400 mg/day	Twice per day	
Levetiracetam (Keppra)	Adjunctive therapy	--	20 mg/kg/day	40 to 60 mg/kg/day	Twice per day	
Phenytoin (Dilantin, Phosphenytoin)	Partial and generalized seizures	--	15-20mg/kg IV for status epilepticus 5-10mg/kg/day	2-8mg/kg/day	10-20mcg/ml twice per day	
Phenobarbital	Neonatal seizures, partial and generalized seizures, myoclonic seizures, status epilepticus	Neonatal seizures, status epilepticus	Status epilepticus: 10 to 20 mg/kg intravenously, then 5 to 10 mg/kg intravenously every 15 to 30 minutes to maximum of 40 mg/kg Younger than 2 months: 3 to 5 mg/kg/day orally or intravenously Older than 2 months: 3 to 5 mg/kg/day	5 to 10 mg/kg/day	One, two, or three times per day	
Ethosuximide (Zarontin)	Absence seizures	--	7.5 mg/kg	15 to 40 mg/kg/day	Twice per day	
Felbamate (Felbatol)	Adjunctive treatment for Lennox-Gastaut, seizure disorder	Partial and generalized seizures – intractable	15 mg/kg/day	45 to 80 mg/kg/day	Twice per day	
Topiramate (Topamax)	Partial seizures, primary generalized seizures, migraine prophylaxis	Migraines	1 mg/kg/day	4 to 6 mg/kg/day	Twice per day	

	Target Serum Levels	Formulations	Side Effects	Severe Adverse Reactions	Management of Side Effects
	4 to 12 mg/L	100 mg/5 mL TYPE? 100 mg chewable 100 mg, 200 mg, 300 mg TYPE?	Weight gain, sedation, impaired attention	Vertigo, aplastic anemia, agranulocytosis	Monitor blood
	50 to 100 mg/L (but up to 150)	125 mg sprinkles 125 mg, 250 mg, 500 mg TYPE? 250 mg, 500 mg TYPE? (equivalent to three-quarters of VPA[WHAT IS THIS?] dose)	Weight gain, hair loss	Thrombocytopenia, anemias	monitor blood, zinc supplementation, use of [selenium-containing?] shampoo, dietary management
	2 to 20 mg/L	2 mg, 5 mg, 25 mg, 100 mg, 150 mg, 200 mg TYPE? 25 mg chewable	Dizziness, headache, sedation	Stevens-Johnson reaction, rash, ataxia; increased risk of rash when given with valproic acid	Steroids, benadryl, discontinue, titrate slowly (especially if used with valproic acid)
	Not established	250 mg, 500 mg, 750 mg TYPE? 100mg/mL TYPE?	Irritability, depression, anxiety	Psychosis, behavioral changes	B-complex vitamin supplement, slow titration
	--	50mg chewables 30mg, 100mg TYPE? 125mg/5mL TYPE?	Gum hyperplasia, facial coarsening, hirsutism	Anemias, ataxia, nystagmus (with elevated blood levels), mania	Dental follow up, blood monitoring
	20 to 40 mg/L	15 mg, 30 mg, 60 mg, 100 mg TYPE? 20 mg/5mL TYPE?	Hyperactivity, sedation, cognitive dulling	Bradycardia, hypotension	Monitor bloods
	40 to 100 mg/L	250 mg TYPE? 250mg/5mL TYPE?	Nausea, vomiting	Gastrointestinal upset, aggression, confusion, insomnia	Give with food; decrease dose
	30 to 100 mg/L	400 mg, 600 mg TYPE? 600 mg/5mL TYPE?	Weight loss, insomnia	Aplastic anemia, liver failure	Monitor chemistry and complete blood count weekly for first month, then monthly; dose in morning and at noon
	9 to 12 mg/L	15 mg, 25 mg sprinkles 25 mg, 50 mg, 100 mg, 200 mg TYPE?	Cognitive dulling, parasthesias, irritability, slurred speech	Kidney stones	Increase dose slowly; do not use with acetazolamide (Diamox), diuretics, or the ketogenic diet; reinforce need for adequate fluid intake

continued on page 8

continued from page 7

Medication (Brand Names)	FDA Indications	Other Common Uses	Starting Dose	Maintenance Dose	Dosage Schedule
Oxycarbazepine (Trileptil)	Partial seizures	Behavior	8 to 10 mg/kg/day	20 to 30 kg: 900 mg/day 30 to 40kg: 1,200mg/day More than 40kg: 1,800 mg/day	Twice per day
Zonisamide (Zonegran)	Partial seizures	Generalized seizures	1 to 2 mg/kg/day	400 to 600 mg/day	One to two times per day
Pregabalin (Lyrica)	Partial seizures	Neuropathy, neuralgia	3 to 5 mg/kg/day	Unknown	Three times per day
Vigabatrin (Sabril)	Infantile spasms		20 to 30 mg/kg/day	100 mg/kg/day (150 mg/kg/day with infantile spasms and tuberous sclerosis)	Twice per day
Gabapentin (Neurontin)	Partial seizures	Sleep, pain	100 mg	--	--
Tiagabine (Gabitril)	Partial and secondarily generalized seizures, Lennox-Gastaut		0.5 to 1 mg/kg/day	9 to 11 mg/kg/day	Twice per day

infantile spasms is adrenocorticotrophic hormone (ACTH) given intramuscularly. Other medications that have shown efficacy include topiramate (Topamax) and vigabatrin (Sabril), which is currently unavailable in the United States. ACTH has the highest responder rate among pharmacologic agents, except perhaps for the use of vigabatrin in those children with tuberous sclerosis and infantile spasms.¹⁷ Mechanisms of action in these medications differ; vigabatrin elevates GABA levels, while it is believed that ACTH suppresses excess production of corticotrophin-releasing hormone, reducing epileptogenicity and neuronal damage.

Initiation of ACTH treatment usually is done as an inpatient. Monitoring of blood chemistry, complete blood count,

urine for glucose, stool for blood, and blood pressure for hypertension is done before and after treatment. Caregivers are taught intramuscular administration of the medication, and referral to a visiting nurse service is made. The child is treated from 2 to 4 weeks with ACTH, with continued monitoring at home and weekly visits to the neurologist. After discharge, blood is drawn at least weekly.

Depending on outcome and protocol, the medication may later be changed to oral prednisone and tapered slowly. Children with infantile spasms have a very high risk of developing other types of epilepsy and frequently become patients with intractable seizures.

Sudden Unexplained Death In

Epilepsy

It is common for anyone witnessing a seizure to assume that the person experiencing the seizure is dying, and one of the first questions asked by the parents of any child with epilepsy is, "Will my child die of a seizure?" There is a higher mortality associated with the diagnosis of epilepsy, but it does vary according to certain risk factors. A recent review of population-based studies from both developing countries and industrial nations found mortality is higher in males than in females, single unprovoked seizures reveal little increase in mortality while poorly controlled seizures have an increased risk of sudden death, and there is little or borderline increase in mortality for people with idiopathic epilepsy. Additionally, mortality in selected popu-

	Target Serum Levels	Formulations	Side Effects	Severe Adverse Reactions	Management of Side Effects
	12 to 35 mg/L	300 mg/5mL TYPE? 150 mg, 300 mg, 600 mg TYPE?	Hyponatremia	Stevens-Johnson reaction	Steroids, diphenhydramine (Benadryl); discontinue medication
	--	50 mg, 100 mg TYPE?	Irritability	Aggression, emotional lability	Slow titration (long half-life); contraindicated with sulfa allergy
	--	25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg TYPE?	SIDE EFFECTS?	ADVERSE EFFECTS	MANAGEMENT
	--	100 mg, 500 mg TYPE?	Sedation, fatigue, depression, confusion	Peripheral vision loss	Wean after 1 year; monitor vision
		100 mg, 300 mg, 400 mg TYPE?	Sedation, rare behavioral problems	Irritability, agitation (usually in children with disabilities)	
	9 to 12 mg/L	25 mg, 50 mg, 100 mg, 200 mg TYPE? 15 mg, 25mg sprinkles	Abdominal pain, headaches	Can worsen seizures	Give with food

lations identifies an increase in mortality in children who have underlying neurological deficits.¹⁸

MANAGEMENT

After it has been determined that an event was a seizure, the next step is to determine whether the event was a response to an acute disorder (eg, fever, hypoglycemia, hyponatremia, hyperglycemia, meningitis, head trauma) or a response to an exogenous factor (eg, alcohol, drugs, toxins, medications that lower the seizure threshold, lack of sleep). If the child has no previous history of seizures and the seizure was precipitated by one of the above events, efforts are directed at correcting the precipitating event, and further work-up is not necessary. The child does not meet

the criteria for epilepsy and does not need to begin preventative medications. Acute provoked seizures are by definition a reaction of the brain to metabolic stress, injury, or inflammation. Again, a diagnosis of epilepsy is made when the child has two or more unprovoked seizures or one unprovoked seizure with an abnormal EEG. At that time, consideration is given as to whether anti-epileptic medication should be initiated.

Medications Used for the Chronic Treatment of Epilepsy

A decision to treat is based on the number of seizures, the time interval between seizures, and abnormalities on the EEG. When there are two or more unprovoked seizures, or one unprovoked seizure with an abnormal EEG, the deci-

sion is usually made to treat with medication.

The general rule for treating epilepsy involves initiation with monotherapy. Overall, about 60% of seizures are controlled with the first anti-epileptic drug.**[REFERENCE]** The goal of epilepsy treatment is to control the seizures with the medication or treatment having the fewest side effects. The decision making process involving which medication to use includes several factors, including the seizure type, existence of an underlying syndrome, age of the child, formulations available, and common side effects.

In the past 10 years, a number of different medications have been approved by the Food and Drug Administration for treatment of recurrent seizures in

TABLE 3.

Testing for new onset events

Test	Indication
Routine electroencephalogram (EEG)	Seizure activity other than febrile seizure
Sleep-deprived EEG	Children age 10 or older; events (seizures) arriving from sleep or when sleep-deprived
Electrocardiogram	Events that may be cardiac in nature; syncope with family history of cardiac problems
Magnetic resonance imagine	Partial onset seizures; usually not available emergently
Computed tomography of the head	Seizures where fracture or possible tumor is suspected (change in level of consciousness, abnormality on examination); used emergently
Video EEG	Equivocal results from routine or sleep-deprived EEG; nocturnal events
Magnetic resonance angiography	Events with visual changes; suspicion of vascular abnormality

children (Table 2). These medications have been used for some time by epileptologists. Specifically, oxcarbazepine (Trileptil) has been approved as monotherapy and adjunctive therapy for partial and secondarily generalized seizures in children 4 and older. Lamotrigine (Lamictil) is approved for use as adjunctive therapy for partial seizures in children 2 and older. Levetiracetam (Keppra) is approved for adjunctive therapy for partial seizures in children four years and older. Topiramate (Topamax) is approved as adjunctive therapy for partial and secondarily generalized seizures and primary generalized tonic-clonic seizures in children older than 2 and for initial monotherapy in children older than 10.

Dosing guidelines and information regarding side effects are included in Table 2. It is important to remember that nearly all of the anti-epileptic drugs carry a risk of bone metabolism abnormalities. For the most part, children on anti-epileptic drugs should also be treated with a multivitamin and possibly calcium carbonate with vitamin D. Folic acid should be supplemented in girls of child-bearing age.⁸

The side effects associated with the

use of anti-epileptic drugs include rash, hirsutism, and weight gain or loss. Severe side effects such as hepatic toxicity, Stevens-Johnson syndrome, and bone marrow toxicity may occur. If these occur, the medication should be stopped and the symptoms treated. These severe reactions cannot be anticipated and require early recognition of symptoms. Fairly frequently, children on anti-epileptic medications may experience behavioral changes and changes in cognition, which are often dose-related.⁸

In all seizures, decisions regarding administration of medication are influenced by the child's age, sex, underlying EEG abnormalities, and epilepsy syndromes. Two-thirds of children with no underlying structural abnormalities and normal development ultimately achieve cessation of seizures. Usually, children are weaned off of medication after being seizure-free for 2 to 5 years while receiving medication and having a normal EEG. Of these, 70% remain seizure-free.¹ Predictors of poor outcome include seizure recurrence in the first months after therapy initiation and developmental delay at onset.⁹

Families and caregivers of children with seizures should be provided with

emergency management guidelines to minimize trips to the emergency department. Rectal diazepam can be administered to stop a seizure and is the only medication currently FDA-approved for acute at-home use for treatment of seizures. Rectal diazepam is available in several different dosages, with all dispensed in either a 10 mg twinpak (with a 4.4-cm tip) or a 20 mg twinpak (with a 6-cm tip.) Dosing should be from 0.2 to 0.5 mg/kg as needed for a seizure lasting more than 5 minutes. The 10 mg can deliver doses of either 5 mg, 7.5 mg, or 10 mg (preset by pharmacist,) while 20 mg can deliver doses of 10 mg, 12.5 mg, 15 mg, 17.5 mg, or 20 mg. The risk of respiratory depression is almost nonexistent with administration of this medication. Families should be provided with information on administration and a plan for when to administer the medication.

ASSOCIATED PROBLEMS IN CHILDREN WITH EPILEPSY

It is well established that children with epilepsy have more associated learning, emotional, and behavioral problems than the general population. It is often management of these associated problems that is more difficult for both the family and the clinician than is the management of the seizures themselves.

Up to 30% of children with epilepsy have cognitive problems severe enough to warrant placement in special schools. Factors contributing to poor academic performance in these children include poorly controlled seizures, underlying brain lesions, side effects of medications and social issues.¹⁹⁻²²

Children with frequent seizures tend to have more behavioral problems, and the families of children experience significant amounts of stress. In fact, children with epilepsy have worse health-related quality of life outcomes than do children with other chronic diseases. This may be result of the stigma associated with epilepsy, including restrictions



Figure 1. Tuberous sclerosis is indicated by a symptom triad of seizures, learning disorder, and facial angiomas.



Figure 2. Patients with Sturge-Weber syndrome normally have a port-wine birthmark and usually have seizures ipsilateral to the birthmark beginning by the second year of life.

from certain physical activities, social exclusion, and high rates of maternal anxiety.^{22,23}

SUMMARY

It is not unusual for the primary care provider to have a child present with unusual paroxysmal events or dermatological lesions that bear further investigation. Although most children with epilepsy are treated and managed by pediatric neurologists, it is imperative that the primary care provider have a clear understanding of associated comorbidities, as well as information on the available anti-epileptic drugs, their side effects, and the need for further monitoring.

Those children with epilepsy whose seizures become intractable, failing to be controlled with three or more medications used appropriately at adequate doses, should be referred to a comprehensive epilepsy center for consideration for other treatments. These may include the ketogenic diet, vagal nerve stimulation, or epilepsy surgery.

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Figure 3. Neurofibromatosis type 1 is associated with multiple café-au-lait spots, neurofibromas, axillary freckling, and Lisch nodules. Abnormalities normally are found on magnetic resonance imaging of the brain.

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