An increasing number of infantile epilepsy syndromes have been recognized. However, a significant number of infants (children aged 1-24 months) do not fit in any of the currently used subcategories. This article reviews the clinical presentation, electroencephalographic findings, evolution, and management of the following entities: early infantile epileptic encephalopathy, early myoclonic epilepsy, infantile spasms/West syndrome, severe myoclonic epilepsy of infancy, myoclonic-astatic epilepsy, generalized epilepsy with febrile seizures plus, malignant migrating partial seizures of infancy, hemiconvulsions-hemiplegia-epilepsy, benign myoclonic epilepsy, and benign familial/nonfamilial infantile seizures. Issues related to their classification are addressed. © 2006 by Elsevier Inc. All rights reserved.


Introduction

An accurate diagnosis is considered the first and most critical step in the management of pediatric epilepsy [1,2]. Delineating epilepsy syndromes serves that purpose. In addition to improving communication between caregivers and establishing clear criteria for research studies, epilepsy syndromes can suggest underlying disease pathophysiology, provide prognostic information to the families, and aid in the selection of appropriate diagnostic tests. Epilepsy syndromes are the rational basis for selection of appropriate antiepileptic drugs, surgical procedures, or alternative treatment options [1,3,4].

The epilepsy syndrome classification system adopted by the International League Against Epilepsy in 1989 [5] has been demonstrated to be reliable and applicable to children [6,7]. Moreover, an increasing number of infantile (1-24 months) epileptic syndromes are being isolated and recognized as such by the majority, thanks to the recent developments in diagnostic techniques, such as video-electroencephalography, brain imaging, and cytogenetics. However, despite this remarkable progress, up to a quarter of infants with epilepsy do not fit in any of the proposed syndromes, or are classified into broad and unspecific categories [8]. It is likely that additional entities are waiting to be defined in this age group [1]. This article reviews the clinical characteristics, electroencephalographic findings, evolution, and management of the infantile epileptic syndromes identified in infancy so far. Their main features are summarized in Table 1, and specific treatment options for some of them are presented in Table 2. Issues related to their classification are addressed at the end of the review, and suggestions for further improvements in the classification of infantile epilepsies are proposed.

Early Infantile Epileptic Encephalopathy With Suppression-Burst (Ohtahara Syndrome)

Early infantile epileptic encephalopathy, or Ohtahara syndrome, is a severe neurologic condition first described in 1976 [9]. It is a rare entity, with a relative prevalence to West syndrome estimated at 1/40 or less [9]. It is characterized by epileptic tonic spasms and a suppression-burst electroencephalogram (Fig 1). The suppression-burst pattern is present in both waking and sleeping states, and appears in the first 3 months of life [9]. Partial tonic seizures can be observed, but myoclonic seizures are rare [9]. Etiology is heterogeneous, and includes brain malformations, migration disorders, mitochondrial diseases, and, rarely, inborn errors of metabolism, such as Leigh’s disease or cytochrome oxidase deficiency [9,10]. The seizures are usually intractable to antiepileptic medications, and the development prognosis is uniformly poor [9]. Surgery can be considered in those patients with cortical malformations, such as cortical dysplasia or hemimegalencephaly. Ohtahara syndrome frequently evolves...
atrophy or dysgenesis. Adrenocorticotrophic hormone
of lissencephaly, and four cases of nonspecific cerebral
case of porencephaly, one case of hydrocephalus, one case
Aicardi syndrome, one case of hemimegalencephaly, one
case of spasms, but were also observed independently. Etiology
spasms. Partial seizures could precede or follow a cluster
pression-burst pattern often disappeared during a cluster of
high-voltage slow wave followed by attenuation, some-
2-5 seconds duration. This pattern was independent of the
and multifocal spikes; severe outcome
First year; partial and generalized seizures, myoclonias; normal EEG at onset; later: generalized spike-waves and multifocal spikes; severe outcome
First year; generalized myoclonic and astatic seizures; interictal parietal theta activity and bilateral spike-waves; variable outcome
First year; continuous electrographic seizures, multiple areas of onset; severe outcome
Variable seizure and developmental phenotype in addition to febrile seizures and afebrile generalized convulsions
Prolonged unilateral febrile seizures; subsequent hemiparesis and partial epilepsy
First 3 years; myoclonic seizures; normal interictal EEG; normal development
First year; partial seizures; normal development

into West syndrome, and for some, later, into Lennox-
Gastaut syndrome [4,11,12]. Controversies exist as to
whether Ohtahara syndrome, West syndrome, and Len-
nox-Gastaut syndrome are part of the same spectrum of
the age-dependent epileptic encephalopathies, or whether
they each represent isolated syndromes with specific characteristics [12,13].

A recent report on 16 patients diagnosed with early infantile epileptic encephalopathy indicated that the age at
first seizure ranged from 1 day to 3 months. There was no
sex predominance. All of the patients had tonic spasms,
either in clusters or isolated. Hemiconvulsions, erratic
focal motor seizures, and asymmetric tonic seizures were
observed in one third to one half of the patients. General-
ized clonic seizures were observed in one patient. The
interictal electroencephalogram was characterized by 1- to
3-second bursts of high-voltage (150-350 μV) slow waves
and multifocal spikes, separated by suppression phases of
2-5 seconds duration. This pattern was independent of the
circadian rhythm. The spasms were accompanied by a
high-voltage slow wave followed by attenuation, some-
times with low-voltage fast activity. The interictal sup-
pression-burst pattern often disappeared during a cluster of
spasms. Partial seizures could precede or follow a cluster
of spasms, but were also observed independently. Etiology
or associated conditions included two suspected cases of
Aicardi syndrome, one case of hemimegalencephaly, one
case of porencephaly, one case of hydrocephalus, one case of
lissencephaly, and four cases of nonspecific cerebral
atrophy or dysgenesis. Adrenocorticotrophic hormone
helped two patients with cryptogenic etiology, but was
ineffective in all others. Three patients had their seizure
activity controlled on zonisamide. This publication was
particularly important because of the prognostic findings.
On evolution, two groups with different prognoses were
identified: one of them included seven patients, who
evolved from Ohtahara syndrome to West syndrome and
later to Lennox-Gastaut syndrome, and all of these patients
died; the second included patients with spike foci on
electroencephalogram: only one patient died, and seven
were seizure-free. Nevertheless, all patients in the second
group were physically and mentally severely handicapped
[14].

Early Myoclonic Epilepsy/Encephalopathy

This rare entity was termed “neonatal myoclonic en-
cephalopathy” in its initial description [15]. It was further
delineated and renamed “early myoclonic epileptic en-
cephalopathy” by Dalla Bernardina et al. in 1983 [16], and
“early myoclonic epilepsy” by Aicardi in 1985 [17]. Like
early infantile epileptic encephalopathy, it is characterized
by intractable seizures with onset during the first 3 months
of life, suppression-burst interictal electroencephalogram,
and poor developmental prognosis [9]. Early myoclonic
epilepsy is, however, distinguished from early infantile
epileptic encephalopathy by its predominant clinical man-
ifestations, erratic myoclonias, and by the presence of a
suppression-burst pattern mainly during sleep. Partial
seizures are also observed, and include tonic spasms,
isolated or in clusters, versive seizures, migrating clonic
seizures, and asymmetric tonic seizures with occasional
secondary generalization [9]. Patients with early myoc-
clonic epilepsy share most electroencephalographic char-
acteristics with patients with early infantile epileptic en-
cephalopathy, although the duration of bursts and
suppression epochs, and the length of burst-burst intervals
are more variable in early myoclonic epilepsy [9,18]. Most
myoclonias have no associated electroencephalographic
changes, and are therefore considered nonepileptic [4,9].
Partial seizures manifest various electrographic patterns of

Table 1. Main characteristics of the epileptic syndromes that present in infancy

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Main Characteristics</th>
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<tr>
<td>Early infantile epileptic encephalopathy</td>
<td>First months; tonic seizures, spasms; suppression-burst; severe outcome</td>
</tr>
<tr>
<td>Early myoclonic epilepsy</td>
<td>First months; myoclonias, spasms; suppression-burst (sleep); severe outcome</td>
</tr>
<tr>
<td>Infantile spasms</td>
<td>First year; spasms; hyspsarrhythmia; developmental delay</td>
</tr>
<tr>
<td>Dravet syndrome</td>
<td>First year; partial and generalized seizures, myoclonias; normal EEG at onset; later: generalized spike-waves and multifocal spikes; severe outcome</td>
</tr>
<tr>
<td>Myoclonic astatic epilepsy</td>
<td>First year; generalized myoclonic and astatic seizures; interictal parietal theta activity and bilateral spike-waves; variable outcome</td>
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<td>Malignant migrating partial seizures of infancy</td>
<td>First year; continuous electrographic seizures, multiple areas of onset; severe outcome</td>
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<tr>
<td>Generalized epilepsy with febrile seizures (+)</td>
<td>Variable seizure and developmental phenotype in addition to febrile seizures and afebrile generalized convulsions</td>
</tr>
<tr>
<td>Hemiconvulsion-hemiplegia-epilepsy</td>
<td>Prolonged unilateral febrile seizures; subsequent hemiparesis and partial epilepsy</td>
</tr>
<tr>
<td>Benign myoclonic epilepsy</td>
<td>First 3 years; myoclonic seizures; normal interictal EEG; normal development</td>
</tr>
<tr>
<td>Benign familial/nonfamilial seizures</td>
<td>First year; partial seizures; normal development</td>
</tr>
</tbody>
</table>

Table 2. Specific treatment options

<table>
<thead>
<tr>
<th>Epileptic Syndrome</th>
<th>Treatment Options</th>
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<tbody>
<tr>
<td>Infantile spasms (West)</td>
<td>Adrenocorticotropic hormone, vigabatrin, ketogenic diet</td>
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<tr>
<td>Dravet</td>
<td>Stiripentol–valproic acid–clobazam, topiramate</td>
</tr>
<tr>
<td>Myoclonic astatic epilepsy</td>
<td>Valproic acid, levetiracetam, ketogenic diet</td>
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<tr>
<td>Benign myoclonic epilepsy</td>
<td>Valproic acid</td>
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rhythmic activity, or irregular spike-waves. Tonic spasms are electrographically similar to the ones observed in early infantile epileptic encephalopathy and West syndrome [9]. Based on a high incidence of familial cases, and on the usual absence of cerebral lesions at onset, genetic factors and inborn errors of metabolism including nonketotic hyperglycinemia play a prominent etiologic role. On evolution, however, lesions such as progressive cortical atrophy or delayed myelination are frequently observed [9]. None of the conventional antiepileptic drugs has demonstrated efficacy. Severe developmental delay is the rule, and mortality is high [9].

Lombroso reported a series of 29 patients with early myoclonic epilepsy. Among them, six manifested perinatal asphyxia, five had brain malformations, eight manifested inborn errors of metabolism, and 10 cases were cryptogenic. Nonketotic hyperglycinemia was diagnosed in four patients. A marked but transitory improvement was observed in one of them. A family history of epilepsy was present in three patients of the cryptogenic category, and two patients were siblings [4]. In the series of Dalla Bernardina et al., two patients were brothers, and six males in four generations had died of an epileptic encephalopathy probably transmitted with an X-linked inheritance. Five patients died during the first 2 years of life. Neuro-pathologic studies were performed in two of them, but failed to reveal any pathologic macroscopic or microscopic findings. Decerebrate posture and microcephaly developed in all survivors [16].

**Infantile Spasms/West Syndrome**

Infantile spasms, or West syndrome, is a form of severe epilepsy observed with a peak frequency between 4 and 9 months of age [11,19]. It was first described in a report by Dr. West regarding his unfortunate son, published in 1841 [20]. Its overall incidence is estimated at 3-4.5/10,000 live births [21-23]. Males are more affected than females in a ratio of 1.4:1 [22]. The spasms are extremely resistant to treatment. They are characterized by a brisk flexion, or, more rarely, extension of the trunk and an extension of the extremities; sometimes followed by a brief tonic posture; they appear in clusters. They may be subtle and may not be recognized as seizures. They can be asymmetric, particularly in symptomatic cases, and appear in sleep or in wakefulness. Development may be normal at onset, but some regression occurs in most children. The typical interictal electroencephalogram reveals hypsarrhythmia, characterized by high-amplitude (up to 500 μV) asynchronous slow waves intermixed with multifocal spikes (Fig 2). It appears in sleep first, and later in wakefulness as well. A modified pattern, with some degree of synchrony and long spike-wave complexes is sometimes observed. The typical electrographic correlate of a spasm is a sharp wave followed by attenuation (electrodecrement) and low-voltage fast activity (Fig 3).

Multiple etiologies have been associated with West syndrome, including perinatal hypoxic-ischemic injuries, tuberous sclerosis, brain malformations, chromosomal abnormalities, and inborn errors of metabolism. In 30% of the cases, no specific etiology is found [2,11]. Infants with
cryptogenic etiology have a better prognosis regarding seizure control and development. In the study by Luth-
vigsson et al., all 6 infants with cryptogenic spasms had a normal or satisfactory outcome [21]. A “benign” form of infantile epileptic spasms has even been described in cryptogenic cases: infants had normal development at onset, and only exhibited a subtle and transitory regression, if any, during the period of spasms [24,25]. Of
It is a severe epilepsy characterized by generalized and unilateral clonic or tonic-clonic seizures appearing in the first year of life, later evolution to other types of seizures, including myoclonias, atypical absences, alternating unilateral seizures, or nonconvulsive status epilepticus. Progressive developmental delay is invariably observed on evolution, usually from the second year on. Tonic seizures are exceptional. All seizures are resistant to treatment [29,30]. Because Dravet syndrome typically presents with a seizure triggered by fever in an otherwise normal infant, it may be indistinguishable from febrile seizures at onset. However, the prolonged character of the first event and the rapid appearance of additional seizures usually allow differentiation of Dravet syndrome from febrile seizures. The term Dravet syndrome was progressively preferred to other proposed denominations, such as severe myoclonic epilepsy in infancy, because myoclonias are not invariably present at onset.

In a recent series, Dravet syndrome accounted for 8.2% of patients who had their first seizure before the age of 3 [29]. Males are more affected than females in a ratio of 2:1 [29]. The interictal electroencephalogram is usually normal at presentation, and later manifests generalized spike-and-wave complexes, as well as focal and multifocal spikes. A theta rhythm in the central and vertex region is observed early in the majority, but tends to disappear with age [13]. Photosensitivity is frequently demonstrated, but is inconstant during the course of the disease [29,30]. It is often a cause of self-stimulation. Massive myoclonias are associated with bursts of irregular spike-and-waves; on the other hand, erratic myoclonias do not correlate with electroencephalographic changes [13].

Convulsive seizures are thought to have a focal onset in the majority of cases, with several foci firing successively and giving them a “falsely generalized” or “unstable” aspect; truly generalized seizures could in fact be less frequent than reported [29]. Atypical absences correspond to generalized 2-3.5 Hz irregular spike-waves [29]. Nonconvulsive status epilepticus is electrographically characterized by diffuse slow waves and intermixed spikes [29]. Neuroimaging studies usually do not reveal brain lesions at onset, but may reveal hippocampal sclerosis on evolution [31]. Genetics plays an important role in Dravet syndrome, and a family history of epilepsy or febrile seizures is present in approximately 25% [29]. Affected monozygotic pairs of twins have been reported. The association with a mutation in the sodium-channel gene

Dravet Syndrome (Severe Myoclonic Epilepsy of Infancy)

Dravet syndrome was described in 1978 [29]. It is a severe epilepsy characterized by generalized and unilateral clonic or tonic-clonic seizures appearing in the first year of life, later evolution to other types of seizures, including myoclonias, atypical absences, alternating unilateral seizures, or nonconvulsive status epilepticus. Progressive developmental delay is invariably observed on evolution, usually from the second year on. Tonic seizures are exceptional. All seizures are resistant to treatment [29,30]. Because Dravet syndrome typically presents with a seizure triggered by fever in an otherwise normal infant, it may be indistinguishable from febrile seizures at onset. However, the prolonged character of the first event and the rapid appearance of additional seizures usually allow differentiation of Dravet syndrome from febrile seizures. The term Dravet syndrome was progressively preferred to other proposed denominations, such as severe myoclonic epilepsy in infancy, because myoclonias are not invariably present at onset.

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SCN1A has been recently discovered, and is present in various proportions of patients. Recent abstracts suggest that de novo truncation mutations are particularly associated with Dravet syndrome. The presence of this mutation is considered supportive, but not necessary to make the diagnosis of Dravet syndrome. γ-aminobutyric acid (GABA) receptor gene GABRG2 mutations have also been described, but only rarely [29]. For some authors, Dravet syndrome is the most severe phenotype in the generalized epilepsy with febrile seizures (+) spectrum [32]. The signification of de novo mutations in families with other forms of epilepsy remains unclear, but a heterogeneous genetic background is likely [29,33]. The long-term prognosis is universally poor. Seizures are extremely difficult to control and remain sensitive to fever or hyperthermia; developmental delay is present in all infants; neurologic abnormalities, such as ataxia and pyramidal signs are frequent; and the mortality rate is high (15.9% in Dravet’s series) [34]. Topiramate is effective [35,36], and stiripentol (not approved in the United States), as add-on therapy to valproic acid and clobazam, has demonstrated significant efficacy on convulsive seizures in a placebo-controlled study on 41 patients [37]. Additional treatment options, such as zonisamide and the ketogenic diet, have also yielded some efficacy in controlling seizure activity [29]. On the other hand, certain drugs, such as phenobarbital, phenytoin, carbamazepine, and lamotrigine, may exacerbate seizures [4,29]. Prophylaxis of fever and hyperthermia should be specifically emphasized in patients with Dravet syndrome.

Myoclonic-Astatic Epilepsy (Doose Syndrome)

Myoclonic-astic epilepsies were described in 1970 [38]. The main characteristics of the epileptic syndrome were already recognized in the initial description. The seizures are primary generalized with myoclonic or astatic components that often lead to severe injuries. They are observed in combination with absences, generalized tonic-clonic or clonic-tonic-clonic seizures (personal observations), tonic seizures, and nonconvulsive status epilepticus with subtle myoclonias. The onset is between 1 and 5 years, most often between 3 and 4 years, in an otherwise normal child. Males are more often affected than females. The interictal electroencephalogram is characterized by bilateral synchronous irregular 2-3 Hz spike-and-wave complexes. Parietal rhythmic theta may be observed independent of the state of vigilance. Myoclonic seizures are accompanied by irregular spikes and polyspikes. The astatic component is characterized by electrographic silence on electromyography, and can present as subtle head drops or massive loss of muscle tone and fall to the ground. Organic brain lesions are rarely encountered [39]. As with Dravet syndrome, a genetic role is strongly suspected. A family history of seizures or electroencephalographic abnormalities was documented in up to 80% of the cases [38], and myoclonic-astic epilepsy was one of the clinical phenotypes encountered in the families in which generalized epilepsy with febrile seizures (+) syndrome was initially described [40]. Outcome is variable. In a study on 52 patients, 85% were developmentally normal at onset, and 77% remained so at 7.5 years follow-up [41,42]. On the other hand, severe developmental delay and intractable seizures have also been described. The persistence of theta rhythms until adolescence and adulthood, failure to develop a stable occipital alpha rhythm, generalized tonic-clonic convulsions during the first year of life, nonconvulsive status epilepticus, and tonic seizures are considered prognostically unfavorable [43]. In our experience, however, patients with myoclonic-astic epilepsy and tonic seizures can have a norm development. Valproic acid is advocated by many [39]. Ethosuximide is effective in treating absence seizures. Levetiracetam and the ketogenic diet have demonstrated promising results in our hands. Comparative drug trials are definitely wanting in this disorder.

Malignant Migrating Partial Seizures of Infancy

Malignant migrating partial seizures in infancy is a severe epileptic disorder described in 1995 [44]. It is characterized by nearly continuous electrographic seizures involving multiple independent areas of onset, beginning in the first 6 months of life in normal infants with developmental delay and intractable seizures. No underlying etiology is evident, but a functional or metabolic dysfunction is suspected. Its prevalence is unknown; series involving only small numbers of patients have been published [44-46].

Coppola et al. reported a series of 14 patients fulfilling these criteria. The spectrum of clinical manifestations was large. All seizures had a motor component; most were focal and accompanied by autonomic manifestations; many migrated from one side of the body to the other, and six of them secondarily generalized. Two patients presented with status epilepticus. Mild clinical features were observed during habitual seizures. The interictal electroencephalogram was normal in three patients at onset, but was always abnormal during evolution, with multifocal spikes and sleep abnormalities. The ictal electroencephalogram was characterized by monomorph rhythmic theta or alpha activity progressively involving adjacent areas before decreasing. Additional seizures beginning in other areas in either hemisphere could commence before the end of the first event, or immediately follow it (Fig 4). Cerebral magnetic resonance imaging was performed in 10 patients and did not reveal any abnormalities. Eleven patients developed microcephaly during the first year of life. Three patients died. Conventional treatments were ineffective, except for the combination of stiripentol and clonazepam in two children, in whom some neurologic improvement was also observed [44].

We and others [47] suspect that there is a wider clinical spectrum of this disorder. In particular, we have observed
Figure 4. (a) Migrating seizure, right-sided onset. Seventeen-month-old female, awake. Mitochondrial disorder. (b) Migrating seizure, transition phase: right-sided fading and independent left onset. (c) Migrating seizure, left-sided continuation and termination.
patients with less-than-constant seizures, and Marsh et al. [47] report patients with slightly better outcomes than those reported by Coppola et al.

***Generalized Epilepsy With Febrile Seizures Plus (GEFS+):***

Generalized epilepsy with febrile seizures (+) was described in 1997 [40]. It is characterized by the association of generalized febrile seizures beyond the age of 6 years and afebrile generalized convulsions; a positive family history of epilepsy with variable phenotypes; and a benign evolution in the majority of cases. The first description in a large family revealed that the clinical spectrum of generalized epilepsy with febrile seizures (+) comprised cases of simple febrile seizures; febrile seizures beyond the age of 6 years (febrile seizures (+)); febrile seizures (+) and absences; febrile seizures (+) and myoclonic seizures; febrile seizures (+) and atonic seizures; and myoclonic-astatic epilepsy. This spectrum was further extended with other types of epilepsy, such as febrile seizures (+) and temporal lobe epilepsy [48].

Dravet syndrome, and cryptogenic Lennox-Gastaut syndrome [32]. The pattern of transmission in the first family suggested an autosomal dominant inheritance. The authors hypothesized that a single major gene defect, with possible additive gene effect, was responsible for the phenotypic variability on the entire spectrum of the generalized epilepsies [40,48]. Extensive genetic analyses in these families allowed the identification of a mutation in the sodium-channel \( \beta 1 \) subunit gene (SCN\( \beta 1 \)) on chromosome region 19q13.1 [49]. Additional mutations were later discovered in other genes, such as the sodium-channel \( \alpha 1 \) subunit gene on chromosome region 2q24 [50], or the GABA\(_ A\) receptor \( \gamma 2 \)-subunit gene on chromosome region 5q34 [51]. These findings underline the genetic complexity of this disorder, which remains to be completely understood. Some have argued that this is not a specific epilepsy syndrome, but rather a description of genetic susceptibility.

***Hemiconvulsions-Hemiplegia-Epilepsy:***

Hemiconvulsions-hemiplegia-epilepsy was described in 1960 [52]. It is characterized by prolonged unilateral febrile seizures followed by ipsilateral hemiparesis, and, later, epilepsy. Pathologic studies in the acute stage revealed hemispheric swelling, hemorrhagic necrotic lesions, and neuronal degeneration. In the chronic stage, atrophy, cystic necrosis, and foci of demyelination were observed. The temporal lobe was by far the most commonly involved region [52]. Vascular causes, such as venous thromboses, were believed to be the most prevalent. According to other authors, this may have been explained by infections involving the head and face, commonly associated with cerebral thromboses. The suggestion was advanced that these cases did not differ in etiology from benign febrile seizures, and that the sequelae were caused by status epilepticus itself [53]. This statement was supported by the fact that the frequency of hemiconvulsions-hemiplegia-epilepsy had considerably decreased in parallel to the introduction of the early use of benzodiazepines in the treatment of febrile convulsions and unilateral seizures [53]. Neuroimaging descriptions also favor the idea that febrile status epilepticus can cause brain injuries, with the demonstration of cytotoxic edema on diffusion-weighted magnetic resonance imaging in the acute phase [54-56], and of atrophy [54] and hypoperfusion on single-photon emission computed tomography studies in later stages [57]. A recent report described the detection of human herpesvirus 6 and 7 deoxyribonucleic acid, and specific antibodies for human herpesvirus 7 in the serum of an 18-month-old patient with generalized febrile convulsions who exhibited early hemispheric edema and late atrophy [56], but the underlying pathophysiologic mechanism remains unknown. Studies specifically addressing the influence of prolonged febrile seizures on temporal lobe epilepsy are currently under way.

***Benign Myoclonic Epilepsy of Infancy:***

Benign myoclonic epilepsy of infancy was described in 1981 [58]. It was initially characterized by the occurrence of easily treatable myoclonic seizures in the first 3 years of life in infants who remained normal on evolution. Except for rare simple febrile seizures, no other types of seizures are usually observed [59]. A family history of epilepsy or febrile convulsions is present in 30% of the cases [60]. Benign myoclonic epilepsy of infancy accounted for less than 1% of all the epilepsies, and 2% of all generalized epilepsies, in unpublished data from the Centre Saint-Paul in Marseilles. Males are more often affected than females in a ratio of approximately 2:1 [59]. The seizures are characterized as brief myoclonic jerks, particularly during drowsiness and, in some cases, are activated by photic stimulation or sudden external stimuli [59]. They usually disappear during sleep. Although generalized tonic-clonic seizures and absence seizures have been described [59], others regard these seizures as exclusionary criteria. The interictal electroencephalogram is normal. The myoclonias are accompanied by generalized spike-waves or polyspike-waves. In contrast, in benign nonepileptic myoclonus of infancy, no electroencephalographic changes are observed during myoclonias. Neuroradiologic investigations do not reveal abnormalities. Seizures are sensitive to valproic acid, which is considered the drug of choice. Sixty-seven of 76 patients (88%) with benign myoclonic epilepsy of infancy became seizure-free on valproate monotherapy [59]. In most cases they disappear in less than 1 year of evolution. Recent data suggest that the neurodevelopmental outcome depends on an early recognition and on appropriate treatment. It is favorable in the great majority, but mild mental retardation can be observed and the real benignity of the syndrome has been questioned [59].
Benign Familial/Nonfamilial Infantile Seizures

This entity is characterized by partial seizures appearing in the first year of life in otherwise normal infants [61,62]. A family history of similar seizures at the same age is frequent, and an autosomal dominant inheritance with incomplete penetrance is suspected [63]. Linkage to chromosome regions 19q, 2q24, and 16p12-q12 has been demonstrated [63,64]. The seizures are characterized by behavioral arrest with versive components, cyanosis, generalized hypertonia, and unilateral myoclonic jerks. Secondary generalization can occur. They resumed at a median age of 14-15 months in a series on 64 cases [62]. The interictal electroencephalogram is normal [61,62]. The ictal electroencephalographic recordings indicate a parieto-occipital onset, with occasional generalization [61,63]. Seizures are well controlled on valproic acid [63]; in mild cases, treatment might not even be necessary. The neurodevelopmental prognosis is always favorable. Its separation from the benign nonfamilial form of infantile partial seizures is controversial. In a study comparing the two entities, Caraballo et al. did not find any electroclinical differences. The only parameter that varied was the presence, in benign familial infantile seizures, of a family history of seizures. Paroxysmal choreoathetosis, a movement disorder occasionally associated with this entity on evolution, was also solely observed in familial cases, but in too small numbers to be considered as a significant finding [62].

Issues and Needs

Some major issues characterize the current classification of epileptic syndromes in infants. First, most of the reported epileptic syndromes are rare and may not be easily recognized. The available data suggest that while these syndromes often carry severe prognoses, they may benefit from specific forms of treatment. Patients with infantile epilepsies should therefore be referred to centers with experience in this domain.

Second, there is a conspicuous absence of precise correlation between metabolic diseases and epilepsy syndromes. It is likely that more detailed reports of seizures and electroencephalographic findings in patients with metabolic defects will help identify additional epilepsy syndromes. Exceptions include early myoclonic epilepsy and West syndrome where metabolic features may be responsible for some of these infantile epilepsies with mixtures of focal and generalized features.

Finally, the International League Against Epilepsy has proposed a diagnostic scheme that is useful for the analysis of patients with epilepsy. This scheme consists of five axes that would allow a variety of approaches dependent on the particular purpose. These axes include ictal semiology, seizure type, epileptic syndrome, etiology, and degree of impairment [65]. Whatever the adopted scheme, we agree that, implicit in this ordering of diagnoses, one must arrive at an accurate seizure classification before an epilepsy syndrome can be established. We believe infantile epilepsies require an electroclinical diagnosis in order to achieve appropriate diagnostic precision. Current efforts are under way to thoroughly establish electroclinical definitions of infantile seizures.

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