Seizures in Childhood

4.0 Contact Hours

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A seizure or convulsion is a paroxysmal, time-limited change in motor activity and behavior that results from abnormal electrical activity in the brain. Seizures are common in the pediatric age group and occur in approximately 10% of children. There are no precise data on the prevalence of epilepsy in children. For most recent studies that report gender, gender-specific incidence in children is higher in males, although seldom significantly so.

Seizure events are broadly classified into two types, depending upon how they start. Generalized seizures are those that start from essentially the entire brain all at once. In contrast, partial seizures are those that start from one part of the brain. This distinction between generalized and partial seizures is important for several reasons including the choice of treatment and outcome. Status epilepticus (SE) is a continuous seizure activity lasting at least 30 minutes or two or more seizures without full recovery of consciousness during the interictal period.

Epilepsy may be associated with almost any cerebral pathology and other cerebral dysgeneses. No specific cause will be found in 70–75% of children.

Upon completion of this course, the learner will be able to:

1. Define seizures
2. Discuss the epidemiology and types of seizures
3. Discuss the various classifications of seizures
4. Discuss the clinical manifestations of various types of seizures
5. Elaborate on the various causes of seizures
6. Discuss the management of seizures

Introduction

A seizure or convulsion is a paroxysmal, time-limited change in motor activity and behavior that results from abnormal electrical activity in the brain. Seizures are common in the pediatric age group and occur in approximately 10% of children. Most seizures in children are provoked by somatic disorders originating outside the brain, such as high fever, infection, syncope, head trauma, hypoxia, toxins, or cardiac arrhythmias. Other events, such as breath-holding spells and gastroesophageal reflux, can cause events that simulate seizures.

Epilepsy describes a syndrome of recurrent, unprovoked seizures. It is derived from the Greek verb epilepsia meaning "to seize upon" or "to take hold of." Epilepsy is not an entity or even a syndrome but rather a symptom complex arising from disordered brain function that itself may be the result of a variety of pathologic processes.

Definitions

Epilepsy:

Epilepsy is a condition characterized by recurrent (two or more) unprovoked seizures separated by more than 24 hours.

Seizure:

A seizure is the clinical manifestation of an abnormal and excessive activity of a set of cortical neurons.

Acute Symptomatic Seizure:

Acute symptomatic seizures occur in close temporal association with a systemic or central nervous system (CNS) insult. About 5% of children with infections of the CNS have acute symptomatic seizures at the time of infection.

Febrile Seizure:

A febrile seizure is a convulsive episode occurring in association with an acute febrile illness. This is actually a subcategory of acute symptomatic seizure, differing only in that all children are exposed to the risk factor.

Neonatal Seizures:

Neonatal seizures are those that occur in the first 28 days of life.

Unprovoked Seizures:

Unprovoked seizures occur in the absence of an identified acute precipitant. In studies in the United States and Iceland, about 25% of newly diagnosed unprovoked seizures in children occur as a single event and never meet criteria for epilepsy.

Epidemiology

There are no precise data on the prevalence of epilepsy in children. The figure of 0.7–0.8% of all school children (aged 5–17 years) is often quoted, and is similar to adult data. The most recent studies report incidence in the first year of life of about 100 per 100,000 children. Incidence falls after the first year. For most recent studies that report gender, gender-specific incidence in children is higher in males, although seldom significantly so. The incidence in African-American children is higher. Most recent studies of epilepsy in developed countries report a slight predominance of partial seizure disorders over generalized seizure disorders.

Classification

Seizure events are broadly classified into two types, depending upon how they start. Generalized seizures are those that start from essentially the entire brain all at once. In contrast, partial (also called “focal” or “local”) seizures are those that start from one part of the brain. This distinction between generalized and partial seizures is important for several reasons. It affects first the observations that must be made during a seizure; second the medical work-up; and third the treatment of a child with seizures.

The seizure type may provide a clue to the cause of the seizure disorder. In addition, precise delineation of the seizure may allow a firm basis for making a prognosis and choosing the most appropriate treatment.

International Classification of Epileptic seizures

- **Focal Seizures (Also known as partial or local seizures)**
    - Simple partial (consciousness retained)
        - Motor
        - Sensory
        - Autonomic
        - Psychic
    - Complex partial (consciousness impaired)
        - Simple partial, followed by impaired consciousness
        - Consciousness impaired at onset
    - Partial seizures with secondary generalization
- **Generalized Seizures**
    - Absence seizures
    - Atypical absence seizures
    - Generalized tonic-clonic seizures
    - Tonic seizures
    - Clonic seizures
    - Myoclonic seizures
    - Atonic seizures
    - Infantile spasms
- **Unclassified Seizures**

Status Epilepticus

Status epilepticus (SE) is defined as a seizure of sufficient duration to provide an enduring epileptic condition. The minimum seizure duration required for the diagnosis of SE has evolved downward from 1 hour to 30 minutes and, as per recent proposals, to 5 minutes. Evolution to shorter times has been based on animal models demonstrating decreased physiologic compensation and brain injury after 30 minutes of continuous generalized tonic clonic seizure activity despite optimal ventilation. Proponents of earlier treatment have noted that typical seizures last less than 2 minutes in adults and children. The currently accepted definition

of SE is that it is the continuous seizure activity lasting at least 30 minutes or two or more seizures without full recovery of consciousness during the interictal period.

Partial Seizures

Partial seizures account for a large proportion of childhood seizures, up to 40% in some series. Partial seizures may be classified as simple or complex; consciousness is maintained with simple seizures and is impaired in patients with complex seizures.

The distinguishing characteristic of simple partial seizures (SPS) is that the patients remain conscious and may verbalize during the seizure. Furthermore, no postictal phenomenon follows the event. Simple partial seizures may be confused with tics; however, tics are characterized by shoulder shrugging, eye blinking, and facial grimacing and primarily involve the face and shoulders. Tics can be briefly suppressed, but partial seizures cannot be controlled. The EEG may show spikes or sharp waves unilaterally or bilaterally or a multifocal spike pattern in patients with SPS.

A complex partial seizure may begin with a simple focal seizure with or without an aura, followed by impaired consciousness; conversely, the onset of the complex partial seizure may coincide with an altered state of consciousness. An aura consisting of vague, unpleasant feelings, epigastric discomfort, or fear is present in approximately one third of children with simple focal seizure and complex focal seizure. The presence of an aura always indicates a focal onset of the seizure. Automatisms are a common feature of CPS in infants and children, occurring in approximately 50–75% of cases. Automatisms develop after the loss of consciousness and may persist into the postictal phase, but they are not recalled by the child. The automatic behavior observed in infants is characterized by alimentary automatisms, including lip smacking, chewing, swallowing, and excessive salivation. These movements can represent normal infant behavior and are difficult to distinguish from the automatisms of CPS.

Spreading of the epileptiform discharge during CPS can result in secondary generalization with a tonic-clonic convulsion.

Generalized seizures

Generalized seizures are extremely common and may follow a partial seizure with a focal onset (second generalization) or occur de novo. They may be associated with an aura, suggesting a focal origin of the epileptiform discharge. It is important to inquire about the presence of an aura, because its presence and site of origin may indicate the area of pathology. Consciousness is severely impaired or lost during a generalized seizure, although this may only be transient if the seizure is very brief.

In a tonic seizure there is a sustained, forceful, rigid contraction of the affected part of the body (usually the whole body). In contrast, in a clonic seizure affected muscles contract and relax rhythmically, usually with the contraction phase being more rapid than the relaxation phase. The amplitude of the clonic contraction tends to increase whilst the rhythm slows towards the end of the seizure. In a tonic-clonic seizure the sustained contraction, typically lasting 10–20 seconds, is followed by rhythmic contractions, often for several minutes.

During absence seizures, there is a brief loss of consciousness causing the affected person to become unresponsive and to stare but there is not usually any loss of posture. Automatisms are common, occurring in at least 50% of children and typically involve the lips (lip-smacking, chewing, swallowing) or hands (fidgeting or washing movements).

Myoclonic seizures comprise extremely rapid, very brief muscular contractions that occur either singly or are repeated only a few times. Myoclonic seizures may occur in prolonged bouts, but there are brief periods of muscular relaxation between the seizures, in contrast to clonic seizures, in which rhythmic contractions persist throughout the period of seizure activity. A sudden, brief reduction in muscle tone, causing a loss of posture, occurs in atonic seizures. Atonic seizures are often associated with myoclonic seizures.

Spasms are seizures in which there are sudden, widespread, muscular contractions (typical examples occurring in infantile spasms). Although spasms were formerly considered to be massive myoclonic seizures, they are now regarded as a separate seizure type. The new,

proposed classification includes ‘epileptic spasms’ as a specific seizure type; ‘infantile’ spasms occur in the first 13–14 months of life and ‘epileptic’ spasms occur in later childhood.

Syndromic classification of epilepsy

The epileptic seizure type is one criterion used to define epileptic syndromes. Epileptic syndromes are determined by seizure type, age of onset, EEG findings (interictal and ictal), associated features, such as neurological findings, family history. Epileptic syndromes are important in the management of epilepsy in terms of predicting prognosis, selecting treatment. The following are the various epileptic syndromes:

<u>Focal (Partial, Localization-Related) Epilepsies</u>

Idiopathic

- Benign infantile seizures (non-familial)
- Benign childhood epilepsy with centro-temporal spikes
- Early-onset benign childhood occipital epilepsy (Panayiotopoulous type)
- Late-onset childhood occipital epilepsy (Gastaut type)

Familial (autosomal dominant)

- Benign familial neonatal seizures
- Benign familial infantile seizures
- Autosomal dominant nocturnal frontal lobe epilepsy
- Familial temporal lobe epilepsy

Symptomatic (or probably symptomatic)

- Limbic epilepsies
- Mesial temporal lobe epilepsy with hippocampal sclerosis
- Mesial temporal lobe epilepsy defined by specific aetiologies
- Other types defined by location and aetiology
- Neocortical epilepsies
- Kojewnikow’s syndrome (Rasmussen’s encephalitis)
- Hemiconvulsion-hemiplegia syndrome

- Other types defined by location and aetiology

Generalized Epilepsies

Idiopathic

- Benign myoclonic epilepsy in infancy
- Epilepsy with myoclonic astatic seizures
- Childhood absence epilepsy
- Epilepsy with myoclonic absences
- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Epilepsy with generalized tonic-clonic seizures only
- Generalized epilepsies with febrile seizures

Reflex Epilepsies

- Idiopathic photosensitive occipital lobe epilepsy
- Other visual sensitive epilepsies
- Primary reading epilepsy
- Startle epilepsy

Epileptic Encephalopathies

- Early myoclonic encephalopathy
- Ohtahara syndrome
- West's syndrome
- Dravet syndrome (severe myoclonic epilepsy in infancy)
- Lennox-Gastaut syndrome
- Landau-Kleffner syndrome
- Epilepsy with continuous spike-waves during slow-wave sleep

Progessive Myoclonic Epilepsies

Seizures Not Necessarily Requiring A Diagnosis Of Epilepsy

- Benign neonatal seizures (non-familial)
- Febrile seizures
- Reflex seizures
- Alcohol-withdrawal seizures
- Drug- or chemically induced seizures
- Immediate and early post-traumatic seizures
- Single, isolated clusters or rarely repeated seizures

Causes of epilepsy

Epilepsy may be associated with almost any cerebral pathology and other cerebral dysgeneses. Although no specific cause will be found in 70–75% of children, aetiology may be demonstrable from the clinical information and examination findings alone. The various causes of epilepsy are:

Malformations

There is a high risk of epilepsy developing in children with neuronal migration disorders and other cerebral dysgeneses. Epilepsy is commonly associated with the cerebral malformations that occur in certain neurocutaneous syndromes, including the cortical tubers of tuberous sclerosis and the leptomeningeal angiomatosis of the Sturge-Weber syndrome. Approximately 60% of children with tuberous sclerosis have epilepsy, but this rises to almost 100% if there are associated severe learning difficulties. Epilepsy occurs in 60–90% of children with Sturge-Weber syndrome. Epilepsy is also relatively common in neurofibromatosis type1. Magnetic resonance imaging (MRI) is far superior to computed tomographic (CT) scanning in the detection of neuronal migration disorders.

Metabolic disorders

Disorders of intermediate metabolism associated with seizures tend to present fairly dramatically in the neonatal period or in early infancy, often at times of intercurrent illness or infection. These disorders can be broadly categorized by measuring the pH, glucose, lactate and

ammonia in the blood and urinary ketones. Neurodegenerative disorders associated with epilepsy progress insidiously during infancy and childhood and many have an identifiable underlying metabolic defect.

Infections

The risk of epilepsy following meningitis or encephalitis is relatively small, but increases if seizures occur during the acute illness. Epilepsy is up to five times more common in patients who convulse during their acute illness than in those who do not. Ten per cent of children develop epilepsy after meningitis and 20% after encephalitis. Epilepsy develops in over 75% of patients requiring drainage of a cerebral abscess. Pertussis vaccination, like other vaccinations, may produce a fever leading to febrile seizures in susceptible children. Intractable seizures, including infantile spasms and the Lennox-Gastaut syndrome, may complicate congenital infections with toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex, other viruses and syphilis.

Head injury

The majority of children who have a head injury do not experience a seizure. The overall risk of epilepsy developing after a head injury is approximately 5%, but it is slightly higher (between 7% and 9%) in children under 5 years of age. Post-traumatic seizures can be classified into three types-

- Immediate—seizures occurring within the first 24 hours (usually within minutes) of the injury
- Early—seizures occurring within the first week of the injury
- Late—seizures occurring months to years following the injury

Hypoxic-ischaemic injury

Hypoxic-ischaemic cerebral injury resulting from cardiorespiratory arrest or drowning is a well-recognized, but rare, antecedent of epilepsy in childhood. Hypoxic-ischaemic encephalopathy (HIE) in the perinatal period is a common cause of ‘late’ epilepsy, including infantile spasms (West’s syndrome). West’s syndrome arising because of a perinatal hypoxic-ischaemic encephalopathy is extremely difficult to treat.

Tumors

Cerebral tumors are a cause of seizures in less than 1–2% of children with epilepsy. This reflects the usual infratentorial (posterior fossa or brain-stem) distribution of pediatric tumors, particularly in children under 6 years of age. In children with brain tumors, 10–20% may present initially with one or more seizures. These tumors are usually astrocytomas, primitive neuroepithelial tumors (PNETs), dysembryoblastic neuroepithelial tumors (DNETs) and oligodendrogliomas or meningiomas.

Hemorrhage

Spontaneous intracranial hemorrhage is rare in childhood, resulting from congenital vascular malformations or acquired disorders such as thrombocytopenia and neonatal vitamin K deficiency. Epilepsy follows a subarachnoid or intracranial hemorrhage in about 20% of cases.

Cerebral palsy

The likelihood of epilepsy varies with the type of cerebral palsy, occurring in about 50–80% of children with hemiplegic or quadriplegic cerebral palsy, and in 20% of those with dystonic or diplegic cerebral palsy. For each type of cerebral palsy, the incidence of epilepsy is highest in those with the most severe learning difficulties.

Febrile seizures

A febrile seizure is generally and practically defined as a convulsion (or seizure) with fever in children aged between 6 months and 5 years without evidence of meningitis or encephalitis

Miscellaneous syndromes

There are several hundred chromosomal abnormalities in which seizures feature, but there are only a few chromosomal disorders that are highly associated with epilepsy. Up to 6–8% of children with Down's syndrome and 20–40% of people with the Fragile X syndrome develop epilepsy, including infantile spasms. In Rett's syndrome, affected girls show

neurodevelopmental regression after initial normal early development, and develop seizures. Up to 80–90% of children with Angelman's syndrome develop seizures.

Investigations

The reasons and aims of investigation in epilepsy are to classify the epilepsy syndrome, identify any obvious etiology that might influence management and facilitate discussion about prognosis and recurrence/genetic risks. The investigation of children with epilepsy falls largely into three areas. They are:

- Electroencephalography
- Neuroimaging
- Others - haematological; metabolic; molecular genetics; histological analysis

Electroencephalography

Electroencephalography is useful in the investigation of epilepsy as:

- An aid to the clinical diagnosis of epilepsy
- For the classification of epilepsy
- For the identification of a structural brain lesion or neurodegenerative disorder
- For monitoring response to treatment
- In the pre-surgical evaluation of epilepsy

Neuroimaging

Scanning the brains of all children with epilepsy is unnecessary. The indications include attempting to identify a cause for the seizures and occasionally for 'reassurance'. Neuroimaging is required in the following groups of children:

- Children who have a neurological deficit/asymmetry (e.g.hemiparesis)
- Children who have evidence of a neurocutaneous syndrome
- Children with evidence of developmental regression
- Children with simple partial seizures
- Children with complex partial seizures (particularly if the seizures have clear frontal or temporal lobe features)
- Children with infantile spasms or myoclonic seizures presenting in the first year of life

- Children with persisting unclassifiable seizures
- Children whose seizures relapse for no obvious reason following initial good control
- Children under the age of 12 months who present with two or more complicated (particularly if focal or unilateral), 'febrile' seizure

CT scan is an appropriate initial scanning technique for the exclusion of a brain tumor. MRI is the preferred imaging technique for children with complex partial seizures and infantile spasms. CT scan involves radiation, unlike MRI, and therefore MRI is generally preferable, particularly if repeat and serial neuroimaging is likely to be required.

Other investigations

The type and extent of 'other' investigations that may be undertaken in children with epilepsy clearly depend on the specific clinical situation and the underlying diagnosis being considered. This is usually most relevant for the myoclonic epilepsies, and neurodegenerative disorders that have epilepsy as a feature.

- Mitochondrial cytopathy - DNA analysis, muscle biopsy (to measure the activity of the respiratory chain enzymes)
- Neuronal ceroid lipofuscinoses—blood analysis (enzyme deficiency, DNA mutation), skin or rectal biopsy
- Other storage disorders—white blood cell (lysosomal) enzyme assay
- Subacute Sclerosing Panencephalitis—serum and CSF measles antibodies
- Angelman syndrome—DNA analysis (microdeletion on chromosome 15)
- Rett syndrome—DNA analysis (MECP2 deletion on chromosome Xq28)

Treatment

Medical treatment

Most clinicians would not recommend starting treatment after a single brief generalized tonic-clonic seizure, but would after a cluster of seizures. Once an anti-epileptic drug (AED) is started, the objective is to achieve complete seizure control without unacceptable side-effects and using the most appropriate formulation that can be taken by the child. It is the identification of the syndrome or the seizure type and safety profile of the drug that determine the choice of

anticonvulsant. Whichever drug is chosen should be introduced gradually to avoid any dose-related side-effects, and increased slowly to its target maintenance dose based on the child's body weight and recommended guidelines. The dose of this drug should be increased to the maximally tolerated level before either adding a second drug (if the first drug has had a partial effect) or substituting another drug (if the first drug was completely ineffective).

The currently recommended first-line drugs in treating the majority of childhood epilepsies are sodium valproate (VPA) for generalized epilepsies and syndromes and carbamazepine (CBZ) for partial (focal) seizures/ epilepsy syndromes. The other medications used are:

	First line	Second line	Third line
Generalized			
Tonic-clonic	sodium valproate, lamotrigine	carbamazepine, topiramate	phenytoin
Myoclonic	sodium valproate	lamotrigine	ethosuximide, clonazepam, phenobarbitone
Tonic	sodium valproate	topiramate, lamotrigine, carbamazepine	clobazam, phenobarbitone
Atonic	sodium valproate	lamotrigine, topiramate	carbamazepine, clobazam, phenobarbitone
Absence	sodium valproate, ethosuximide	lamotrigine	clobazam topiramate
Partial			
Simple/complex	carbamazepine	topiramate, gabapentin, clobazam,	lamotrigine, vigabatrin, phenytoin
Infantile spasms	vigabatrin	nitrazepam, prednisolone	topiramate, ACTH, pyridoxine

Most clinicians would usually suggest attempted withdrawal of an AED after a seizure-free period of 2–3 years; this is essentially an arbitrary figure. Predictive factors for relapse after withdrawal of medication included partial seizures, seizure onset occurring after 12 years of age and an identified cause for the epilepsy. In the absence of these factors it may therefore be worth considering withdrawal of antiepileptic medication after 12 months of seizure freedom, rather than the currently recommended but arbitrary period of 24 months.

Surgical treatment

Any patient with partial seizures refractory to optimal doses of conventional AEDs and whose prognosis for spontaneous seizure remission is poor should be considered for surgical treatment. The surgical treatment of epilepsy, once undertaken, is irreversible. It is therefore crucial to ensure that, firstly, the child has epilepsy which is resistant to antiepileptic medication, and, secondly, that surgery is likely to either prevent or at least markedly reduce further seizures. The commonly performed procedures are:

- Resective - temporal and extratemporal lobe, multilobar or hemispherectomy
- Functional –stereotactic , disconnective

Resective surgery aims to be curative whereas disconnective surgery is more palliative. Surgery must be undertaken in a recognized, national center with comprehensive pre- and post-surgical (including psychological) evaluation and support facilities.

Other treatment

The indications for using alternative treatments, their efficacy and their precise modes of action have not been fully established, yet they are frequently used in children with intractable epilepsy.

The ketogenic diet -

The observation that seizure frequency may be decreased during fasting often, but not invariably, at times of intercurrent illness led to the development of the ketogenic diet, which reproduces some of the metabolic effects of fasting. Ketosis is achieved by supplying the majority of dietary calories as fat, with adequate protein, carbohydrate and added vitamins and

minerals to maintain nutrition. The ketogenic diet can achieve a greater than 50% reduction in seizures in 50–60% of children.

Steroids -

Steroids have been prescribed for the 'intractable' childhood epilepsies, including West's syndrome, severe myoclonic epilepsy in infancy, the Lennox-Gastaut syndrome, electrical status epilepticus of slow-wave sleep (ESESS) and the Landau-Kleffner syndrome. Prednisolone (2–4 mg/kg per day) or ACTH (10–20 IU/day) is given for varying and arbitrary periods ranging from a couple of weeks to many months.

Intravenous immunoglobulins -

Immunoglobulin infusions have been used in the Lennox-Gastaut syndrome and other intractable epilepsies. This treatment may be most effective in some of the acute epileptic encephalopathies, including Rasmussen's encephalitis.

Management of status epilepticus

Convulsive and non-convulsive status epilepticus are medical and neurological emergencies. In convulsive status the time-interval between onset of seizures and the start of effective therapy is important in determining the prognosis, largely through preventing any secondary brain damage.

Management includes –

- Maintaining a patent airway and adequate cardiorespiratory function
- Correct positioning of the child
- Identifying and treating any precipitating factors
- Stopping the seizure as quickly as possible
- Preventing any secondary brain damage by maintaining homeostasis
- Preventing seizure recurrence

Current accepted practice is to use an intravenous short-acting benzodiazepine (lorazepam or diazepam) bolus first and then to give a second dose if the seizure continues. In infants and

young children venous access may be difficult, and to avoid unnecessary delay, rectal administration of a benzodiazepine (diazepam, 0.5 mg/ kg or lorazepam 0.1 mg/kg) or paraldehyde should be given rapidly.

If status persists or a seizure recurs within 10–15 minutes then the child should be given rectal paraldehyde and intravenous phenytoin. The initial ‘loading’ dose of phenytoin is 18 mg/kg. If status persists, the child must be stabilized first and then transferred to intensive care, principally to provide cardiorespiratory support and to prevent/minimize any secondary medical complications. Status persisting on admission to intensive care requires barbiturate anesthesia.