Epilepsy Syndromes with Onset in Neonates & Infants

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Disclosures relevant to this presentation

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Member ILAE Task Force on Neonatal Seizures 2013-17

Member ILAE Task Force on Nosology & Definitions 2017-21

Member ILAE Task Force on Etiology Specific Syndromes 2021-25
ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions

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An epilepsy syndrome is a characteristic cluster of clinical and EEG features often supported by specific etiological findings (structural, genetic, immune and infectious
The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures

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FIGURE 1 Relative occurrences of common etiologies of neonatal seizures in term infants. Adapted from, 5-7, ILAE

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Epilepsy syndrome

Seizure type (all focal onset)
- Electro-clinical
- Electrographic only

Etiology
- Hypoxic-ischaemic
- Structural
  - Vascular
  - Brain malformation
- Genetic
- Infectious
- Metabolic
- Unknown

Co-morbidities

Presentation
- Critically ill or with clinical suspicion

Differential diagnosis
- Video EEG / amplitude integrated EEG

Seizures
- (with EEG correlate)
- (without clinical signs)

Seizure type
- Electro-clinical
- Electrographic only
- Unclassified
- Motor
- Non-motor
- Sequelae
Classification should guide clinical management
ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions
**Self-limited epilepsies**
- Self-limited neonatal epilepsy (SeLNE)
- Self-limited familial neonatal-infantile epilepsy (SeLFNIE)
- Self-limited infantile epilepsy (SeLIE)
- Genetic epilepsy with febrile seizures plus (GEFS+)
- Myoclonic epilepsy in infancy (MEI)

**Developmental and epileptic encephalopathies (DEE)**
- Early infantile developmental and epileptic encephalopathy (EIDEE)
- Epilepsy in infancy with migrating focal seizures (EIMFS)
- Infantile epileptic spasms syndrome (IESS)
- Dravet syndrome (DS)

**Etiology-specific syndromes**
- KCNQ2-DEE
- Pyridoxine-dependent (ALDH7A1)-DEE (PD-DEE)
- Pyridox(am)ine 5'-Phosphate Deficiency (PNPO)-DEE (PSPD-DEE)
- CDKL5-DEE
- PCDH19 clustering epilepsy
- Glucose Transporter 1 Deficiency Syndrome (GLUT1DS)
- Sturge Weber syndrome (SWS)
- Gelastic seizures with hypothalamic hamartoma (GS-HH)
Epilepsies where there is likely to be spontaneous remission

- Self-limited neonatal epilepsy (SeLNE)
- Self-limited familial neonatal-infantile epilepsy (SeLFNIE)
- Self-limited infantile epilepsy (SeLIE)
- Genetic epilepsy with febrile seizures plus (GEFS+)
- Myoclonic epilepsy in infancy (MEI)
Epilepsies where developmental impairment is related to both the underlying etiology independent of epileptiform activity and the epileptic encephalopathy

- Early infantile developmental and epileptic encephalopathy (EIDEE)
- Epilepsy in infancy with migrating focal seizures (EIMFS)
- Infantile epileptic spasms syndrome (IESS)
- Dravet syndrome (DS)
Syndromes due to specific genetic, structural, immune and infectious etiologies where there are consistent electroclinical features, management and prognostic implications.

**Etiology-specific syndromes**

- **KCNQ2-DEE**
- Pyridoxine-dependent *(ALDH7A1)-DEE (PD-DEE)*
- Pyridox(am)ine 5’-Phosphate Deficiency *(PNPO)-DEE (P5PD-DEE)*
- **CDKL5-DEE**
- **PCDH19** clustering epilepsy
- Glucose Transporter 1 Deficiency Syndrome *(GLUT1DS)*
- Sturge Weber syndrome *(SWS)*
- Gelastic seizures with hypothalamic hamartoma *(GS-HH)*
<table>
<thead>
<tr>
<th>Mandatory</th>
<th>Alerts</th>
<th>Exclusionary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizures</td>
<td>Seizures are characterized by focal tonic features at onset, affecting the head, face, and limbs. Focal clonic or tonic seizures may alternate sides from seizure to seizure, and may evolve to bilateral tonic or clonic seizures</td>
<td>Clinical history suggestive of utero seizures</td>
</tr>
<tr>
<td>EEG</td>
<td>Interictal: Mild background slowing</td>
<td>Interictal: Persistent focal slowing or moderate or greater background slowing not limited to the postictal period</td>
</tr>
<tr>
<td>Age at onset</td>
<td>Onset after first month of age</td>
<td>Burst suppression pattern</td>
</tr>
<tr>
<td>Development at onset</td>
<td>Significant neurological examination abnormalities, excluding incidental findings</td>
<td>Hypsarrhythmia</td>
</tr>
<tr>
<td>Neurological exam</td>
<td>Neuroimaging documenting a causal lesion for seizures</td>
<td>Total: Lack of EEG correlates with clinical symptoms</td>
</tr>
<tr>
<td>Imaging</td>
<td>Lack of pathogenic variant in gene associated with this syndrome, most commonly KCNQ2 or KCNQ3 OR Lack of family history suggesting AD inheritance with incomplete penetrance</td>
<td>Weak positive or negative for seizures including intracranial infection, ischemic or hemorrhagic stroke, hypoxic-ischemic brain injury, significant metabolic disturbances</td>
</tr>
<tr>
<td>Other studies - genetics</td>
<td>Lack of family history suggesting AD inheritance with incomplete penetrance</td>
<td>Moderate to severe neurodevelopmental disability</td>
</tr>
<tr>
<td>Course of illness</td>
<td>Mild neurodevelopmental delay long-term</td>
<td></td>
</tr>
<tr>
<td>MRI or ictal EEG required for diagnosis?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Syndrome without laboratory confirmation:** In resource-limited regions, SeLNE can be diagnosed without EEG and MRI in a neonate with a family history suggestive of familial SeLNE who meets all other mandatory and exclusionary clinical criteria and has no Alerts. However, the clinical history of affected family members should be consistent with the expected course for SeLNE, and careful follow-up of the patient is required to ensure their course is also consistent with this syndrome.

Abbreviations: EEG, electroencephalogram; MRI, magnetic resonance imaging; SeLNE, self-limited neonatal epilepsy.
Early Infantile Developmental & Epileptic Encephalopathy replaces the terms Ohtahara syndrome and Early Myoclonic Encephalopathy

<table>
<thead>
<tr>
<th>TABLE 5</th>
<th>Diagnostic criteria for early infantile developmental and epileptic encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mandatory</td>
</tr>
<tr>
<td>Seizures</td>
<td>Tonic and/or myoclonic seizures</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>EEG</td>
<td></td>
</tr>
<tr>
<td>Age at onset</td>
<td>Birth to 3 months (adjusted for prematurity)</td>
</tr>
<tr>
<td>Development at onset</td>
<td></td>
</tr>
<tr>
<td>Neurological exam at onset</td>
<td></td>
</tr>
<tr>
<td>Early Comorbidities</td>
<td>Developmental impairment is present prior to or shortly after seizure onset</td>
</tr>
</tbody>
</table>
| Course of illness | Abnormal neurodevelopment including intellectual disability | Are MRI or ictal EEG required for diagnosis?  
An MRI is not required for diagnosis but is strongly recommended to exclude structural causes 
An ictal EEG is not required in an infant with characteristic clinical features where the interictal EEG shows burst-suppression, multifocal discharges with diffuse slowing |

Syndrome without laboratory confirmation: In resource-limited regions, this syndrome cannot be diagnosed without an interictal EEG.
FIGURE 5  A 4-week-old boy with Early Infantile DEE. He presented on day 2 of life with sequential seizures with a prominent tonic component and severe encephalopathy. The EEG (20 microvolt/mm, 30 mm/s) shows a burst-suppression pattern. Genetic testing showed a KCNQ2 pathogenic variant. The patient showed a marked reduction in seizures with carbamazepine but remained profoundly delayed
Dravet syndrome

<table>
<thead>
<tr>
<th></th>
<th>Mandatory</th>
<th>Alerts</th>
<th>Exclusionary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seizures</strong></td>
<td>Recurrent focal clonic (hemiconic) febrile and afebrile seizures (which often alternate sides from seizure to seizure), focal to bilateral tonic-clonic, and/or generalized clonic seizures</td>
<td>No history of prolonged seizures (&gt;10 min) Lack of fever sensitivity as a seizure trigger</td>
<td>Epileptic spasms Early infantile SCN1A DEE</td>
</tr>
<tr>
<td><strong>EEG</strong></td>
<td>Normal EEG background without interictal discharges after age 2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age at onset</strong></td>
<td>1–20 months</td>
<td>1–2 months or 15–20 months</td>
<td></td>
</tr>
<tr>
<td><strong>Development at onset</strong></td>
<td>Developmental delay at seizure onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neurological exam</strong></td>
<td>Focal neurological findings (other than Todd’s paresis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td></td>
<td>MRI showing a causal focal lesion</td>
<td></td>
</tr>
<tr>
<td><strong>Other testing: i.e., genetics, and so on</strong></td>
<td>Lack of pathogenic SCN1A or other causal variant</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Course of illness</strong></td>
<td>Drug-resistant epilepsy Intellectual disability</td>
<td>Good efficacy with prophylactic sodium-channel agents including carbamazepine, oxcarbazepine, and phenytoin</td>
<td></td>
</tr>
</tbody>
</table>

**Is MRI or ictal EEG required for diagnosis?**

- An MRI is not required for diagnosis but is highly recommended to exclude other causes.
- An ictal EEG is not required for diagnosis.

**Possible evolving syndrome:** In a child <12 months who presents with a prolonged hemiconic or bilateral tonic-clonic seizure with fever, and no other underlying cause, the possibility of Dravet syndrome should be considered. Further convulsive seizures (often with fever, and if prolonged or hemiconic) would allow more definitive diagnosis of Dravet syndrome. A diagnosis would be further supported by the finding of a pathogenic SCN1A variant.

**Syndrome without laboratory confirmation:** In resource-limited regions, Dravet syndrome can be diagnosed in children without Alerts who meet all other clinical mandatory and exclusionary criteria, without EEG, MRI, and genetic testing.
Syndrome papers provide overviews. Review the literature for finer details of each syndrome.
Infantile epileptic spasms syndrome

<table>
<thead>
<tr>
<th>Table 7</th>
<th>Diagnostic criteria for infantile epileptic spasms syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mandatory</strong></td>
<td><strong>Alerts</strong></td>
</tr>
<tr>
<td>Seizures</td>
<td>Flexor, extensor or mixed epileptic spasms which often occur in clusters</td>
</tr>
<tr>
<td>EEG</td>
<td>Interictal: Hypsarrhythmia, multifocal or focal epileptiform discharges (that might be seen quickly after the spasms onset)</td>
</tr>
<tr>
<td>Age at onset</td>
<td>1–24 months (while epileptic spasms may begin later, this would not be ISS)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Developmental slowing after spasms onset but may be absent early in the course (difficult to determine in a child with existing significant developmental disorders)</td>
</tr>
</tbody>
</table>

**Is MRI or ictal EEG required for diagnosis?**
An MRI is not required for diagnosis but is highly recommended to evaluate for underlying cause.
An ictal EEG is not required for diagnosis provided the interictal study shows hypsarrhythmia or epileptiform abnormalities or developmental delay. In the absence of hypsarrhythmia or epileptiform anomalies, an ictal recording is required.

**Possible evolving syndrome:** Infants with preceding brain injury, developmental brain malformations, or specific genetic conditions, including early-infantile DEE, who show significant interictal EEG abnormalities (high amplitude, background slowing, and/or multifocal discharges) should be watched carefully for the development of clinical epileptic spasms. However, the syndrome of ISS cannot be diagnosed prior to onset of the mandatory seizure type.

**Syndrome without laboratory confirmation:** In resource-limited regions, an interictal EEG is highly recommended. However, if EEG is unavailable, if clear clusters of typical epileptic spasms are witnessed by an experienced clinician (in person or on video recording), with the other clinical mandatory and exclusionary criteria, ISS can be diagnosed.
## Etiology specific syndrome - Gelastic seizures with hypothalamic hamartoma

### TABLE 15 Diagnostic criteria for gelastic seizures with hypothalamic hamartoma

<table>
<thead>
<tr>
<th></th>
<th>Mandatory</th>
<th>Alerts</th>
<th>Exclusionary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizures</td>
<td>Gelastic seizures with mechanical, mirthless laughter, inappropriate to context</td>
<td>Seizure frequency less than daily</td>
<td></td>
</tr>
<tr>
<td>EEG</td>
<td>Interictal: Generalized or focal background slowing (excluding immediate postictal period) Ictal: Gelastic seizures may lack ictal EEG correlate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset</td>
<td>Onset &gt;5 years of age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Development at onset</td>
<td>Clear developmental delay at seizure onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurological exam</td>
<td>Focal neurological findings (other than Todd's paresis) or generalized hypotonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging</td>
<td>Hypothalamic hamartoma (may require thin slices through the hypothalamic region to confirm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Course of Illness</td>
<td>Drug-resistant epilepsy</td>
<td>Lack of behavioral problems including aggression, impulsivity, and hyperactivity</td>
<td></td>
</tr>
</tbody>
</table>

**Is MRI or ictal EEG required for diagnosis?**
- An MRI is required for diagnosis
- An ictal EEG is not required for diagnosis. Furthermore, gelastic seizures may lack ictal correlate on EEG

**Syndrome without laboratory confirmation:** In resource-limited regions, HH-GS cannot be diagnosed in the absence of an MRI, as gelastic seizures may arise from other brain regions.
Precision medicine drives classification in the epilepsies

"A treatment approach in which disease treatment and prevention is tailored to individual variability in genes, environment and lifestyle for each person"

Medical therapy, surgical treatment, metabolic therapy, gene related therapy
ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions

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Epilepsy Syndromes with Onset in Childhood

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Outline

- Historical overview
- Purposes of the ILAE Task Force for Nosology
- Process of defining syndromes
- Definition and Classification of syndromes
- Core criteria and related Delphi process
- Further definitions
- Conclusions
Historical overview

1983, Centre Saint Paul, Marseille: first attempt of epileptic syndromes' classification

1984, "Guide Bleu"

1985, Proposal for Classification of Epilepsies and Epileptic Syndromes

1989, Revised Classification

2017, new Classification of the Epilepsies and Operational Classification of Seizure Types
Define epilepsy syndromes delineating “typical” features, a range of “accepted” findings and “alerts” features rarely seen in a syndrome.

Use a clear lexicon employing descriptive syndromic names avoiding “named” syndromes where possible.

Create a resource available worldwide.

Identify group of related syndromes.

Purposes of the ILAE Task Force on Nosology
Process of defining syndromes

- Literature review through July 2019
- Current criteria listed on EpilepsyDiagnosis.org
- Expert opinion from original Task Force members
**Definition and Classification**

**Epileptic syndrome**: a characteristic cluster of clinical and EEG features, often supported by specific etiological findings (structural, genetic, metabolic, immune and infectious).

 Syndromes are divided based on age at onset and on syndrome type (generalized epilepsy syndromes, focal epilepsy syndromes, focal and generalized epilepsy syndromes and syndromes associated with Developmental and/or Epileptic Encephalopathy (DÉE) or Progressive Neurological Deterioration).

4 groups:
1. Neonatal and Infantile onset (for the purpose of the proposed classification infancy was defined as the period up to age 24 months
2. Childhood onset
3. Variable age at onset
4. Idiopathic Generalized Epilepsies.
- DEE: an epilepsy associated with developmental impairment due to either the underlying etiology, the superimposed epileptic activity or both.

- The term DEE is more challenging to apply when epilepsy begins later in life, following a normal development, e.g. in Rasmussen Syndrome.

- Thus, the concepts of Epilepsy Syndromes with DEE and Epilepsy Syndromes with Progressive Neurological Deterioration to encompass the group of syndromes associated with cognitive impairment with or without other neurological deterioration and recognize that this impairment may be due to the underlying etiology, superimposed epileptic activity, or both.
Template for clinical data for syndromes

- Epidemiology
  - Clinical Context, e.g. age at onset, sex ratio, etc.
  - Natural history evolution, e.g. evolution from or to other syndromes, response to ASMs, etc.

- Comorbidities
  - Seizures type(s)
  - EEG findings

- Neuroimaging findings
  - Genetic findings and other laboratory studies
  - Differential diagnosis
International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions

Nicola Specchio | Elaine C. Wirrell | Ingrid E. Scheffer | Rima Nabbout
Kate Riney | Pauline Samia | Marilisa Guerreiro | Sam Gwer
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Edouard Hirsch | Sam Wiebe | Helen J. Cross | Emilio Perucca
Solomon L. Moshé | Paolo Tinuper | Stéphane Auvin
• Not for all patients
• Syndrome diagnosis
→ syndrome management
→ prognosis

ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology

Epilepsy Syndromes

Epilepsy types

Focal
Generalized
Combined
Generalized & Focal
Unknown

Seizure types

Focal
Generalized
Unknown

Etiology

Co-morbidities

Unknown
Immune
Metabolic
Infectious
Genetic
Structural
What’s new?

New names for Epilepsy Syndromes with Onset in Childhood and new classification

Self-limited focal epilepsies

Generalized Epilepsies

Developmental and/or Epileptic Encephalopathies
Self-limited focal epilepsies

- Self-Limited Epilepsy with Centrotemporal Spikes
- Self-Limited Epilepsy with Autonomic Seizures
- Childhood Occipital Visual Epilepsy
- Photosensitive Occipital Lobe Epilepsy

Generalized Epilepsies

- Childhood Absence Epilepsy
- Epilepsy with Eyelid Myoclonia
- Epilepsy with Myoclonic Absence

Developmental and/or Epileptic Encephalopathies

- Epilepsy with Myoclonic-Atonic Seizures
- Lennox-Gastaut syndrome
- Developmental and/or Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep
- Hemiconvulsion-Hemiplegia-Epilepsy Syndrome
- Febrile Infection-Related Epilepsy Syndrome
Updated 2022 ILAE guidance

- Epidemiology
- Clinical: age at onset, history, neurological exam
- Natural history: drug responsiveness, likelihood of remission, comorbidities, evolution
- Seizure type(s)
- EEG features: typical findings, if ictal EEG is needed
- Neuroimaging
- Genetics
- Other lab findings, if relevant
- Differential diagnosis

Mandatory features
Exclusionary features
Alerts: atypical features
Core diagnostic criteria
Self-limited focal epilepsies

- Childhood Epilepsy with CT Spikes
- Rolandic Epilepsy

Self-Limited Epilepsy with Centrotemporal Spikes

- Late-onset (Benign) Occipital Epilepsy or Idiopathic childhood Occipital Epilepsy – Gastaut type
- Early Onset (Benign) Occipital Epilepsy

Late-onset (Benign) Occipital Epilepsy

Self-Limited Epilepsy with Autonomic Seizures

Early Onset (Benign) Occipital Epilepsy

Panayiotopoulos syndrome

- Idiopathic Photosensitive Occipital Lobe Epilepsy

Photosensitive Occipital Lobe Epilepsy
Self-Limited Focal Epilepsies (SeLFE) of Childhood

Self-Limited Epilepsy with Centrotemporal Spikes (SeLCTS)
- Age-dependent
- Normal child - normal intellect, examination
- Classical seizure semiology
- Characteristic EEG features
- MRI: No structural lesion
- Remission in adolescence

Benign Focal Epilepsy of Childhood
Benign Rolandic Epilepsy
Benign Epilepsy with Centro-Temporal Spikes
Self-Limited Focal Epilepsies (SeLFE) of Childhood

Self-Limited Epilepsy with Autonomic Seizures (SeLEAS)

Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)
- Age-dependent
- Normal child - normal intellect, examination
- Classical seizure semiology
- Characteristic EEG features
- Remission in adolescence

Panayiotopoulos syndrome
Early-onset benign occipital epilepsy
Self-Limited Focal Epilepsies (SeLFE) of Childhood

- **Self-Limited Epilepsy with Autonomic Seizures (SeLEAS)**
- **Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)**
  - Age-dependent
  - Normal child - normal intellect, examination
  - Classical seizure semiology
  - Characteristic EEG features
  - Remission in adolescence
- **Childhood Occipital Visual Epilepsy (COVE)**
- **Gastaut syndrome**
- **Late-onset benign occipital epilepsy**
Self-Limited Focal Epilepsies (SeLFE) of Childhood

- Self-Limited Epilepsy with Autonomic Seizures (SeLEAS)
- Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)
- Childhood Occipital Visual Epilepsy (COVE)
- Photosensitive Occipital Lobe Epilepsy (POLE)

- Self-Limited Focal Epilepsies (SeLFE) of Childhood
- Age-dependent
- Normal child - normal intellect, examination
- Classical seizure semiology
- Characteristic EEG features
- Remission in adolescence

Idiopathic photosensitive occipital lobe epilepsy
Self-Limited Focal Epilepsies (SeLFE) of Childhood

- Onset median 7 yrs (range 4-10 yrs)
- Aura: Buccal paraesthesia
- Hemifacial tonic or clonic features
- Drooling, speech arrest – dysarthria, dysphasia
- Focal to bilateral tonic-clonic (FBTC)
- Within 1-2 hrs of falling asleep or prior to awakening
- Remit mid to late adolescence
9 yr boy with SeLECTS
Awake EEG: high amplitude right centrotemporal discharges
9 yr boy with SeLECTS
Asleep EEG: increased and higher amplitude discharges
9 yr boy with SeLECTS
Ictal rhythm: L centrotemporal rhythmic spikes ↑ amplitude, ↓ frequency
Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)

**Mandatory**
- **Seizures**: Focal seizures with dysarthria, sialorrhea, dysphasia
- **EEG**: High amplitude, centrotemporal biphasic epileptiform abnormalities
- **Course of illness**: Remission by mid to late adolescence. No developmental regression

**Alerts**
- **Seizures**: Focal motor or generalized convulsive status epilepticus >30 min.
- **EEG**: Sustained focal slowing not limited to the postictal phase. Lack of sleep activation of centrotemporal abnormalities
- **Age at onset**: >12 years at onset
- **Development at onset**: Moderate to profound intellectual disability
- **Neurological exam**: Hemiparesis or focal neurological findings, other than Todd's paresis

**Exclusionary**
- **Seizures**: Generalized tonic-clonic seizures during wakefulness.
- **Age at onset**: <3 years of >14 years at onset
- **Development at onset**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep (suggests EE-SWAS)
- **Imaging**: Causal lesion on brain MRI
- **Course of illness**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep suggests evolution to EE-SWAS
Self-Limited Focal Epilepsies (SeLFE) of Childhood

Self-Limited Epilepsy with Autonomic Seizures SeLEAS

- Onset 3-6 y (range 1–14 y)
- Focal autonomic seizures
  - Prominent vomiting and retching
  - Malaise
  - Pallor or flushing
  - Abdominal pain
  - Cardiorespiratory changes
  - Head and eye deviation
- Remits early – mid adolescence
SeLEAS

Awake: Rare posterior quadrant spikes

Asleep: Increase in frequency and amplitude of bilateral posterior discharges
Self-Limited Epilepsy with Autonomic Seizures (SeLEAS)

Mandatory
- **Seizures**: Focal autonomic seizures, with or without impaired awareness. Autonomic symptoms often involve prominent retching and vomiting, but may also include malaise, pallor, flushing, abdominal pain, pupillary or cardiorespiratory changes.
- **EEG**: High amplitude, focal or multifocal epileptiform abnormalities which increase in drowsiness and sleep.
- **Course of illness**: Remission by early to mid-adolescence. No developmental regression.

Alerts
- **Seizures**: Seizure frequency greater than monthly.
- **EEG**: Sustained focal slowing not limited to the postictal phase. Unilateral focal abnormalities in a consistent focal area across serial EEGs.
- **Age at onset**: <3 years or >8 years at onset.
- **Development at onset**: Moderate to profound intellectual disability.
- **Neurological exam**: Hemiparesis or focal neurological findings, other than Todd's paresis.

Exclusionary
- **Age at onset**: <1 year or >14 years at onset.
- **Development at onset**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep (suggests EE-SWAS).
- **Imaging**: Causal lesion on brain MRI.
- **Course of illness**: Neurocognitive regression with a continuous spike-and-wave pattern in sleep suggests evolution to EE-SWAS.
Self-Limited Focal Epilepsies (SeLFExE) of Childhood

- Focal sensory visual seizures
  - Elementary visual phenomena
  - Multicoloured circles
  - ± awareness
  - ± head and eye deviation
  - Awake
Awake: posterior spikes

Sleep: ↑ posterior spikes

Ictal: bilateral posterior low voltage fast activity
most prominent posterior regions
**Childhood Occipital Visual Epilepsy (COVE)**

**Mandatory**

- **Seizures:** Focal sensory visual seizures with elementary visual phenomena (multi-colored circles), with or without impaired awareness, and with or without motor signs (deviation of the eyes or turning of the head). Seizures arise predominantly or exclusively from wakefulness.
- **EEG:** Occipital spikes or spikes-and-wave abnormalities (awake or sleep).

**Alerts**

- **Seizures:** Prolonged seizure lasting >15 minutes. GTCS during wakefulness.
- **EEG:** Sustained focal slowing not limited to the postictal phase.
- **Age at onset:** <6 years or >14 years at onset.
- **Development at onset:** Intellectual disability.
- **Neurological exam:** Any significant neurological examination abnormality.

**Exclusionary**

- **Seizures:** Drop (tonic or atonic) seizures. Atypical absences. Progressive myoclonus.
- **Age at onset:** <1 year or >19 years at onset.
- **Development at onset:** Neurocognitive regression.
- **Neurological exam:** Persistent visual field deficit.
- **Imaging:** Causal lesion on brain MRI. Cerebral occipital lobe calcifications.
- **Course of illness:** Neurocognitive regression. Development of myoclonic seizures, ataxia, spasticity.
Photosensitive Occipital Lobe Epilepsy POLE

- Focal sensory visual seizures
- May evolve to BTCS
- Triggered by photic stimuli
- Conscious head version ‘chasing the sun’ before loss of awareness
- Head and eye deviation
POLE Interictal: diffuse spike-wave elicited by eye closure
Discharge stops on eye opening
Photosensitive Occipital Lobe Epilepsy (POLE)

**Mandatory**
- **Seizures**: Focal sensory visual seizures (see text), which may evolve to bilateral tonic-clonic seizures. Seizures are triggered by photic stimuli, such as flickering sunlight.
- **EEG**: Occipital epileptiform abnormalities facilitated by eye closure and IPS.

**Alerts**
- **Seizures**: Prolonged seizures lasting >15 minutes.
- **EEG**: Sustained focal slowing not limited to the postictal phase. Photoparoxysmal response at slow photic frequency (1-2 Hz) (suggest CLN2 disease).
- **Age at onset**: <4 years >17 years at onset.
- **Development at onset**: Moderate to profound intellectual disability.
- **Neurological exam**: Any significant neurological examination abnormality.

**Exclusionary**
- **Seizures**: Eyelid myoclonia. Progressive myoclonus.
- **Age at onset**: <1 year or >50 years at onset.
- **Development at onset**: Neurocognitive regression.
- **Neurological exam**: Permanent visual field deficit.
- **Imaging**: Causal lesion on brain MRI.
Self-Limited Focal Epilepsies (SeLFE) of Childhood

Self-Limited Epilepsy with Autonomic Seizures (SeLEAS)
- Age-dependent
- Normal child - normal intellect, examination
- Classical seizure semiology
- Characteristic EEG features
- Remission in adolescence

Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)
- Range 1-14 years (peak 3-6 years)
  Multifocal high voltage spikes
- Range 4-10 years (peak 7 years)
  Centrottemporal spikes
  Occipital spikes, fixation-off sensitivity
  Range 15 months-19 years (peak 8-9 years)

Childhood Occipital Visual Epilepsy (COVE)
- Range 4-7 years (mean 11 years)
  Occipital spikes

Photosensitive Occipital Lobe Epilepsy (POLE)
- Idiopathic photosensitive occipital lobe epilepsy
Genetic Generalized Epilepsies of Childhood are a group of condition characterized by genetic etiology with complex inheritance, namely with polygenic basis.

- A positive family history of epilepsy is frequent.
- Cognition, neurological examination and response to drugs are variable.
- Seizure’s semiology, and EEG features are specific for each of the syndromes included in this group.

*discussed in the paper on IGE syndromes
Generalized Epilepsies

- Petit mal
- Pyknolepsy

Childhood Absence Epilepsy

- Jeavons Syndrome

Epilepsy with Eyelid Myoclonia

- Bureau and Tassinari syndrome

Epilepsy with Myoclonic Absence
Generalized Epilepsy Syndromes of Childhood

Childhood Absence Epilepsy

Epilepsy with Eyelid Myoclonia (E-EM)

Epilepsy with Myoclonic Absence (EMA)

- Classical seizure semiology
- Characteristic EEG features
- Genetic
- ± family history of epilepsy
- Normal/intellectual disability
- Variable drug response

Developmental /and Epileptic Encephalopathies

Myoclonic-Atonic Epilepsy (MAE)
Mandatory

- **Seizures**: Eyelid myoclonia
- **EEG**: Eye closure and intermittent photic stimulation elicits fast (3-6 Hz) generalized polyspikes or polyspike-and-wave

**Alerts**

- **Seizures**: Inability to induce eyelid myoclonia in the office by slow eye closure during exposure to bright light in an untreated patient. Myoclonic jerks affecting limbs – strongly consider JME
- **Neurological exam**: Focal neurological findings
- **Imaging**: Potentially relevant abnormal neuroimaging, excluding incidental findings

**Exclusionary**

- **Seizures**: Any of the following seizure types:
  - Myoclonic-absence seizures
  - Focal seizures
- **EEG**: Focal slowing. Consistently unilateral focal spikes. Generalized slow spike-and-wave at frequency <2.5 Hz (unless it is at the end of a higher frequency burst). Diffuse background slowing that is not limited to the postictal period. Lack of EEG correlate with typical clinical event
- **Age at onset**: <2 years or >14 years at onset
- **Imaging**: Abnormal neuroimaging with causative lesion
- **Course of illness**: Progressive cognitive decline over the course of the epilepsy

**Epilepsy with Eyelid Myoclonia (EEM)**
Epilepsy with Eyelid Myoclonia: Ictal EEG in 14-year-old patient with. Background activity is normal. Each time the patient closes the eyes (eye closure artifact is seen) there is a generalized polyspike-and-wave discharge lasting between 6 and 8 seconds clinically associated with eyelid myoclonia. During the second event, soon after eye closure, there is a fast activity discharge that builds up.
Epilepsy with Myoclonic Absence (EMA)

Mandatory

- **Seizures**: Myoclonic absence seizures as predominant type
- **EEG**: Regular 3 Hz generalized spike-and-wave time-locked with the myoclonic jerks

Alerts

- **Neurological exam**: Moderate or greater intellectual disability. Focal neurological findings

Exclusionary

- **Seizures**: Focal seizures. Atonic, Myoclonic-Atonic or Tonic seizures
- **EEG**: Focal slowing. Consistently unilateral focal spikes. Generalized slow spike-and-wave at frequency <2 Hz (unless it is at the end of a higher frequency burst). Diffuse background slowing that is not limited to the postictal period.
- **Age at onset**: <1 year or >12 years at onset
- **Imaging**: Abnormal neuroimaging with causative lesion
- **Course of illness**: Progressive cognitive decline over the course of epilepsy
Epilepsy with Myoclonic Absences: Ictal polygraphic EEG recording in an 8-year-old child with showing a paroxysmal generalized 3 Hz spike-and-wave discharge. EMG channels (right and left deltoids) show bilateral myoclonic jerks synchronous with epileptiform abnormalities, and between jerks there is a sustained increase in muscle tone.
Developmental and/or Epileptic Encephalopathies

- Epileptic Encephalopathy with Continuous Spike-and-Wave in Sleep
- Atypical (Benign) Partial Epilepsy (pseudo-Lennox syndrome)
- Hemiconvulsion-Hemiplegia-Epilepsy Syndrome
- Acute encephalitis with refractory, repetitive partial seizures (AERRPS)
- Febrile Infection-Related Epilepsy Syndrome
- Devastating epileptic encephalopathy in school-aged children (DESC)
- Lennox-Gastaut syndrome
- Doose syndrome
- Epilepsy with Myoclonic-Atonic Seizures

Developmental and/or Epileptic Encephalopathy with Spike-and-Wave Activation in Sleep
Spectrum of conditions:
- cognitive, language, behavioral and motor regression associated with marked spike-and-wave activation in sleep.
- Regression is seen within weeks from the EEG pattern.
- Landau-Kleffner syndrome is a specific sub-type of EE-SWAS, where regression affects mainly language with an acquired auditory agnosia.
Developmental Epileptic Encephalopathy with spike-and-wave activation in sleep (DEE-SWAS) and Epileptic Encephalopathy with spike-and-wave activation in sleep (EE-SWAS)

**Mandatory**
- **EEG:** Slow (1.5-2Hz) spike-and-wave abnormalities in N-REM sleep. Abnormalities are markedly activated in sleep.
- **Development at onset:** Cognitive, behavioral or motor regression or plateauing temporally related to SWAS on EEG.
- **Long term outcome:** Remission of SWAS pattern on EEG by mid adolescence, although EEG often remains abnormal.

**Alerts**
- **Seizures:** Tonic seizures during sleep.
- **EEG:** Generalized paroxysmal fast activity in sleep (consider Lennox-Gastaut syndrome). Generalized slow spike-and-wave <2.5 Hz in both awake and asleep states (consider Lennox-Gastaut syndrome).
- **Age at onset:** >1 and <2 years at onset.

**Exclusionary**
- **Seizures:** Epileptic spasms.
- **Age at onset:** <1 year or >12 years at onset.
Epilepsy with Myoclonic Atonic Seizures (EMAtS)

- Onset between 2 and 6 years
- Myoclonic–atonic seizures
  - brief myoclonic jerk
  - affecting the proximal muscles, often associated with a slight vocalization, followed by a very brief atonic component
- Myoclonic, absences, GTC, tonic, non-convulsive SE
Epilepsy with Myoclonic Atonic Seizures (EMAtS)

Mandatory

- **Seizures**: Myoclonic- atonic seizures
- **EEG**: Generalized 2-6 Hz spike-wave or polyspike-and-wave abnormalities

Alerts

- **Seizures**: Tonic seizures within 12 months of epilepsy onset
- **EEG**: Generalized paroxysmal fast activity in sleep. Generalized slow spike-and-wave <2 Hz. Photoparoxysmal response at low frequencies (suggests CLN2 disease)
- **Development at onset**: Moderate to severe developmental delay preceding seizure onset
- **Neurological exam**: Focal neurological findings

Exclusionary

- **Seizures**: Epileptic spasms or ISS prior to diagnosis. Focal seizures
- **EEG**: Persistent focal abnormalities. Hypsarrhythmia
- **Age at onset**: <6 months or >8 years at onset
- **Imaging**: Causal lesion on MRI
Epilepsy with Myoclonic Atonic Seizures: Interictal and ictal polygraphic EEG recordings in a 3-year-old child.

A. Interictal EEG shows bilateral posterior slow waves (4-6 Hz). There are generalized abnormalities characterized by high amplitude spikes and spike-and-wave abnormalities intermingled with high amplitude delta waves without any clinical changes.
Epilepsy with Myoclonic Atonic Seizures: Interictal and ictal polygraphic EEG recordings in a 3-year-old child. B. and C. Examples of myoclonic atonic seizures associated with a generalized spike-and-wave discharge of brief duration. EMG channels show loss of tone in the deltoids (B) and in nuchal and sternocleidomastoid muscles (C). Clinically, the child experiences abrupt falls with both events.
Lennox-Gastaut syndrome (LGS)

- 1-2% epilepsies
- Onset 3-7 y (< 18 y)
- 20% evolve from Infantile Spasms
- Multiple seizure types – Tonic seizures
- Cognitive ± behavioral problems
- Developmental slowing or regression

Gastaut et al, 1966, ’75; Camfield et al, 1996
Lennox-Gastaut syndrome (LGS)

- Tonic seizure
- ± atypical absence, myoclonic, FIAS, GTC, spasms, NCSE
- GSSW, GPFA
- Onset < 18 y
- Mild – profound ID

- Onset > 10 y
- PPR at slow frequency 1-2 Hz (? CLN2 disease)

- Persistent focal discharge without generalized spike-wave
Lennox-Gastaut Syndrome: Interictal and ictal polygraphic EEG recordings.
A. Generalized slow spike-and-wave abnormalities (between 2 and 2.5 Hz) are seen, lasting 8 seconds, not associated with any clinical signs.
Lennox-Gastaut Syndrome: Interictal and ictal polygraphic EEG recordings

B. Generalized paroxysmal 10 Hz fast activity. The discharge is seen during sleep and is not associated with any clinical signs.
Lennox-Gastaut Syndrome: Interictal and ictal polygraphic EEG recordings

C. Ictal EEG showing a generalized electro-decremental response lasting 4 seconds associated with bilateral tonic contraction of the upper limbs, consistent with a generalized tonic seizure.
Further definitions

**Syndrome-in-Evolution**
Syndromes that lack all Mandatory diagnostic features at onset but take time to evolve, e.g., Rasmussen Syndrome early in the course, prior to appreciation of imaging findings.

**Syndrome Without Laboratory Confirmation**
Minimum criteria for diagnosis in resource-limited regions, which have little or no access to EEG, advanced neuroimaging or genetic studies.

**Etiology-specific epilepsy syndrome**
Syndromes in which there is a specific etiology for the epilepsy associated with a clearly defined, relatively uniform and distinct clinical phenotype as well as consistent EEG, neuroimaging and/or genetic results.
Conclusions

- The major goal of the Task Force was to reach consensus regarding which entities met epilepsy syndrome criteria and then define each one, using a rigorous consensus-gathering process and creating a resource available worldwide.

- Identified Mandatory, Exclusionary and Alerts criteria for each syndrome.

- Used descriptive names of syndromes as opposed to eponyms; retained some terms as ‘Dravet syndrome’, ‘Lennox-Gastaut syndrome’ and ‘Rasmussen syndrome’.

- Introduced the term Syndrome-in-Evolution, Syndrome Without Laboratory Confirmation, “Etiology-Specific Epilepsy Syndromes”.

- Not included specific treatment recommendations.
Acknowledgments

- **Neurology**
  - Marina Trivisano
  - Luca de Palma
  - Nicola Pietrafusa
  - Alessandro Ferretti
  - Paola De Liso
  - Lucia Fusco
  - Federico Vigevano

- **Clinical Trial Center**
  - Susanna Livadiotti
  - Giorgia Copponi
  - Alessandra Simonetti
  - Giuseppe Pontrelli

- **Neurosurgery**
  - Carlo Marras
  - Alessandro De Benedictis
  - Andrea Carai

- **Psychology**
  - Simona Cappelletti
  - Ilaria Tondo
  - Simonetta Gentile

- **Neuroradiology**
  - Daniela Longo
  - Camilla Rossi Espagnet
  - Lorenzo Figà-Talamanca

- **SPECT-PET**
  - Carmen Garganese

- **Physics**
  - Antonio Napolitano

- **Neuropathology**
  - Francesca Diomedi

- **Genetics**
  - Enrico Bertini
  - Antonio Novelli
  - Marco Tartaglia
  - Alessandra Terraciano

- **EEG Technicians**
  - Giusy Carfi' Pavia
  - Claudia Volponi

- **Nurses**
  - Tommaso Renzetti
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  - Costanza Calabrese

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