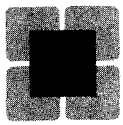

# Pediatric epilepsy syndromes: an overview

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THE CLASSIFICATION of epileptic seizures has contributed to the rational therapy of epileptic seizures since the advent of the newer antiepileptic drugs, many of which have a relative specificity for reduction in particular seizure types.[1] Classification has also aided in communication between physicians and researchers by standardizing terminology, which is critical in providing uniformity for the exchange of information.

In the past 20 years, it has become evident that, particularly in children, it is possible to identify epileptic syndromes of which individual seizures are but one manifestation.[2] The seizure bears the same resemblance to the syndrome as a pigment does to a painting. While the seizure is part of the syndrome that draws attention to the condition, the composition of the syndrome is based on a variety of contributions made by family history, age at onset, presence or absence of abnormal neurologic or psychologic findings, presence or absence of interictal electroencephalographic (EEG) abnormalities as well as specific ictal EEG components, a particular natural history (sometimes suggesting spontaneous resolution and at other times, progression), response to medication, and developmental complications. Some of these syndromes carry with them a specific pathologic, chromosomal or biochemical signature.

Apart from its usefulness in communication, such a classification has significant implications for treatment. Obviously, in management of a condition which is potentially benign, one would avoid use of potentially toxic or cognitively stultifying medications, which might produce side effects worse than the condition under consideration. In conditions which are self-limited in time, one might choose to discontinue medication at an early age. For conditions in which medication is required on a continuing basis into adult life by virtue of the nature of the underlying syndrome, one might prescribe medications which are relatively nonteratogenic for patients approaching the age at which this consideration is germane.

In the identification of syndromes, two dichotomies are used: first, the separation of epilepsies composed of generalized seizures from those composed of partial seizures, and, secondly, the separation of epilepsies which are idiopathic or primary from those which are symptomatic or secondary. By and large, idiopathic or primary epileptic syndromes occur in children who have usually made more progress, frequently demonstrate a positive family history of similar seizure types, and have no demonstrable underlying pathology. Seizures in patients of this type tend to be relatively self-limited and responsive to medication. The EEG usually has normal background interictal activity. On the other hand, symptomatic, secondary, or lesional epileptic syndromes are associated with underlying cerebral disease which imparts an abnormality in development, in neurologic examination or in ancillary investigative findings. In children with symptomatic epilepsies, the EEG background is frequently abnormal in the interictal period, a family history of similar seizures is usually missing, response to medication is frequently variable and less predictable than in the primary epilepsies, and the possibility of spontaneous resolution is considerably less.

Similar epileptic seizures may occur in different syndromes. Thus, absence seizures may be seen in both primary and secondary epilepsies as may myoclonus, infantile spasms, or generalized tonic-clonic convulsions. Even partial seizures in childhood may be indicative of either primary epilepsies such as benign rolan-

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dic epilepsy or lesional epilepsies.

The following are syndromes defined in the proposed International Classification of Epilepsies and Epileptic Syndromes first published by the Commission on Classification and Terminology of the International League Against Epilepsy. (These appeared in *Epilepsia* in 1985 and were subsequently modified.) The definitions also derive from the work of a subsequent Study Group for Research in Infantile Epilepsy.[3] Many of these syndromes will be discussed and amplified in this publication by investigators who have made major contributions in their elucidation.

### Benign childhood epilepsy with centrotemporal spikes

This is a syndrome of brief, simple, partial, hemifacial motor seizures, frequently with associated somatosensory symptoms, which have a tendency to evolve into generalized tonic-clonic seizures (GTCS).[4–11] Both seizure types are often related to sleep. Onset occurs between 3 and 13 years of age (peak, 9 to 10), and recovery before ages 15 to 16. Genetic predisposition is frequent, and there is male predominance. The EEG has blunt high-voltage centrotemporal spikes, often followed by slow waves that are activated by sleep and tend to spread or shift from side to side.

### Childhood epilepsy with occipital paroxysms

This syndrome is, in general respects, similar to the previous one.[12] The seizures start with visual symptoms (amaurosis, phosphenes, illusions, or hallucinations), and are often followed by hemiclonic seizures or automatisms. In one quarter of the cases, seizures are immediately followed by migrainous headache. The EEG shows paroxysms of high-amplitude spike waves or sharp waves recurring rhythmically on the occipital and posterior temporal areas of one or both hemispheres, but only when the eyes are closed. During seizures, the occipital discharge may spread to the central or temporal region. At present, no definite statement on prognosis is possible.

### Benign neonatal familial convulsions

These are rare, dominantly inherited disorders, usually manifesting on the second and third days of life, with clonic or apneic seizures and no specific EEG criteria.[13] History and investigations reveal no etiologic factors. About 14% of these patients later develop epilepsy.

### Benign neonatal convulsions

These are very frequently repeated clonic or apneic seizures occurring around the fifth day of life, without known etiology or concomitant metabolic disturbance.[14] Interictal EEG often shows alternating sharp theta waves. There is no recurrence of seizures, and psychomotor development is not affected.

### Benign myoclonic epilepsy in infancy

This form is characterized by brief bursts of generalized myoclonus that occur during the first or second year of life in otherwise normal children who often have a family history of convulsions or epilepsy.[15] EEG recordings show generalized spike waves occurring in brief bursts during the early stages of sleep. These attacks are easily controlled by appropriate treatment. They are not accompanied by any other types of seizures, although GTCS may occur during adolescence. The epilepsy may be accompanied by a relative delay of intellectual development and minor personality disorders.

### Childhood absence epilepsy (pyknolepsy)

This syndrome occurs in children with a strong genetic disposition who are otherwise normal; onset occurs at school age (peak manifestation, ages 6 to 7).[16–19] It appears more frequently in girls than in boys, and is characterized by very frequent (several to many per day) absences. The EEG reveals bilateral, synchronous symmetrical spike waves, usually three per second, on a normal background activity. During adolescence, GTCS often develop. Otherwise, absences may remit or, more rarely, persist as the only seizure type.

### Juvenile absence epilepsy

The absences of this syndrome are the same as in pyknolepsy, but absences with retropulsive movements are less common.[20] Age at manifestation is at or near puberty, and sex distribution is equal. Seizure frequency is lower than in pyknolepsy, with absences occurring less frequently than every day, in most cases sporadically. Association with GTCS is frequent, and they precede the absence manifestations more often than in childhood absence epilepsy, occurring on awakening. Not infrequently, these patients also have myoclonic seizures. The spike waves are often faster than three per second. Response to therapy is excellent.

### Juvenile myoclonic epilepsy (impulsive petit mal)

This syndrome usually appears during puberty and is characterized by seizures with bilateral, single or repetitive, arrhythmic, irregular myoclonic jerks, predominantly in the arms.[21–24] Sudden falls are sometimes caused by the jerks. No disturbance of consciousness is noticeable. The disorder may be inherited, and sex distribution is equal. Often there are GTCSs and, less often, infrequent absences. Seizures usually occur shortly after awakening and in many cases are precipitated by sleep deprivation. Interictal and ictal EEG have rapid, generalized, often irregular spike waves and polyspike waves; there is no close phase correlation between EEG spikes and jerks. Frequently, the patients are photosensitive. Response to appropriate drugs is good.

### Epilepsy with GTCS on awakening

This is a syndrome with onset usually in the second decade of life.[25] The grand mal seizures in most cases are presumably GTCS and occur exclusively or predominantly (over 90% of the time) shortly after awakening regardless of the time of day, or in a second seizure peak in the evening period of relaxation. If there are other seizures, these are likely to be absences or myoclonic, as in juvenile myoclonic epilepsy. Seizures may be precipitated by sleep deprivation and other external factors, and there is a significant correlation with photosensitivity. Genetic predisposition is relatively frequent. The EEG shows one of the patterns of idiopathic generalized epilepsy.

### West syndrome (infantile spasms, Blitz-Nick-Salaam Krampfe)

Usually, West syndrome consists of a characteristic triad: infantile spasms, arrest of psychomotor development, and hypsarrhythmia, although one of the elements may be missing.[26–31] Spasms may be flexor, extensor, lightning, or nods, but most commonly are mixed. Onset peaks between 4 and 7 months and always comes before 1 year. Boys are more commonly affected, and the prognosis is generally poor. West syndrome may be separated into two groups. The symptomatic group is characterized by the previous existence of brain damage signs (psychomotor retardation, neurologic signs, radiologic signs, or other types of seizures) or by a known etiology. The smaller, cryptogenic group is characterized by the absence of previous signs of brain damage and of known etiology. The prognosis is based, in part, on early therapy with adrenocorticotropic hormone (ACTH) or oral steroids. However, it principally depends on the etiology. Cryptogenic cases, when treated early, have had favorable prognoses without psychic impairment or later epilepsy, whereas in symptomatic cases, the prognosis is grave for normal development and for seizure control with ACTH.

### Lennox-Gastaut syndrome

This syndrome manifests itself in children from 1 to 8 years of age, but appears mainly in preschool-age children.[32–35] The most common seizure types are tonic-axial, atonic, and absence seizures, but other types such as myoclonic, GTCS, or partial are frequently associated with this syndrome. Seizure frequency is high, as is status epilepticus (stuporous states with myoclonias, tonic, and atonic seizures). The EEG usually has abnormal background activity, slow spike waves of less than three per second, and often, multifocal abnormalities. During sleep, bursts of fast rhythms (around ten per second) appear. In general, there is mental retardation. Seizures are difficult to control, and the development is usually unfavorable. In 60% of the cases, the syndrome occurs in children suffering from a previous encephalopathy, but it is primary in other cases.

### Epilepsy with myoclonic-astatic seizures

Manifestation begins between 7 months and 6 years, most often from 2 to 5 years, and (unless it begins in the first year) with twice as many boys affected as girls.[36,37] There is frequently hereditary predisposition and usually a normal developmental background. The seizures are myoclonic, astatic, myoclonic-astatic, absences with clonic and tonic components, and tonic-clonic. Status frequently occurs. Tonic seizures develop late in the course of unfavorable cases. The EEG, initially often normal except for four- to seven-per-second rhythms, may have irregular fast spike wave or polyspike wave. Course and outcome are variable.

### Epilepsy with myoclonic absences

This syndrome is clinically characterized by absences accompanied by severe bilateral rhythmical clonic jerks, often associated with a tonic contraction.[38] On the EEG, they are always accompanied by bilateral, synchronous, and symmetrical discharge of rhythmical spike wave at three per second, similar to those in childhood absence. These seizures occur many times a day. Awareness of the jerks may be maintained. Associated seizures are rare. Age at onset is about 7 years, and there is a male preponderance. Prognosis is less

favorable than in pyknolepsy because of mental deterioration, resistance to therapy of the seizures, and possible evolution to other types of epilepsy such as Lennox-Gastaut syndrome.

### Early myoclonic encephalopathy

The principal features of this syndrome are onset before 3 months of age, initially fragmentary myoclonus, then erratic partial seizures, massive myoclonias, or tonic spasms. The EEG is characterized by suppression-burst activity, which may evolve into hypsarrhythmia. The course is severe, psychomotor development is arrested, and death may occur in the first year. Familial cases are frequent and suggest the influence of one or several congenital metabolic errors, but there is no constant genetic pattern.

The status of early infantile epileptic encephalopathy with suppression bursts, described by Ohtahara et al[39] in relation to early myoclonic encephalopathy, is at present unclear, especially in view of its ictal features and its frequent evolution into a syndrome indistinguishable from West syndrome.

### Neonatal seizures

Neonatal seizures differ from those of older children and adults. The most frequent neonatal seizures are described as subtle because their clinical manifestations are frequently overlooked. These include tonic, horizontal deviation of the eyes with or without jerking, eyelid blinking or fluttering, sucking, smacking or other buccal-lingual oral movements, swimming or pedaling movements, and occasionally, apneic spells. Other neonatal seizures occur as tonic extension of the limbs, mimicking decerebrate or decorticate posturing. These are seen particularly in premature infants. Multifocal clonic seizures are characterized by clonic movements of a limb, which may migrate to other body parts; or there may be focal clonic seizures, which are much more localized. In the latter, the infant is usually not conscious. Rarely, myoclonic seizures may occur, and the EEG pattern is frequently that of suppression-burst activity. The tonic seizures have a poor prognosis because they often accompany intraventricular hemorrhage. The myoclonic seizures also carry a poor prognosis because they are frequently a part of the early myoclonic encephalopathy syndrome.

### Severe myoclonic epilepsy in infancy

Severe myoclonic epilepsy is a recently defined syndrome.[40] Characteristics include family history of epilepsy or febrile convulsions, normal development before onset, seizures beginning during the first year of life in the form of generalized or unilateral febrile clonic seizures, secondary appearance of myoclonic jerks, and often partial seizures. EEGs show generalized spike waves and polyspike waves, early photosensitivity, and focal abnormalities. Psychomotor development is retarded from the second year of life on, and ataxia, pyramidal signs, and interictal myoclonus appear. This type of epilepsy is very resistant to all forms of treatment.

### Epilepsy with continuous spike waves during slow-wave sleep

This syndrome results from association of various seizure types, partial or generalized, occurring during sleep, and atypical absences when awake.[41] Tonic seizures do not occur. The characteristic EEG pattern consists of continuous diffuse spike waves during slow-wave sleep, which is seen after the onset of seizures. Duration varies from months to years. Prognosis is guarded because of the appearance of neuropathologic disorders, despite the usually benign evolution of seizures.

### Acquired epileptic aphasia (Landau-Kleffner syndrome)

The Landau-Kleffner syndrome is a childhood disorder associating an acquired aphasia, multifocal spikes, and spike-and-wave discharges.[42] Epileptic seizures and behavioral and psychomotor disturbances occur in two thirds of the patients. There is verbal auditory agnosia and rapid reduction of spontaneous speech. For the most part, the seizures are generalized convulsive or partial motor. They are rare, and remit before the age of 15 years, as do the EEG abnormalities.

### Kojewnikow's syndrome

Two types of Kojewnikow's syndrome are now recognized, but only one of these two types is included among the epileptic syndromes of childhood because the other type is not specifically related to this age. The first type represents a particular form of rolandic partial epilepsy, in both adults and children, and is related to a variable lesion of the motor cortex.[43] Its principal features are motor partial seizures, always well localized; often late appearance of myoclonias in the same site where there are somato-motor seizures; an EEG with normal background activity and focal paroxysmal abnormalities (spikes and slow waves); occurrence at any age in childhood and adulthood; frequently demonstrable etiology (tumoral, vascular); and no progressive

evolution of the syndrome (clinical, EEG, or psychological), except the evolutive character of the causal lesion. The childhood disorder, suspected to be of viral etiology, has onset between 2 and 10 years (peak, 6 years) with seizures that are motor partial seizures, but are often associated with other types.[44] Fragmentary motor seizures appear early in the course of the illness, and are initially localized but later become erratic and diffuse, and persist during sleep. A progressive motor deficit follows, and mental deterioration occurs. The EEG background activity shows asymmetric and slow diffuse delta waves, with numerous ictal and interictal discharges that are not strictly limited to the rolandic area.

### Progressive myoclonic epilepsy

This epileptic syndrome includes patients with several disease entities, including juvenile Gaucher's disease and cherry-red spot myoclonus syndrome, juvenile ceroid lipofuscinosis and Lafora body disease, which have distinct clinical and pathologic findings.[45–47] Onset is in childhood or adolescence; neurologic deficits involve visual, cerebellar, pyramidal or extrapyramidal systems. The conditions are progressive and myoclonus is prominent. Mental deterioration may occur, though this is not prominent in dyssynergia cerebellaris myoclonica and cherry-red spot myoclonus syndrome. We use the term "non-Lafora progressive myoclonus epilepsy" for what has also been called Unverricht-Lundborg disease, degenerative progressive myoclonus epilepsy or Baltic myoclonus.[48–50]

In defining an epileptic syndrome as an epileptic disorder characterized by a cluster of signs and symptoms customarily occurring together, one hopes to achieve a clarification of etiology and a basis for the evaluation of therapy. With time, some of these syndromes will be found to have specific genetic and therefore biochemical and potentially remediable underlying causation. Likely candidates for this include pyknoleptic petit mal and juvenile myoclonic epilepsy. Others will be reclassified, as they probably represent a potpourri of conditions with a common end result. Such conditions include the West and the Lennox-Gastaut syndromes. At present the categorization of the epilepsies into syndromes has at least the potentially useful goal of providing a guideline for devising treatment plans and formulating putative prognoses.

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