

# An Overview of Childhood Epilepsy, Classification, Diagnosis, and Treatment Approaches

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**Abstract:** The Epilepsies are persistent neurological disorders identified by a predisposition for frequent epileptic seizures. Epilepsy/seizure disorder is the most common youth neurologic condition, disorders in children, impacting 4-10 children per 1,000. We aimed by this study to overview the epilepsy in pediatric from different perspective, epidemiological evaluation, diagnosis approaches, and treatment options. MIDLINE, Google Scholar, and EMBASE databases were comprehensively searched for childhood epilepsy related articles published before to December 2016, the literature searched included most of studies that are evidence based supported, and discussing the diagnosis and treatment approaches for pediatric epilepsy, moreover references list of each identified study were searched for more relevant articles. The spectrum of epilepsy syndromes in childhood is large. Diagnosis of an epilepsy syndrome provides insight into the scientific course, assists forecast outcome, and directs the best treatment plan. EEG medical diagnosis, and much better aetiological diagnosis, specifically supported by neuroimaging, has assisted to clarify the diversity of epilepsy in children, and has actually enhanced management.

**Keywords:** Childhood Epilepsy, epilepsy syndromes, Classification, Diagnosis.

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## 1. INTRODUCTION

The Epilepsies are persistent neurological disorders identified by a predisposition for frequent epileptic seizures <sup>(1)</sup>. Epilepsy/seizure disorder is the most common youth neurologic condition, disorders in children, impacting 4-10 children per 1,000 <sup>(2)</sup>, and a significant public health issue <sup>(3)</sup>. Kids identified with epilepsy face considerable difficulties. The seizures themselves, especially when poorly controlled, might be disabling and interfere with the child's ability to find out, whereas secondary influences, such as preconception and lack of knowledge about the condition can negatively affect psychological and social function <sup>(4,5,6)</sup>. In addition, children with epilepsy frequently show comorbidities that impact developmental development and psychological health, consisting of attention-deficit/ hyperactivity condition (ADHD) <sup>(7,8,9)</sup>. Knowledge of the public health of childhood epilepsy and of existing functioning of children with this condition will help notify the advancement of systems of care that move beyond a narrow focus on seizure control to deal with ramifications of the condition for the child's social, psychological, and developmental well-being <sup>(3,10)</sup>.

The seizure is the symptom of an irregular, hypersynchronous discharge of a population of cortical neurons <sup>(10,11)</sup>. This discharge may produce subjective symptoms or goal indications, in which case it is a medical seizure, or it may be apparent only on an electroencephalogram (EEG), in which case it is an electrographic (or subclinical) seizure. Clinical seizures are typically classified in accordance with the International Classification of Epileptic Seizures (**Table 1**) <sup>(11)</sup>. The medical diagnosis of a specific seizure type, and of a specific type of epilepsy (epilepsy syndrome), directs the diagnostic workup of these patients and their initial treatment <sup>(11)</sup>.

Table 1: Annotated International Classification of Epileptic Seizures <sup>(11)</sup>

<p><b>I. Partial seizures (seizures beginning locally)</b></p> <p><b>A. Simple partial seizures (consciousness not impaired)</b></p> <ol style="list-style-type: none"> <li>1. with motor symptoms</li> <li>2. with somatosensory or special sensory symptoms</li> <li>3. with autonomic symptoms</li> <li>4. with psychic symptoms</li> </ol> <p><b>B. Complex partial seizures (with impairment of consciousness)</b></p> <ol style="list-style-type: none"> <li>1. beginning as simple partial seizures and progressing to impairment of consciousness                     <ol style="list-style-type: none"> <li>a. without automatisms</li> <li>b. with automatisms</li> </ol> </li> <li>2. with impairment of consciousness at onset                     <ol style="list-style-type: none"> <li>a. without automatisms</li> <li>b. with automatisms</li> </ol> </li> </ol> <p><b>C. Partial seizures (simple or complex), secondarily generalized</b></p>
<p><b>II. Generalized seizures (bilaterally symmetric, without localized onset)</b></p> <p><b>A. Absence seizures</b></p> <ol style="list-style-type: none"> <li>1. true absence ('petit mal')</li> <li>2. atypical absence</li> </ol> <p><b>B. Myoclonic seizures</b></p> <p><b>C. Clonic seizures</b></p> <p><b>D. Tonic seizures</b></p> <p><b>E. Tonic-clonic seizures ('grand mal')</b></p> <p><b>F. Atonic seizures</b></p>
<p><b>III. Unclassified seizures</b></p>

**OBJECTIVES:**

Epilepsy is a very serious neurological condition, and can be a devastating disorder especially among children, but in other hand many other diseases could mimic epilepsy such; some cardiac arrhythmias or syncope. Therefore, we aimed by this study to overview the epilepsy in pediatric from different perspective, epidemiological evaluation, diagnosis approaches, and treatment options.

**2. METHODOLOGY**

MIDLINE, Google Scholar, and EMBASE databases were comprehensively searched for childhood epilepsy related articles published before to December 2016, the literature searched included most of studies that are evidence based supported, and discussing the diagnosis and treatment approaches for pediatric epilepsy, moreover references list of each identified study were searched for more relevant articles to our concerned topic. We included only those articles with human subject and populations of children aged less than 15 years old. we also restricted our search for English language trails.

**3. RESULTS & DISCUSSION**

➤ **Epidemiological review of epilepsy among children:**

According to one identified study <sup>(12)</sup> that examine the prevalence of epilepsy among children, it is estimated worldwide that 10.5 million children under 15 years have active epilepsy, representing about 25% of the global epilepsy population <sup>(12)</sup>. Of the 3.5 million individuals who establish epilepsy yearly, 40% are younger than 15 years, and more than 80% live in establishing countries. Population-based studies on childhood-onset epilepsy <sup>(12)</sup> show yearly occurrence rates of 61-124 per 100 000 in establishing nations, and 41- 50 per 100000 in developed nations.6 Incidence falls gradually from around 150 per 100 000 in the first year of life to 45- 50 per 100000 after the age of 9 years <sup>(12)</sup>. Cumulative occurrence research studies suggest that as much as the age of 15 years, 1.0 - 1.7%of children will have at least one unprovoked seizure, and 0 .7- 0.8 % duplicated seizures <sup>(13,14)</sup>. Frequency rates in Europe and North America vary from 3.6- 6.5 per 1000, whereas Latin and african American studies report rates of 6.6-17 per 1000 <sup>(12)</sup>.

**Epilepsy in Children with Cerebral Palsy (CP):**

CP is a developmental disability defined by motor or posture irregularities secondary to a non-progressive brain disruption that has taken place in early advancement. The brain irregularity may happen in the prenatal, perinatal, or postnatal period<sup>(15)</sup>. CP can be categorized in accordance with symptoms (spastic, extrapyramidal, or blended); or based upon topography (quadriplegia, diplegia, or hemiplegia)<sup>(16)</sup>. The incidence of CP worldwide is estimated to be 2.0 - 2.5 per 1,000 live births<sup>(17)</sup> and the frequency rate is around 1.2 - 2.5 per 1,000 in early school age children<sup>(18)</sup>. The occurrence of epilepsy is five times more common in patients with CP compared to normal children<sup>(19)</sup>. Data combined from several studies including 1,918 children<sup>(20)</sup> found that usually 43% (range 35- 62%) of children with CP develop seizures. The epilepsy onset is typically within the very first year of life, lots of had history of neonatal seizures, and there is an increased occurrence of status epilepticus. In addition, these patients had a lower chance of ending up being seizure totally free, and treatment with an extra second-line antiepileptic drug is most likely<sup>(20)</sup>.

**➤ General aspects of prognosis of pediatric epilepsy:**

Most children with epilepsy can be divided into four primary prognostic groups<sup>(21)</sup>. The very first group is the benign epilepsies e.g, benign rolandic epilepsy (20-- 30% of patients), where remission occurs after a couple of years and treatment can typically be avoided. The second group is the pharmacosensitive epilepsies e.g, many children with lack epilepsy (30% of patients), in which seizure control is quickly achieved by medication and spontaneous remission happens after a couple of years. The 3rd one is the pharmacodependent epilepsies, in which drug treatment will manage seizures, however no spontaneous remission occurs e.g, juvenile myoclonic epilepsy and many cases of symptomatic focal epilepsy (20% of patients). Drug withdrawal is followed by relapse and treatment will be lifelong. The fourth group is the pharmacoresistant (or refractory) epilepsies, with poor prognosis (13-17% of patients). The definition of pharmacoresistance is arbitrary and refers to both the frequency and severity of seizures for an individual child. Resistance to drugs can usually be forecasted early after an inadequate action to initial proper treatment<sup>(22)</sup>.

Children with developmental issues, structural main nerve system (CNS) lesions, or focal neurologic deficits have a 37% risk of having another seizure within 1 year and 60% risk of having another seizure within 3 years.

If a child has a 2nd unprovoked seizure, the risk for further seizures is greater than 50%, even amongst children without other risk factors<sup>(23,24,25)</sup>. Identifying the seizure as part of a syndrome has extra predictive value. For instance, patients with simple febrile seizures will likely have spontaneous remission as they get in school-age years; nevertheless, patients with juvenile myoclonic epilepsy are most likely to have long-lasting seizure reoccurrence<sup>(26)</sup>.

**➤ Diagnosis:**

The evaluation of a child with suspected seizure begins with a total history. A comprehensive description of the episode in question consisting of child's responsiveness during the episode, duration of episode, existence of alerting signs, and postictal modifications is necessary in the medical diagnosis of seizure. Developmental assessment and neurological evaluation may clarify the underlying neurological condition. The diagnosis of seizure needs an EEG and this may show interictal findings particular of specific seizures types like lack epilepsy. In the majority of instances, however, continuous video EEG for a minimum of 23 hr is essential to catch and identify the events of issue<sup>(27,28)</sup>. The EEG will also permit assessment of EEG background, which along with interictal activities and seizure type will assist in seizure classification. A brain MRI is shown in children with developmental impairments and seizures. Additional work up including hereditary and metabolic testing might be required in the suitable medical setting<sup>(35,36)</sup>

***Evaluation procedures for diagnosis of epilepsy in children:***

**A) Electroencephalogram (EEG)** is suggested for the diagnosis of epileptic seizure, kind of seizure, and electroclinical syndrome, sometimes giving ideas for etiology. A typical EEG does not leave out epilepsy diagnosis. An EEG with epileptiform discharges in a child without seizures or cognitive or language regression does not establish the diagnosis of epilepsy. 5-8% of regular children might have epileptiform discharges on the EEG<sup>(27,28)</sup>.

**B) Cerebral imaging** may reveal the etiology of epilepsy, (might reveal structural irregularities in some cases). A determined sore might or may not be the cause of epilepsy. It is essential to correlate the type of seizure and approximated origin (localization) from medical and EEG details and the identified lesion. Most often the neuroimaging assessment is not an emergency (29). The Committee for Neuroimaging of ILAE published guidelines for imaging infants and children with recent-onset epilepsy<sup>(30)</sup>.

**C) Genetic testing** and recognizing the predisposition genes for epilepsy are essential for both research and medical practice<sup>(31)</sup>. Mutations analysis and their neurophysiological and neurodevelopmental effects might contribute to comprehending the seizure vulnerability procedures. This might further add to new AEDs (antiepileptic drugs) advancement or finding solutions against pathophysiologic mechanisms of epilepsy (antiepileptogenic treatments). Genetic screening may clarify etiologic medical diagnosis and may anticipate the risk for epilepsy of in households with positive epilepsy history. More than 20 genes with function in epilepsy susceptibility have been described. Among the most valued discoveries for the epilepsy diagnosis was for instance the SCN1A gene, associated with a lot of cases of Dravet syndrome (severe epileptic encephalopathy defined by extended hemiclonic seizures activated by fever in infants less than 1 year). This electroclinical syndrome has particular: action to numerous AEDs, prognosis and associated conditions<sup>(32)</sup>.

**D) Metabolic testing** might also add to the etiologic diagnosis of epilepsy for instance presentation of high levels of pipercolic acid (indirect biomarker) in plasma and CSF<sup>(32)</sup> and of alpha-aminoacidic semialdehyde in urine and plasma (particular biomarker with some exceptions)<sup>(33)</sup> in pyridoxine-dependent epilepsy support the medical diagnosis, which can be even more confirmed by hereditary screening and demonstration of aldehyde dehydrogenase 7A1 (ALDH7A1) anomalies<sup>(34)</sup>. Other scientific evaluations, beside preliminary neurological and neurodevelopmental evaluation: psychiatric, ophthalmological, hearing, in addition to psychological screening contribute to defining the associated disabilities. Preferably these should be done given that the preliminary medical diagnosis for a full assessment of children and adolescents with epilepsy<sup>(35)</sup>.

#### ➤ **Treatment options of childhood epilepsy:**

##### **Goals of Therapy:**

The targets of treatment vary significantly in the common drug-sensitive epilepsies and in the complex drug-resistant types. In the very first group, seizure control without adverse events, with potentially one drug and in the most practical and least pricey way, is a reasonable target. Drug choices for these purposes vary bit. For complex and serious epilepsies, the primary objective ought to not always be total seizure control at all expenses. Such an attitude would cause drug escalation and to heavy polytherapies with extreme cognitive side-effects, the effects which might be even worse than those of seizures. There is an increased risk for seizure getting worse with heavy polytherapies<sup>(36,37)</sup>. For that reason, reducing seizure frequency need to be attempted as a result step making sure the very best possible lifestyle, which results from the balance between cognitive side-effects of drugs, and intrinsic seriousness and frequency of seizures. Moms and dads generally understand this point of balance effectively and must constantly be thoroughly paid attention to.

##### **Pharmacological treatment:**

Monotherapies with valproate or carbamazepine have revealed comparable efficiency and excellent tolerability in children with newly identified focal epilepsy with or without secondary generalization<sup>(38)</sup>. Phenytoin, phenobarbital, carbamazepine, and valproate had a comparable effectiveness, with 20% of children being seizure-free and 73% accomplishing a 1-year remission by 3 years of subsequent<sup>(39)</sup>. Phenobarbital caused extreme sedative sideeffects and phenytoin had low tolerability. More recent drugs might supply alternative monotherapies, however very few relative regulated trials are readily available in children<sup>(42)</sup>. Two class I studies used topiramate in children older than 3 years, 146 or than 6 years,<sup>(40)</sup> with new or just recently diagnosed focal epilepsy. Greater dosages of topiramate were more effective than lower doses,<sup>(41)</sup> and 100 or 200 mg/day were equivalent in safety to 600 mg carbamazepine and 1250 mg valproate<sup>(40)</sup>. Use of set doses, nevertheless, is flawed with respect to optimisation dosage research studies. Oxcarbazepine and phenytoin had a similar efficacy, however discontinuation rate was greater for phenytoin. 148 Studies that have actually been done on newly identified focal epilepsy may have masked particular drug impacts on aetiologically homogeneous syndromes. Regardless of this constraint, it is now advised that children with recently detected focal epilepsy are initiated on either carbamazepine or valproate, which topiramate is considered as an alternative monotherapy<sup>(42)</sup>. Lamotrigine and gabapentin are possibly fascinating initial monotherapies, although the only offered two studies<sup>(42)</sup> did not consist of children. Proof about the effectiveness of monotherapy with zonisamide, tiagabine, and levetiracetam is insufficient<sup>(42)</sup>. Controlled trials in pharmaco-resistant focal epilepsies have actually shown the effectiveness of add-on topiramate,<sup>(43)</sup> lamotrigine,<sup>(44)</sup> oxcarbazepine,<sup>(45)</sup> gabapentin,<sup>(46)</sup> and clobazam<sup>(47,48)</sup>. However, advancement of tolerance obstructs the long term use of clobazam. Evidence about add-on effectiveness of levetiracetam, tiagabine, and zonisamide is insufficient<sup>(49)</sup>. When assessing the patient's reaction to the various drugs, it is smart to check out whether a surgical choice is possible. Nevertheless, because attempting the many drugs now readily available would need a long period of time, surgery must be thought about soon after resistance to two proper drugs has actually been shown<sup>(50,51)</sup>.

***Surgery treatment:***

The indications and level of a resection will depend upon the definition of the epileptogenic zone,<sup>(52)</sup> which includes the ictal beginning zone (ie, the neurophysiologically defined cortical area where seizures are initiated), but does not always correspond to the epileptogenic lesion. Removal of an epileptogenic sore, without defining and eliminating the epileptogenic zone (lesionectomy), produces seizure control in a significant proportion of patients,<sup>(53)</sup> however delineation and removal of the entire epileptogenic zone, or at least the ictal beginning zone, enhances the result of lesionectomy<sup>(54)</sup>.

#### 4. CONCLUSION

The spectrum of epilepsy syndromes in childhood is large. Diagnosis of an epilepsy syndrome provides insight into the scientific course, assists forecast outcome, and directs the best treatment plan. EEG medical diagnosis, and much better aetiological diagnosis, specifically supported by neuroimaging, has assisted to clarify the diversity of epilepsy in children, and has actually enhanced management. This method will enable the epilepsy diagnosis to be in accordance with existing knowledge in the field in a substantial percentage of cases, and little patients to receive the most suitable treatment for their disease. Epilepsy surgery is an essential choice for a couple of wellselected people, however need to be thought about with excellent care when there is no evident underlying brain sore.

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