ABSTRACT

The impact of childhood-onset epilepsy ranges from mild to catastrophic. Although many children outgrow seizure disorders or are able to maintain good seizure control, other children will go on to develop intractable forms of epilepsy. Epilepsy syndromes can be classified according to the usual age of onset. Identifying the syndrome helps to guide treatment selection and management. Healthcare providers must weigh the benefits of treatment against the adverse effects. Currently, there are limited data regarding the use of antiepileptic drugs in pediatric patients. When developing a treatment plan, clinicians must remember that children are not merely small adults. Treatment goals must be tailored to each child, taking into consideration the child’s and the family’s needs.


THE PEDIATRIC PATIENT WITH NEWLY DIAGNOSED EPILEPSY: PLANNING FOR A LIFETIME

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CHILDHOOD-ONSET EPILEPSY can range from being a mild inconvenience to a catastrophic illness. Some children will outgrow their seizure disorder, other children will have excellent seizure control, and some children will have seizure disorders that become intractable. Population-based studies indicate that at least 50% of childhood-onset epilepsies go into remission. Although a large percentage of children outgrow their epilepsy, it is just the beginning of a lifelong experience for many. Several of the childhood-onset epilepsies consist not only of seizures but can also include behavioral problems and cognitive impairment. Correct diagnosis, early intervention, and optimal treatment are necessary to minimize consequences and provide the most opportunities for the highest quality of life. This article reviews the most common epilepsy syndromes that begin in infancy, childhood, and adolescence.

SEIZURE SYNDROMES

Descriptive diagnosis of seizures can be made on 1 or 2 levels. The more basic descriptive diagnosis is based on the type of seizure. A broader descriptive diagnosis can be made by categorizing the condition as an epileptic syndrome or as a specific type of epilepsy. Approximately 50% of the cases of childhood epilepsy can be categorized at this level.

A seizure syndrome is defined as a cluster of signs and symptoms that customarily occur together, including type of seizure or seizures, electroencephalography (EEG) patterns, age of onset, neurological examination findings, psychomotor development, etiology, and clinical course. The International League Against Epilepsy currently uses 2 sets of criteria in...
defining epilepsy syndromes. The first classifies seizure type as generalized or as partial. There is also a sub-classification system based on the etiology of the disorder: symptomatic (known causes), cryptogenic (probably caused by some undetermined brain disorder), and idiopathic (no underlying cause other than possible hereditary predisposition).

Whether a seizure syndrome is idiopathic or symptomatic is significant in terms of prognosis. Idiopathic syndromes usually occur in the absence of neurological dysfunction, and development is normal. Seizures are typically self-limiting and respond to medication. Symptomatic syndromes are associated with cerebral disease or malformation, abnormal development, and lack of response to medication. Cryptogenic epilepsy presumably has an underlying cause, thus presents more often like symptomatic epilepsy. All these criteria must be taken into consideration when dealing with childhood epilepsy. Some types of childhood epilepsy may not require treatment because their prognosis is excellent without therapy. This is especially true for children who are neurologically normal and exhibit benign syndromes, such as febrile seizures or benign rolandic epilepsy. In contrast, children with brain damage or one of the symptomatic or cryptogenic epilepsies should be treated immediately. The Table lists the classes of epilepsy syndromes according to age at onset.

### Pediatric Epilepsy Syndromes

Febrile seizures are the most common type of seizures encountered in early life. The usual occurrence is in a healthy child with normal development, age 6 months to 2 years, and with a viral illness and a high fever. The seizures are classified as simple or complex. Simple febrile seizures last less than 15 minutes and lack any fociality; complex febrile seizures last longer and may have focal features or recur within 24 hours. The EEG readings are usually nonspecific. Prognosis is favorable and chronic treatment with antiepileptic drugs (AEDs) is not recommended. Rectal benzodiazepines may be prescribed to abort another attack if one occurs. Most children with febrile seizures do not have recurring seizures after 5 years of age. Approximately 2% to 4% of children who have febrile seizures develop epilepsy.

Infantile spasms, also known as West syndrome, are a unique form of seizure disorder limited almost entirely to infants during the first year of life. It is usually associated with developmental delay and a characteristic EEG pattern called hypsarrhythmia, which indicates chaotic brain activity. The most common seizures are described as “jackknife” or “salaam” seizures, but extensor or focal features are not uncommon. West syndrome has many causes, including tuberous sclerosis and various prenatal or acquired encephalopathies. In many cases, the cause cannot be determined. These cases are called cryptogenic and are thought to have better outcomes than symptomatic

<table>
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<tr>
<th>Neonatal Period</th>
<th>Infancy</th>
<th>Early Childhood (toddler and preschool age)</th>
<th>Childhood (school age), Adolescence, and Young Adulthood</th>
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<tr>
<td>Benign neonatal convulsions</td>
<td>Febrile seizures</td>
<td>Epilepsy with myoclonic absences</td>
<td>Childhood absence epilepsy</td>
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<td>Benign neonatal familial convulsions</td>
<td>Early infantile epileptic encephalopathy</td>
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<td>Miscellaneous neonatal seizures</td>
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<td>Infantile spasm (West syndrome)</td>
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<td>Reflex epilepsies (eg, photosensitive epilepsy, reading epilepsy)</td>
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<td>Severe myoclonic epilepsy of infancy</td>
<td>Epilepsy with continuous spike waves during slow-wave sleep</td>
<td>Juvenile absence epilepsy</td>
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<td>Benign myoclonic epilepsy of infancy</td>
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<td>Benign partial epilepsy of infancy</td>
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<td>Benign infantile familiar convulsions</td>
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<td>Symptomatic/cryptogenic partial epilepsies</td>
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cases. Regardless of cause, normal developmental outcome is reported in only 10% to 15% of patients. Infantile spasms remain medically resistant despite the emergence of new drugs and have been treated traditionally with corticosteroids. Vigabatrin has been reported to be effective, especially in patients with tuberous sclerosis. Surgery may be the treatment of choice in some cases in which a localized brain abnormality can be identified.

Dravet syndrome, or severe myoclonic seizures in infancy, is becoming increasingly recognized. Seizures typically begin in the first year of life, usually with febrile convulsions or clonic seizures. Myoclonic and/or partial and/or absence seizures occur between 2 and 3 years of age. Seizures are sometimes prolonged. The results of the EEG may initially be normal, but interictal generalized spike-wave complexes and/or generalized polyspike waves are seen within the second year of life. Developmental delay usually appears in the second year and unsteadiness of gait is also present. The overall outcome is poor. Virtually all patients continue to have seizures, and Dravet syndrome remains one of the most intractable forms of childhood epilepsy. Motor function remains poor in adolescents and in young adults, and a persistent tremor is common. Initially, it is easy to misdiagnose this condition as febrile convulsions. However, some factors may raise a red flag, including a low degree of fever (often below 100.5°F), seizures that last for more than 15 to 30 minutes, and a unilateral localization. Most striking is the frequent recurrence of the seizures (usually within 2 months after the first episode) and the occurrence of febrile seizures. The prognosis is poor in terms of seizure outcome and cognitive development.

Lennox-Gastaut syndrome occurs between 1 and 9 years of age, with peak occurrences between 3 and 5 years. Multiple seizure types occur, including tonic, atonic, myoclonic, and atypical absence seizures. An abnormally slow background and spike-wave discharges dominate the EEG and severe cognitive impairment is a routine occurrence. Seizures are generally resistant to treatment. The prognosis for seizure control and learning ability remain poor. Recurrent status epilepticus is common, and approximately 90% of patients have mental retardation or behavioral problems. Those cases that begin as infantile spasms seem to have an especially poor prognosis. Treatment is difficult, as AEDs are often ineffective. Some success has been attained with nonpharmacologic treatments, such as the ketogenic diet and vagal nerve stimulation (VNS). Surgery is considered in some cases. Resective surgery is sometimes attempted if a lesion is thought to be responsible for the syndrome. The surgical intervention often includes a corpus callosotomy for the treatment of the drop attacks which are responsible for multiple injuries to the patient. Once again, even if some degree of seizure freedom is attained, cognitive outcome is usually grim.

Childhood absence epilepsy (CAE) usually begins between 6 and 7 years of age. CAE is idiopathic and is characterized by brief absence seizures, normal neurological development, normal brain imaging, and 3-Hz spike-and-wave activity on the EEG. CAE is more common in girls and often there is a family history. It responds well to the proper AED therapy. The older AEDs valproate and ethosuximide have been the medications of choice, but the newer AED lamotrigine is presently included as a first-line drug. Other newer AEDs may also be effective for CAE. These seizures often remit and are not associated with any cognitive or behavioral impairment.

Benign partial epilepsy with centrotemporal spikes, or benign rolandic epilepsy (BRE), is the most common epilepsy seen in childhood. It usually begins between the ages of 3 and 13 years, with the peak incidence between 8 and 10 years in neurologically healthy children. The EEG is characterized by centrotemporal spikes. Seizures usually occur within hours of the patient falling asleep. Sensorimotor symptoms may affect the tongue, lips, and gums and may be followed by a unilateral seizure involving the face, tongue, pharynx, and larynx. Parents often describe hearing a noise, such as a clucking sound. The child is unable to speak, and there is excessive drooling. Consciousness is preserved unless the seizure evolves into a generalized tonic-clonic seizure. Treatment is sometimes withheld because of the self-limiting nature of this syndrome, which remits by age 16 years. Children are often not treated unless they have daytime events or recurrent nighttime events that interfere with their quality of life.

Juvenile myoclonic epilepsy (JME) is characterized by the onset of myoclonic jerks and tonic-clonic seizures, usually between the ages of 10 and 20 years. Patients may also have absence seizures. Seizures are exacerbated by sleep deprivation, alcohol, and stress. A 4- to 6-Hz spike-wave discharge is seen on the EEG.
Approximately 33% of the patients are photosensitive. JME is often misdiagnosed if the history of early morning myoclonus is not obtained. Seizures usually respond well to medication. Valproate has been the treatment of choice, but the increased risk for teratogenicity with valproate has led to the more recent use of lamotrigine. JME tends to be a lifelong disorder, and patients and parents must be counseled regarding the possibility of ongoing pharmacologic treatment, even in the absence of seizures.

Although the syndromes described in this section are the most prevalent syndromes seen in pediatric neurology, this does not lessen the importance of the others mentioned in the Table. For example, the partial epilepsies resulting from a known or occult cerebral lesion account for a substantial number of patients with refractory epilepsy. These partial epilepsies are a little more difficult to discuss in syndromic terms. The EEG patterns depend largely on the location, type, and extent of abnormality. Age of onset varies significantly.

**PROGNOSIS AND OUTCOMES**

Identifying the epilepsy syndrome is helpful on several different levels. It can aid in AED selection because some syndromes have a more favorable response to a specific drug. It can also provide information to the family with regard to prognosis and outcome. A benign, self-limited epilepsy syndrome can be differentiated from a malignant, chronic disorder. Identifying the epilepsy syndrome helps to guide parental education and counseling. Healthcare providers can assure parents of children with BRE that the children will outgrow their epilepsy. Parents can be told that although most children with idiopathic seizure disorders have normal intelligence and do well in social and academic arenas, some do not. Although the prognosis for seizure outcome may be good, that does not ensure the absence of learning or social problems secondary to the epilepsy. Even children with benign syndromes and less severe epilepsy can be at risk for social and emotional problems.

**TREATMENT OF MALIGNANT SYNDROMES: EFFICACY AT WHAT PRICE?**

Although some children with benign epilepsy syndromes are at risk for behavioral and learning difficulties, children with cryptogenic and symptomatic epilepsies often develop these problems. Behavior, learning, and emotional problems are more likely in this group of children as a result of the underlying lesion, the effect of frequent and early expression of seizures, or the adverse effects of AEDs.

It is difficult to sort out the negative effects of medication on behavior and cognition because of the multiple factors involved, such as the underlying brain disease, which can affect the child's behavior and ability to learn. How a family adapts and copes with the condition may have an effect, to a degree, on a child's ability to learn and certainly can contribute to negative behavior patterns of the child. The response of the outside community to the child's seizures and other disabilities can also impact a child's behavior. However, many of these children have such frequent and severe seizures, parents and practitioners are often in a no-win situation.

Most studies of cognitive impairment and AEDs report inconclusive findings. There is some evidence that high blood levels caused by traditional AEDs, such as phenytoin, phenobarbital, and primidone, are significantly associated with cognitive decline. However, there are no well-designed, randomized, prospective studies that firmly establish the cognitive and behavioral effects of AEDs in children that can be
used as a guide in prescribing these drugs. This group of children presents an overwhelming challenge for the practitioner, who must weigh seizure control against medication side effects.

The AEDs have also been associated with metabolic side effects. Valproate has been associated with weight gain in adolescents and in adults. The potential for weight gain when receiving treatment with AEDs should be considered carefully, especially with the increasing number of children who are obese. Valproate has also been shown to suppress bone growth and has been associated with short stature.

Children with more resistant epilepsies are placed on multiple medications, often at fairly high dosages, because of the lack of response to one medication at the recommended dosage. As the dosage and blood levels of AEDs increase, the adverse effects also increase. Multiple medications are likely to cause more problems with cognition and behavior in children, especially in those children with associated neurological disorders. Treatment must be assessed continually in children with drug-resistant seizures. The goal of treatment is freedom from seizures without side effects, which must be weighed against the adverse effects of the drugs. The effects of a seizure may only last for several minutes a day out of the child’s life as opposed to the constant effects of medication.

PHARMACOLOGICAL CONSIDERATIONS IN CHILDREN

In pediatrics, it is well known that children are not simply small adults, which includes the way in which children respond to medications. As a child matures, the way the body absorbs, distributes, metabolizes, and eliminates medication all change. Dosing requirements differ with chronological age, and even children of the same age may require different dosing. However, there are basic rules to consider when formulating dosage regimens for young patients. Larger initial doses (mg/kg) are needed in infants because of their large volume of distribution. However, because of an infant’s decreased elimination capacity, doses need to be administered more frequently to prevent drug accumulation and resulting toxicity. If a young child is having problems tolerating a sedating AED, giving the medication in 3 divided doses rather than 2 may help.

Because many children are placed on AEDs at a young age, it is often hard for parents to recognize medication effects. Questions should be phrased so that the examiner can determine sedative and cognitive signs. For example, instead of asking if young children are sleepy, ask exactly how much they sleep. If a 5-year-old is taking a nap after school, it is probably a medication side effect. Language and learning abilities should also be assessed with detailed questioning. Developmental levels must be included when evaluating medication side-effect profiles.

INTRACTABILITY AND ALTERNATIVE TREATMENTS

Intractability is generally defined as inadequate seizure control despite appropriate medical therapy or as adequate seizure control but with unacceptable side effects. This is a subjective concept and the issue becomes more complicated in children. With the more malignant epilepsy syndromes, such as West syndrome, Lennox-Gastaut, and Dravet syndrome, physicians must think differently about infantile and early childhood epilepsy. Seizures are not the only problem or even the main problem; for many of these children, developmental, cognitive, and behavioral issues are as important as the seizures and must be taken into consideration when making therapeutic decisions. The intractability of these seizures is assessed easily, and early interruption of the epileptic activity is desirable.

The best possible treatment for these disorders may or may not be pharmacological. Other therapies should be considered if a child is not responding well to medications. The ketogenic diet, VNS, and surgery are all therapies to be considered in children with medically intractable epilepsy. These therapies are viable alternatives to multiple-medication regimens, which often do not relieve patients of their seizures. In some cases, these therapies may eliminate the need for medication or reduce the amount of medication needed and may contribute to increased alertness and improvement in overall function. The ketogenic diet can significantly improve seizure control in children with medically intractable epilepsy; approximately 30% to 50% of patients have a marked or complete cessation of seizures or a reduction in the seizure severity. The diet also can result in improved alertness and behavior. This improvement may be a consequence of seizure reduction or withdrawal of medication or a direct result of the diet. In studies of infantile spasms, the ketogenic diet was found to be a safe, well-tolerated, effective treatment. It has also been found to decrease atonic and myoclonic seizures in children.
with Lennox-Gastaut syndrome. VNS has shown particular promise for catastrophic syndromes, such as Lennox-Gastaut, and severe myoclonic seizures of infancy. Given the poor response to medication in children with these syndromes, VNS should certainly be considered as an adjunctive therapy.

Despite the addition of multiple new AEDs over the past 10 years, up to 40% of patients remain refractory to medical treatment. The possibility always exists that a child's seizures, no matter how severe, may remit in time. Surgery should be considered early if deleterious effects of seizures on a child's biological, developmental, and psychosocial state are evident and should not always be considered a treatment of last resort. Studies show that intractability can be determined early. Seizure freedom can now be achieved in very young children who were previously not considered good surgical candidates because of the extent of their epileptic focus and neurological impairment. Although seizure cessation in children with symptomatic and/or cryptogenic epilepsy does not necessarily improve cognition and development, parental reports indicate that a child's quality of life improves significantly with cessation of frequent seizures.

CONCLUSIONS

In all pediatric epilepsy syndromes, outcome is influenced greatly by the underlying cause. In many cases, even if seizures can be controlled, associated behavior and learning problems will persist. However, even a major brain disorder associated with cognitive impairment may be improved, at least in part, by adequate treatment. The goals of therapy must be carefully considered and specific for the individual child. In addition, optimum outcomes are dependent on the presence of an informed and participating family. The family must first understand the disorder and the impact epilepsy will have on the child's life, in addition to their own. For example, parents of children with benign rolandic epilepsy whose seizures will ultimately remit will not face the same chronic and intense challenges that parents of children with more severe epilepsy syndromes may endure. However, even a child with a benign seizure syndrome can develop educational and social issues. Parents must be aware of potential problems and decrease the likelihood of occurrence if possible. When a child has a diagnosis of Lennox-Gastaut syndrome, the parents must be informed about the inevitability of cognitive and behavioral problems. Improved parental understanding of their child's epilepsy will ideally lead to improved epilepsy management. Parents must educate themselves about the different treatment modalities, thus they can play an active part in the decision-making process and be aware of medical and nonmedical options and interventions. Nurses can then work collaboratively with families to ensure that appropriate referrals and resources are in place, such as neuropsychological services and any other ancillary therapies and resources.

Nurses must not overlook the need for education and support to the family and child with a benign epilepsy syndrome or well-controlled seizures. At office visits, the healthcare provider should ask about a child's behavior, school performance, socialization, and family dynamics. Children should be included in their own care as much as developmentally possible. Questions should be addressed directly to children when they are old enough to understand and to respond. Parents and children should be encouraged to seek support from the Epilepsy Foundation and other organizations that may offer community-based services, information, and assistance.

REFERENCES

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