

# Early infantile epileptic encephalopathy

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## Abstract

*Early infantile epileptic encephalopathy (EIEE) or Ohtahara syndrome is the earliest form of age-dependent encephalopathies, which include also [West syndrome](#) and [Lennox-Gastaut syndrome](#). This rare syndrome is characterized by a very early onset, during the first months of life, with frequent tonic spasms and a suppression-burst pattern on electroencephalogram. Partial motor seizures may occur. Brain imaging usually discloses gross structural abnormalities in the majority of cases. Metabolic disorders were present in a few cases. The course is severe with early death or marked psychomotor retardation and intractable seizures with frequent evolution to [West syndrome](#). Antiepileptic drugs remain as first-line treatment. EIEE constitutes along with the neonatal or early myoclonic encephalopathy the group of "epileptic encephalopathies with suppression-burst pattern" or "severe neonatal epilepsies with suppression-burst pattern".*

## Key-words

Early infantile epileptic encephalopathy, early infantile epileptic encephalopathy with suppression-burst, Ohtahara syndrome, suppression-burst pattern, early myoclonic encephalopathy, cerebral malformation, West syndrome

## Disease name / synonyms

- Early infantile epileptic encephalopathy (EIEE)
- Early infantile epileptic encephalopathy with suppression-burst
- Ohtahara syndrome.

[West syndrome](#) and [Lennox-Gastaut syndrome](#).

EIEE is characterized by a very early onset - mainly within 1 month and often within the first 10 days of life-, frequent tonic spasms and a suppression-burst pattern on EEG (Ohtahara, 1978; Ohtahara *et al.*, 1987, 1992; Aicardi and Ohtahara 2002).

## Definition / diagnostic criteria

Early infantile epileptic encephalopathy (EIEE) or Ohtahara syndrome is the earliest form of age-dependent encephalopathies, which include also

## Differential diagnosis

[Early myoclonic encephalopathy \(EME\)](#) or [neonatal myoclonic encephalopathy \(NME\)](#)

EME is characterized by an early onset (during the first month of life) of partial or erratic myoclonus, massive myoclonus, partial motor seizures and late tonic spasms. The EEG shows a suppression-burst pattern (Aicardi, 1992). The course is severe, as neurological development is very poor and 50% of reported patients were dead in the first year of life. Metabolic disorders, especially non ketotic hyperglycinaemia, are mostly found but the proportion of cryptogenic cases is high.

EME shares with EIEE the age of occurrence, the suppression-burst pattern on EEG, the poor epileptic prognosis and the development of encephalopathy. The main differences are the seizures types, myoclonic in the EME and tonic spasms in the EIEE, and the etiology, metabolic with few familial cases in EME and sporadic with brain malformation in EIEE.

These two syndromes constitute the major part of severe neonatal epilepsies with suppression-burst patterns (Aicardi and Ohtahara, 2002). The distinction between these two conditions may be difficult since in the neonatal period brief spasms are difficult to distinguish from generalized myoclonus, including with polygraphic recording. However, from the therapeutic point of view, the distinction has great importance since Vigabatrin might improve EIEE, but not EME (Nabbout and Dulac, 2003).

#### **Unclassified severe neonatal epilepsies with suppression-burst patterns**

Some children with neonatal seizures and suppression-burst pattern do neither fulfil the criteria of EIEE nor those of EME (Schlumberger *et al.*, 1992).

#### **Infantile spasms ([West syndrome](#))**

This syndrome is characterized by a triad of spasms, psychomotor deterioration and a disorganized EEG designed as hypsarrhythmia. It mainly occurs after 3 months of life. Most survivors of EIEE evolve to West syndrome. These 2 syndromes belong to the group of age-dependent encephalopathies. They share several features as tonic spasms, severe and continuous epileptic activity, and severe mental delay. The age group is younger for EIEE.

#### **Etiology**

A majority of cases of EIEE are associated with structural brain damage (Ohtahara *et al.*, 1992). It includes [Aicardi syndrome](#), [Hemimegalencephaly](#), [Porencephaly](#), cerebral atrophy and dento-olivary-dysplasia (Robain and Dulac, 1992). Metabolic disorders were present in a few cases and consisted of [cytochrome-c oxidase deficiency](#) (Williams *et al.*, 1998), [Leigh's encephalopathy](#) (Tatsuno *et al.*, 1984).

#### **Clinical description**

The onset of seizures is within the first 2 months of life, mainly within 1 month and often within the first 10 days of life. The main type of seizures is tonic spasms, which occur in clusters or singly, both in the awake and sleep state. In addition, partial motor seizures are observed in more than half of the cases. Myoclonic seizures are rare (Ohtahara, 1978) and erratic myoclonus is not a feature (Schlumberger *et al.*, 1992). The neurological examination shows variable signs - depending on the brain malformation- and is frequently asymmetrical. The suppression-burst pattern is the most characteristic finding on EEG. Bursts last 2-6 seconds and comprise high voltage slow waves mixed with spikes whereas suppression period lasts 3-5 seconds. Spasms are ictal events characterized by diffuse synchronization, with an initial high amplitude slow wave (Martin *et al.*, 1981) or a fast activity (Yamatogi and Ohtahara, 1981).

#### **Diagnostic methods**

The diagnosis of this syndrome is established on clinical and EEG criteria (*cf* clinical description). Due to the predominant role of structural damage, brain imaging is the most important diagnostic evaluation. Computed tomography (CT) and magnetic resonance imagery (MRI) reveal often-specific anomalies from the onset of clinical symptoms. Metabolic investigations are indicated in case of normal or non-specific imaging abnormalities.

#### **Epidemiology**

This syndrome was first identified by Ohtahara (Ohtahara, 1978). Nearly 50 cases are reported in the literature with a detailed description for 35 of them (Ohtahara, 1978; Schlumberger *et al.*, 1992; Bermejo *et al.*, 1992; Clarke *et al.*, 1987; Martin *et al.*, 1981). The major series is that of Ohtahara who described 15 patients (Ohtahara *et al.*, 1992) with one additional case in 2002 (Yamatogi and Ohtahara). Schlumberger *et al.* (1992) studied 23 patients with suppression-burst pattern and without any evidence of perinatal anoxic-ischaemic distress. Eight of them fulfilled the criteria of EIEE, 7 of them fulfilled the criteria of EME and 8 were unclassified.

#### **Genetic counselling**

No familial cases of EIEE have been reported. However, familial cases are frequent in EME (Aicardi, 1992; Wang *et al.*, 1998; Dalla Bernardina *et al.*, 1983) and an autosomal recessive inheritance is suggested even when no metabolic disorder is found.

## Treatment

Treatment of EIEE is disappointing. The spasms are less responsive to ACTH and/or corticoids than in West syndrome. Vigabatrin (50-100 mg/Kg/d) is occasionally helpful. Two patients with focal cortical dysplasia were improved after hemispherectomy in one patient (Pedespan *et al.*, 1995) and a more restricted resection in the other (Komaki *et al.*, 1999).

## Unresolved questions

The syndromes EIEE and EME are considered to be the 2 main syndromes of the group of severe neonatal epilepsies with suppression-burst pattern. Although they are well defined, the identification of the seizures pattern and the distinction between massive myoclonia and spasms may be difficult especially when we lack a good EEG video registration. Moreover, a number of cases remain difficult to classify

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