# Review of ILAE Epilepsy Syndromes 2022

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# Epilepsy Syndromes 2022

Agenda

- Onset in neonates and infants (up to age 2 years)
- Onset in childhood
- Variable ages onset (pediatric and adult patients)
- Idiopathic generalized epilepsies

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Epilepsia

SPECIAL REPORT

# 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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Epilepsia

SPECIAL REPORT

# ILAE definition of the Idiopathic Generalized Epilepsy Syndromes: Position statement by the ILAE Task Force on Nosology and Definitions

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Epilepsia

SPECIAL REPORT

# 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[1] | Elaine C. Wirrell[2] | Ingrid E. Scheffer[3] | Rima Nabbout[4] | Kate Riney[5,6] | Pauline Samia[7] | Marilisa Guerreiro[8] | Sam Gwer[9] | Sameer M. Zuberi[10] | Jo M. Wilmshurst[11] | Elissa Yozawitz[12] | Ronit Pressler[13] | Edouard Hirsch[14] | Sam Wiebe[15] | Helen J. Cross[16] | Emilio Perucca[17,18] | Solomon L. Moshé[19] | Paolo Tinuper[20,21] | Stéphane Auvin[22]

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Epilepsia

SPECIAL REPORT

# International League Against Epilepsy classification and definition of epilepsy syndromes with onset at a variable age: position statement by the ILAE Task Force on Nosology and Definitions

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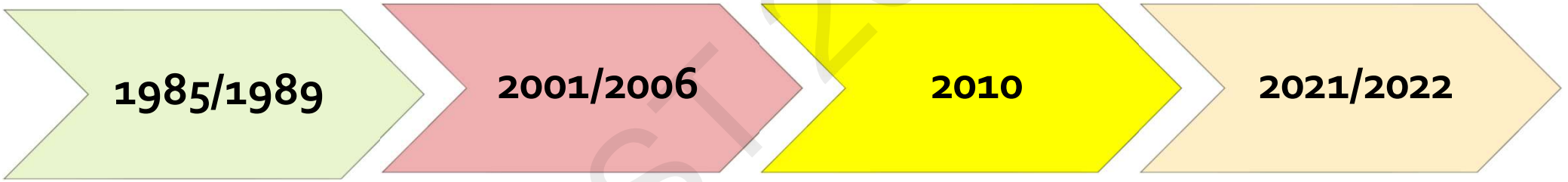
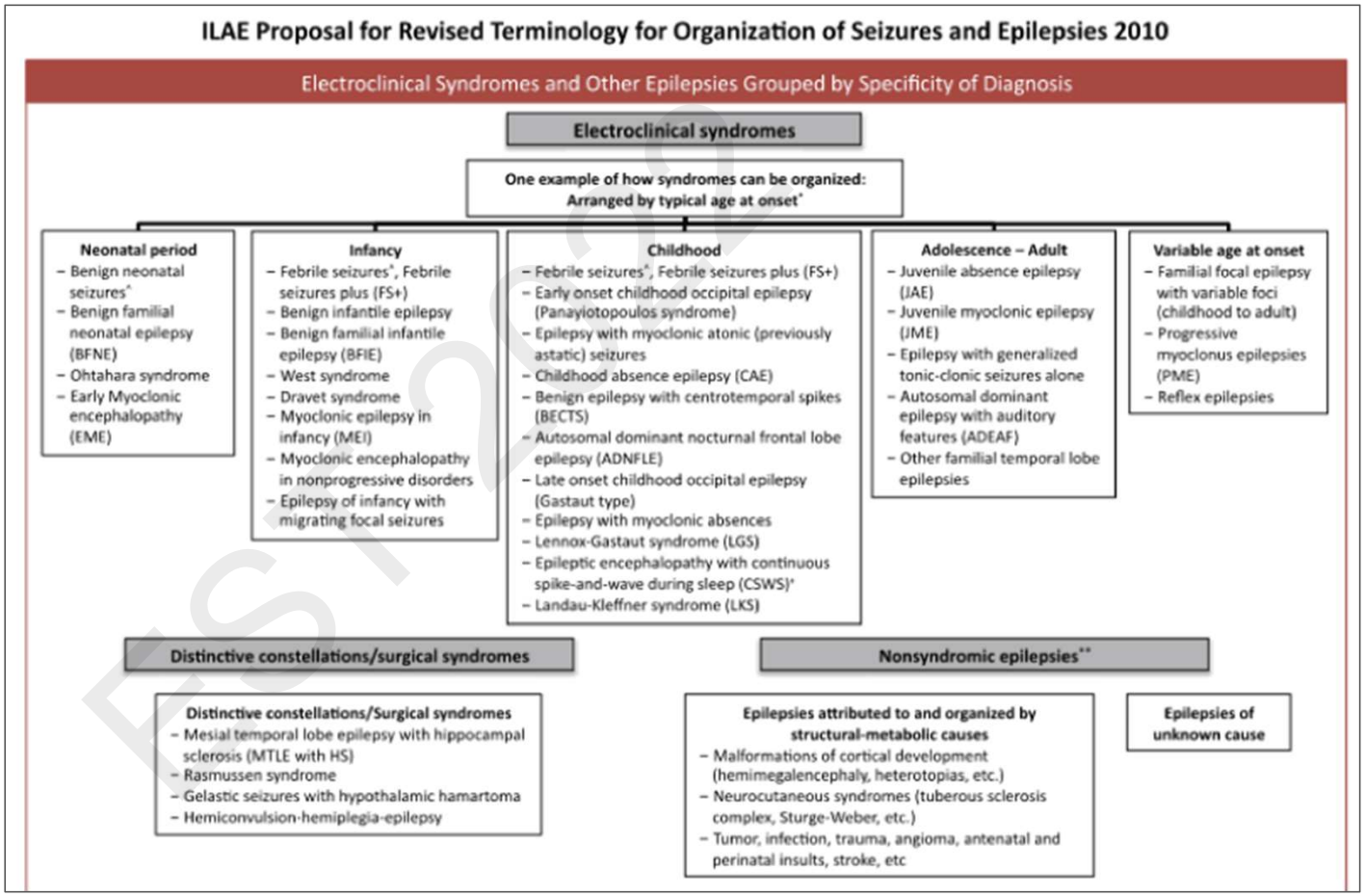
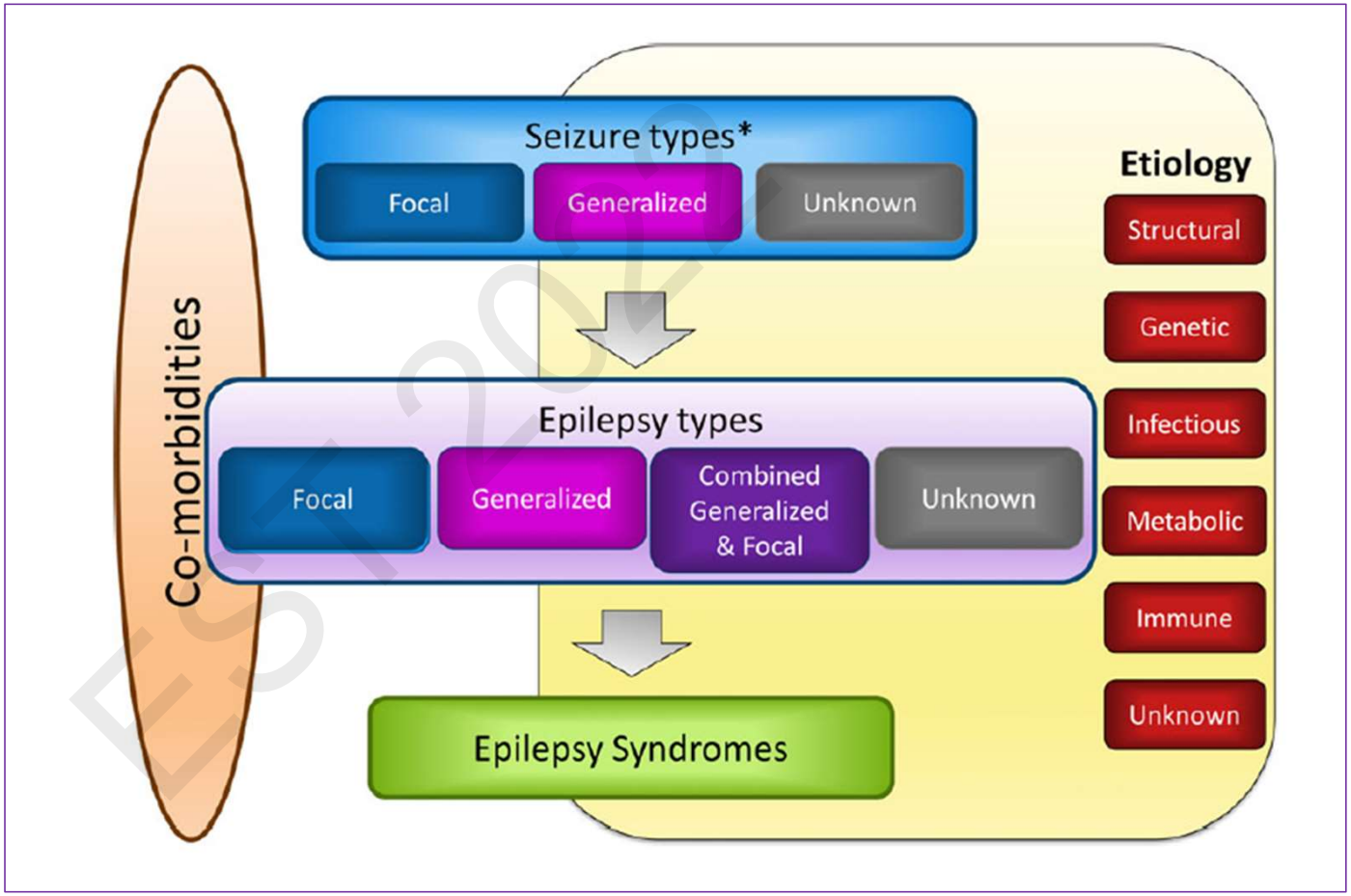
# Epilepsy Syndromes 's Journey



# Epilepsy Syndromes **2010**

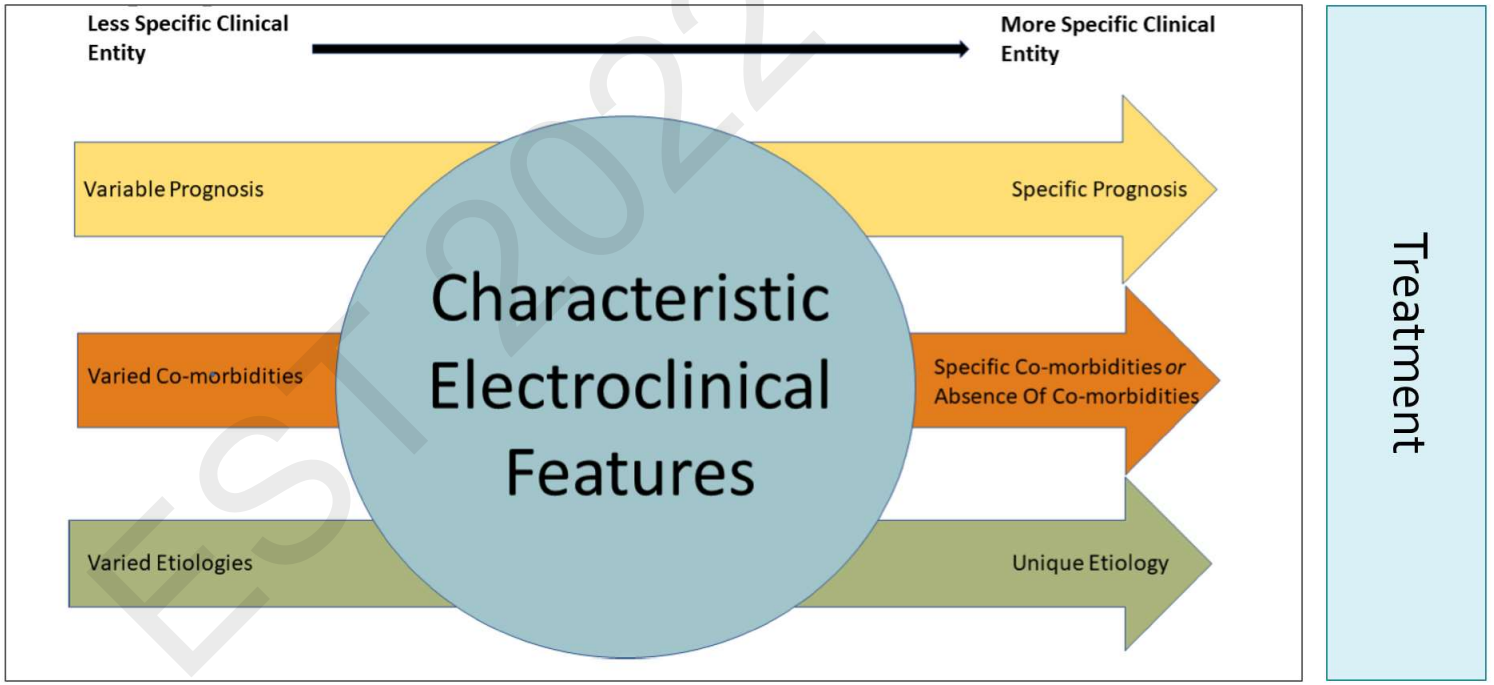


# Epilepsy Classification **2017**



# The Nosology and Definitions Task Force, ILAE 2017-2021

# Epilepsy Syndromes 2022






*Wirrel E, et al. Epilepsia 2022;00:1–3*

| Age onset | Type of epilepsy | | | |
|---|---|---|---|---|
| | Focal | Focal and/or generalized | Generalized | Syndromes with DEE or with progressive neurological deterioration |
| Neonates & infants | | | | |
| Childhood | | | | |
| Variable age | | | | |
| Idiopathic generalized epilepsies | | | | |

| Position paper | Type of epilepsy | | | |
|---|---|---|---|---|
| | Focal | Focal and/or generalized | Generalized | Syndromes with DEE or with progressive neurological deterioration |
| Epilepsy syndromes with onset in neonates and infants[22] | • Self-limited (familial) neonatal epilepsy<br>• Self-limited (familial) infantile epilepsy<br>• Self-limited familial neonatal-infantile epilepsy | • Genetic epilepsy with febrile seizures plus | • Myoclonic epilepsy in infancy | • Early infantile DEE<br>• Epilepsy of infancy with migrating focal seizures<br>• Infantile epileptic spasms syndrome<br>• Dravet syndrome<br>• Etiology-specific DEEs<br>  • *KCNQ2*-DEE<br>  • Pyridoxine-dependent and pyridox(am)ine 5′ phosphate deficiency DEE<br>  • *CDKL5*-DEE<br>  • *PCDH19* clustering epilepsy<br>  • GLUT1DS-DEE<br>  • Sturge–Weber syndrome<br>  • Gelastic seizures with HH |
| Epilepsy Syndromes with onset in childhood[23] | Self-limited focal epilepsies<br>• Self-limited epilepsy with centrotemporal spikes<br>• Self-limited epilepsy with autonomic seizures<br>• Childhood occipital visual epilepsy<br>• Photosensitive occipital lobe epilepsy | | • Epilepsy with myoclonic absences<br>• Epilepsy with eyelid myoclonia | • Epilepsy with myoclonic–atonic seizures<br>• Lennox–Gastaut syndrome<br>• DEE or EE with spike-and-wave activation in sleep<br>• Febrile infection-related epilepsy syndrome<br>• Hemiconvulsion–hemiplegia–epilepsy |
| Epilepsy syndromes with onset at a variable age[24] | • Mesial temporal lobe epilepsy with hippocampal sclerosis<br>• Familial mesial temporal lobe epilepsy<br>• Sleep-related hypermotor (hyperkinetic) epilepsy<br>• Familial focal epilepsy with variable foci<br>• Epilepsy with auditory features | Epilepsy with reading-induced seizures | | Rasmussen syndrome<br>Progressive myoclonus epilepsies |
| Idiopathic generalized epilepsies[21] | | | • Childhood absence epilepsy<br>• Juvenile absence epilepsy<br>• Juvenile myoclonic epilepsy<br>• Epilepsy with generalized tonic–clonic seizures alone | |









*Epilepsia. 2022;00:1–16*[9]

## Mandatory

- Criteria that must be present to diagnose the syndrome

## Alerts

- Absent criteria in vast majority of patients but rarely can be seen
- Rethink the diagnosis
- R/O other conditions

## Exclusionary

- Criteria that must be absent to diagnose the syndrome





*Epilepsia. 2022;00:1–16*

# Syndrome Core Diagnostic Criteria

| | Mandatory | Alert | Exclusionary |
|---|---|---|---|
| Seizure type | | | |
| EEG | | | |
| Age at onset | | | |
| Development at onset | | | |
| Neurological exam | | | |
| Are MRI or Ictal EEG required For Dx | | | |
| Other studies-genetic | | | |
| Syndrome without laboratory confirmation | | | |

# Text explanation

- Epidemiology
- Clinical context
- Course of illness
- Seizures
- EEG (+ example picture)
- Genetics
- DDx

# Abbreviations

| Syndrome group | Syndrome name | Abbreviation |
|---|---|---|
| Neonatal–infant | *CDKL5*-developmental and epileptic encephalopathy | *CDKL5*-DEE |
| | Dravet syndrome | DS |
| | Early infantile developmental and epileptic encephalopathy | EIDEE |
| | Epilepsy of infancy with migrating focal seizures | EIMFS |
| | Genetic epilepsy with febrile seizures plus | GEFS+ |
| | Gelastic seizures with hypothalamic hamartoma | GS-HH |
| | Glucose transporter 1 deficiency syndrome | GLUT1DS |
| | Infantile epileptic spasm syndrome | IESS |
| | *KCNQ2*-developmental and epileptic encephalopathy | *KCNQ2*-DEE |
| | Myoclonic epilepsy in infancy | MEI |
| | Protocadherin 19 clustering epilepsy | *PCDH19* clustering epilepsy |
| | Pyridoxine-dependent (*ALDH7A1*) developmental and epileptic encephalopathy | PD-DEE |
| | Pyridox(am)ine 5′-phosphate deficiency (*PNPO*) developmental and epileptic encephalopathy | P5PD-DEE |
| | Self-limited familial neonatal–infantile epilepsy | SeLFNIE |
| | Self-limited infantile epilepsy | SeLIE |
| | Self-limited neonatal epilepsy | SeLNE |
| | Sturge–Weber syndrome | SWS |





*Epilepsia. 2022;00:1–16*

# Abbreviations

| | | |
|---|---|---|
| Child | Childhood occipital visual epilepsy | COVE |
| | Developmental and epileptic encephalopathy with spike-and-wave activation in sleep | DEE-SWAS |
| | Epileptic encephalopathy with spike-and-wave activation in sleep | EE-SWAS |
| | Epilepsy with eyelid myoclonia | EEM |
| | Epilepsy with myoclonic absences | EMA |
| | Epilepsy with myoclonic–atonic seizures | EMAtS |
| | Febrile infection-related epilepsy syndrome | FIRES |
| | Hemiconvulsion–hemiplegia epilepsy syndrome | HHE |
| | Lennox–Gastaut syndrome | LGS |
| | Photosensitive occipital lobe epilepsy | POLE |
| | Self-limited epilepsy with autonomic seizures | SeLEAS |
| | Self-limited epilepsy with centrotemporal spikes | SeLECTS |
| Idiopathic generalized epilepsies | Childhood absence epilepsy | CAE |
| | Epilepsy with generalized tonic–clonic seizures alone | GTCA |
| | Juvenile absence epilepsy | JAE |
| | Juvenile myoclonic epilepsy | JME |
| Variable age | Epilepsy with auditory features | EAF |
| | Epilepsy with reading-induced seizures | EwRIS |
| | Familial focal epilepsy with variable foci | FFEVF |
| | Familial mesial temporal lobe epilepsy | FMTLE |
| | Mesial temporal lobe epilepsy with hippocampal sclerosis | MTLE-HS |
| | Progressive myoclonus epilepsies | PME |
| | Rasmussen syndrome | RS |
| | Sleep-related hypermotor (hyperkinetic) epilepsy | SHE |

*Epilepsia. 2022;00:1–16*

# Propose: Term

- **Syndrome-in-evolution**
- **Syndrome without laboratory confirmation**

# Epilepsy Syndromes 2022

## Onset in Neonates and Infants

(up to age 2 years)

# Onset in Neonates and Infants

**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)**

- Ealy 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 (P5PD-DEE)
- *CDKL5*-DEE
- *PCDH19* clustering epilepsy
- Glucose Transporter 1 Deficiency Syndrome (GLUT1DS)
- Sturge Weber syndrome (SWS)
- Gelastic seizures with hypothalamic hamartoma (GS-HH)

# Self-limited Epilepsy Syndrome

| | |
|---|---|
| **Self-limited (Familial) neonatal epilepsy (SeLNE), d2-d7** | • Familial = *KCNQ2, KCNQ3* (AD pattern)<br>• Non-familial = de novo pathogenic gene variants of the gene above |
| **Self-limited (Familial) neonatal-infantile epilepsy (SeLFNIE), d2-7 mo** | • *SCN2A, KCNQ2* (AD pattern)<br>• De novo in non-familial |
| **Self-limited (Familial ) infantile epilepsy, (SeLIE) , 3 -20 mo** | • Former= benign familial (and non-familial) infantile seizure<br>• *PRRT2* pathogenic variants (AD pattern)- PKD in childhood/adult<br>• Also *SCN8A, SCN2A* |
| **Genetic epilepsy w febrile seizures plus spectrum inc febrile seizures+** | • GEFS+: < 6 mo - > 6 yrs. *SCN1B, SCN1A*, etc<br>• FS+ : typical febrile beyond age of 6 yrs<br>• Family trait and de novo in GEFS+ gene |
| **Myoclonic epilepsy in infancy (MEI)** | • Onset 6 mo-5 yrs<br>• GTC may be seen in later life |

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# Self-limited (familial) neonatal epilepsy (SeLNE)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | 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 | Clinical history suggestive of in utero seizures | Epileptic spasms<br>Myoclonic seizures<br>Generalized tonic seizures<br>Generalized tonic-clonic seizures |
| EEG | | Interictal: Mild background slowing | Interictal: Persistent focal slowing or moderate or greater background slowing not limited to the postictal period<br>Burst suppression pattern<br>Hypsarrhythmia<br>Ictal: Lack of EEG correlate with clinical symptoms |
| | | | Onset after first month of age |
| | | | Any degree of encephalopathy |
| Imaging | | | Neuroimaging documenting a causal lesion for seizures |
| Other studies – genetics | | Lack of pathogenic variant in gene associated with this syndrome, most commonly *KCNQ2* or *KCNQ3* OR<br>Lack of family history suggesting AD inheritance with incomplete penetrance | Other acute symptomatic cause of seizures including intracranial infection, ischemic or hemorrhagic stroke, hypoxic-ischemic brain injury, significant metabolic disturbances |
| Course of illness | | Mild neurodevelopmental delay long-term<br>Lack of remission of epilepsy after 6 months of age<br>Drug-resistant epilepsy | Moderate to severe neurodevelopmental disability |
| *Are MRI or ictal EEG required for diagnosis?*<br>A nonlesional MRI is required to diagnose this syndrome<br>An ictal EEG is not required for diagnosis | | | |

**Interictal EEG**

: B/G = normal or abnormal (minor)

: d/c = C, CT , FT area

**Ictal EEG**

: B/G attenuation → repetitive spike wave CT

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# Self-limited familial neonatal-infantile epilepsy (SeLFNIE)

**Interictal EEG**
: B/G = normal
: d/c = posterior region or widespread slowing

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal tonic seizures with head and eye deviation, followed by other tonic and clonic features and may evolve to bilateral tonic clonic seizures | Sequential seizures | Epileptic spasms<br>Myoclonic seizures |
| EEG | | Interictal: Mild background slowing | Interictal: Persistent focal slowing or moderate or greater background slowing not limited to the postictal period<br>Burst suppression pattern<br>Hypsarrhythmia<br>Ictal: Lack of EEG correlate with clinical symptoms |
| | | intracranial infection, ischemic or hemorrhagic stroke, hypoxic-ischemic brain injury, significant metabolic disturbances | Encephalopathy |
| Neurological exam | | Significant neurological examination abnormalities, excluding incidental findings | |
| Imaging | | | Neuroimaging documenting a causal lesion for seizures |
| Other studies – genetics, and so on | | Lack of pathogenic variant in genes associated with this syndrome (usually *SCN2A*) | |
| Course of illness | | Mild neurodevelopmental delay long-term<br>Lack of remission of epilepsy by age 2 years<br>Drug-resistant epilepsy | Moderate to severe neurodevelopmental disability |

*Are MRI or ictal EEG required for diagnosis?*
A nonlesional MRI is required to diagnose this syndrome
An ictal EEG is not required for diagnosis

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# Self-limited (familial) infantile epilepsy (SeLIE)

**Interictal EEG**
: B/G = normal
**Ictal EEG**
: focal d/c temporal/posterior head region

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal seizures occur with behavioral arrest, impaired awareness, automatisms, head/eye version, and clonic movements (often alternating from one side to the other and progressing to a hemiclonic or focal to bilateral tonic-clonic seizure) | Prolonged or focal clonic (hemiclonic) seizures (>10 min) | Epileptic spasms<br>Myoclonic seizures<br>Sequential seizures<br>Tonic seizures |
| | | | Interictal:<br>Persistent focal slowing or moderate or greater background slowing not limited to the postictal period<br>Hypsarrhythmia |
| | | | Age at onset <1 month or >36 months |
| onset | | | Moderate to profound delay<br>Neurocognitive regression |
| Neurological exam | | Significant neurological examination abnormalities, excluding incidental findings | |
| Imaging | | | Causal lesion on brain MRI |
| Other studies – genetic, etc | | Lack of pathogenic variants found in *PRRT2*, *SCN2A*, *KCNQ2*, or *KCNQ3* OR<br>Lack of family history suggesting autosomal dominant inheritance with incomplete penetrance | |
| Course of illness | | Lack of remission by late childhood | Neurocognitive regression with myoclonic seizures, ataxia, spasticity |

*Are MRI or ctal EEG required for diagnosis?*
A neuroimaging MRI is required to diagnose this syndrome
An ictal EEG is not required for diagnosis

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# Genetic epilepsy with febrile seizures plus (GEFS+)

- AD with variable penetrance
- Phenotypes: febrile seizure (gen/focal), myoclonic-atonic seizures, DS, IGE, GGE and focal epilepsies
- Hallmark : febrile seizure and febrile seizure plus (FS+)
- FS+ = febrile seizures persisting after 6 years and/or evolving to afebrile seizure

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# Myoclonic epilepsy in infancy (MEI)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Myoclonic seizures (see text) | Afebrile generalized tonic-clonic seizure or generalized clonic at time of epilepsy onset | Any of the following seizure types:<br>• Absence seizures<br>• Atonic seizures<br>• Epileptic spasms<br>• Focal impaired awareness seizures<br>• Focal clonic (hemiclonic) seizures<br>• Myoclonic-absence seizures<br>• Tonic seizures |
| EEG | Normal background | Interictal: Lack of generalized spike-wave discharge on sleep recording<br>PPR at low frequency photic stimulation (suggest CLN2 disease) | Ictal: Recorded myoclonic event without EEG correlate<br>Interictal:<br>Hypsarrhythmia<br>Generalized slow spike-wave (<2.5 Hz) |
| Age at onset | | | Age at onset of myoclonic seizures ≤4 months or >3 years |
| Development at onset | | Speech delay at time of diagnosis<br>Moderate to profound ID | |
| Neurological exam | | Significant neurological examination abnormalities, excluding incidental findings | Dysmorphism or other congenital anomalies (suggests chromosomal disorder) |
| Imaging | | | Significant neuroimaging abnormalities |
| Other studies – genetics, and so on | | | Low CSF glucose or pathogenic *SLC2A1* variants (Glut1DS) |
| Course of illness | | | *Neurocognitive regression* |
| *Are MRI or ictal EEG required for diagnosis?*<br>A nonlesional MRI is required for diagnosis<br>An ictal EEG is not required for diagnosis but should be strongly considered if the interictal sleep recording does not show generalized spike-wave to confirm that myoclonus is epileptic | | | |
| *Syndrome without laboratory confirmation*: In resource-limited regions, at a minimum, a sleep EEG showing generalized spike-wave is required to make this diagnosis | | | |

# Epileptic Encephalopathies (EE)

- Epileptic activity itself → severe cognitive and behavioral impairments above ad beyond that expected from underlying etiology
- Frequent epileptiform activity associated w dev slowing and often regression
- May occur on a background of normal or abnormal development

# Developmental and Epileptic Encephalopathies

- EE:
- **DE**: Refers to developmental impairment without frequent epileptiform activity, such as in a child or adult with intellectual disability.
- **DE**: There is onset of a condition manifesting with cognitive, neurological, or psychiatric impairment, stagnation, or regression, due directly to the underlying etiology
- DEE: Both developmental and epileptic contributes to the patient's condition

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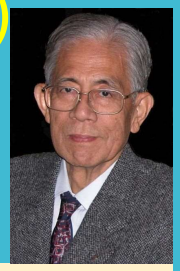
# Early infantile developmental and epileptic encephalopathy (EIDEE)



Includes Ohtahara syndrome and EME

: Onset in the first 3 months of life

: Abnormal PE, development impairment

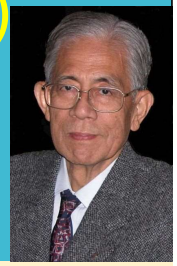
: Formerly Ohtahara syndrome (EIEE) and Early Myoclonic Encephalopathy (EME)

: ≥ 1 seizure types: tonic sz, myoclonic sz, epileptic spasms and sequential sz

: May evolve into Infantile Spasms Syndrome

: Co-morbid movement disorders: myoclonus, chorea, dystonia, tremor

# Early infantile developmental and epileptic encephalopathy (EIDEE)



Includes Ohtahara syndrome and EME

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Tonic and/or myoclonic seizures | | |
| EEG | | | |
| Age at onset | | | |
| Development at onset | | historically | |
| Neurological exam at onset | | Normal neurological examination, although it is acknowledged that this can be challenging to assess historically or in an infant who has had very frequent seizures and/or received ASMs that may alter their exam | |
| Early Comorbidities | Developmental impairment is present prior to or shortly after seizure onset | | |
| Course of illness | Abnormal neurodevelopment including intellectual disability | | |

1. Tonic seizures.
2. Myoclonic seizures.
3. Epileptic spasms.
4. Sequential seizures, may include tonic, clonic, and/or autonomic components, as well as automatisms without a single predominant seizure type

*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, multi-focal discharges with diffuse slowing

*Syndrome without laboratory confirmation*: In resource-limited regions, this syndrome cannot be diagnosed without an interictal EEG

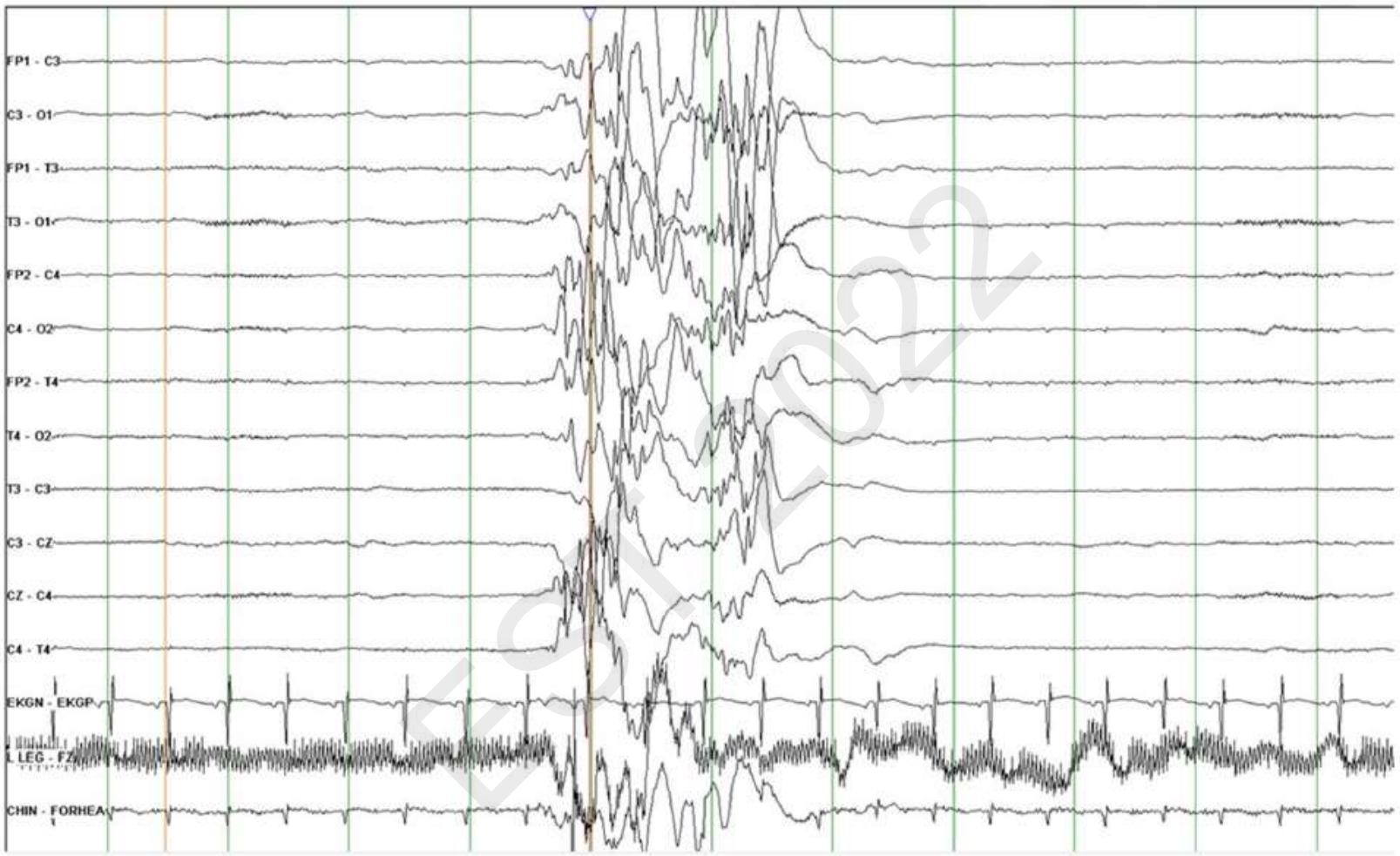
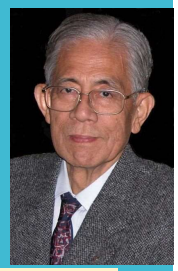



**FIGURE 5** A 4-week-old boy with Early Infantile DEE. He presented on day 2 of life with sequential seizures with a prominent tonic component and severe encephalopathy. The EEG (20 microvolt/mm, 30 mm/s) shows a burst-suppression pattern. Genetic testing showed a *KCNQ2* pathogenic variant. The patient showed a marked reduction in seizures with carbamazepine but remained profoundly delayed

# Early infantile developmental and epileptic encephalopathy (EIDEE)



Includes Ohtahara syndrome and EME

## MRI

- To exclude surgical remediable lesions
- For certain genetic etiologies: normal→ volume loss → atrophy

## Metabolic

- Metabolic Ix: UOA, PAA, lactate, $NH_3$, acylcarnitine profile, CU
- CSF(glucose/lactate/pyruvate, aa), neurotransmitters

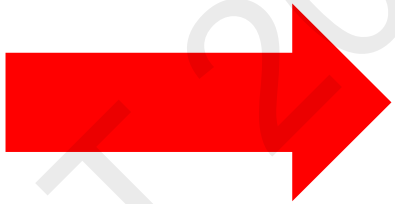
## Genetic Test

- Chromosome microarray, karyotype
- Gene panel: WES, WGS

e.g.

- KCNQ2-DEE
- SCN2A-DEE, SCN8A-DEE
- STXBP1-DEE
- CDKL5-DEE
- KCNT1-DEE
- UBA5-DEE

Early infantile developmental and epileptic encephalopathy (EIDEE)



Infantile epileptic spasms syndrome IESS

Includes Ohtahara syndrome and EME

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# Infantile epileptic spasms syndrome (IESS)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Flexor, extensor or mixed epileptic spasms which often occur in clusters | | |
| EEG | Interictal:<br>Hypsarrhythmia, multifocal or focal epileptiform discharges<br>(that might be seen quickly after the spasms onset) | Interictal:<br>Normal EEG<br>Suppression-burst pattern | Ictal:<br>Normal EEG during recorded clinical events of suspected spasms |
| Age at onset | 1–24 months (while epileptic spasms may begin later, this would not be ISS) | Age at onset 1–2 months | |
| Comorbidities | Developmental slowing after spasms onset but may be absent early in the course (difficult to determine in a child with existing significant developmental disorders) | | |

*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

8

# Epilepsy of infancy with migrating focal seizures (EIMFS)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal/multifocal tonic or clonic seizures, with or without subtle behavioral arrest and prominent autonomic features<br>Seizures migrate from one hemisphere or lobe to another clinically<br>Seizure frequency rapidly increases in the first weeks and months, often progressing to status epilepticus | | Myoclonic seizures |
| EEG | Ictal recording shows a migrating pattern (this might be missed if a prolonged video EEG is not performed)<br>Interictal: Multifocal discharges | Interictal:<br>Suppression burst pattern prior to medication<br>Single persistent epileptic focus on EEG<br>Hypsarrhythmia | |
| Age at onset | <12 months | Onset 6–12 months | |
| Development at onset | | Severe delay prior to seizure onset | |
| Neurological exam | | Significant abnormalities on neurological examination prior to seizure onset | |
| Comorbidities | Developmental plateauing or regression with frequent seizures | | |
| Imaging | | | Abnormal neuroimaging with structural causal lesion |
| Course of illness | Neurodevelopmental delay | Seizure freedom<br>Lack of brain atrophy on MRI | |
| *Is MRI or ictal EEG required for diagnosis?*<br>An MRI is required for diagnosis to exclude a causal structural etiology<br>An ictal EEG may not be required if clinical migration is observed. However, an ictal EEG is strongly recommended to document a migrating pattern | | | |
| *Syndrome without laboratory confirmation*: In resource-limited regions, EIMFS can be diagnosed on clinical observation of seizure migration without EEG or MRI, provided all other clinical mandatory and exclusionary criteria are met | | | |

9

# Dravet Syndrome (DS)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Recurrent focal clonic (hemiclonic) febrile and afebrile seizures (which often alternate sides from seizure to seizure), focal to bilateral tonic-clonic, and/or generalized clonic seizures | No history of prolonged seizures (>10 min)<br>Lack of fever sensitivity as a seizure trigger | Epileptic spasms<br>Early infantile *SCN1A* DEE |
| EEG | | | |
| Age at onset | | | |
| Development at c | | | |
| Neurological exa | | | |
| Imaging | | | MRI showing a causal focal lesion |
| Other testing: ie, and so on | | | |
| Course of illness | | including carbamazepine, oxcarbazepine, and phenytoin | |

- Myoclonic seizures
- Focal impaired awareness seizures
- Focal to bilateral tonic-clonic seizures
- Atypical absence seizures
- Atonic seizures
- Nonconvulsive status epilepticus (originally termed obtundation status)
- Tonic and tonic-clonic seizures mainly in sleep and in clusters

*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 hemiclonic 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 hemiclonic) 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

# Epilepsy Syndromes 2022

## Onset in Childhood



*Specchio N et al. Epilepsia. 2022;00:1–45*

# Onset in Childhood

## Onset in Childhood

Onset 2-12 years

- 3 main groups

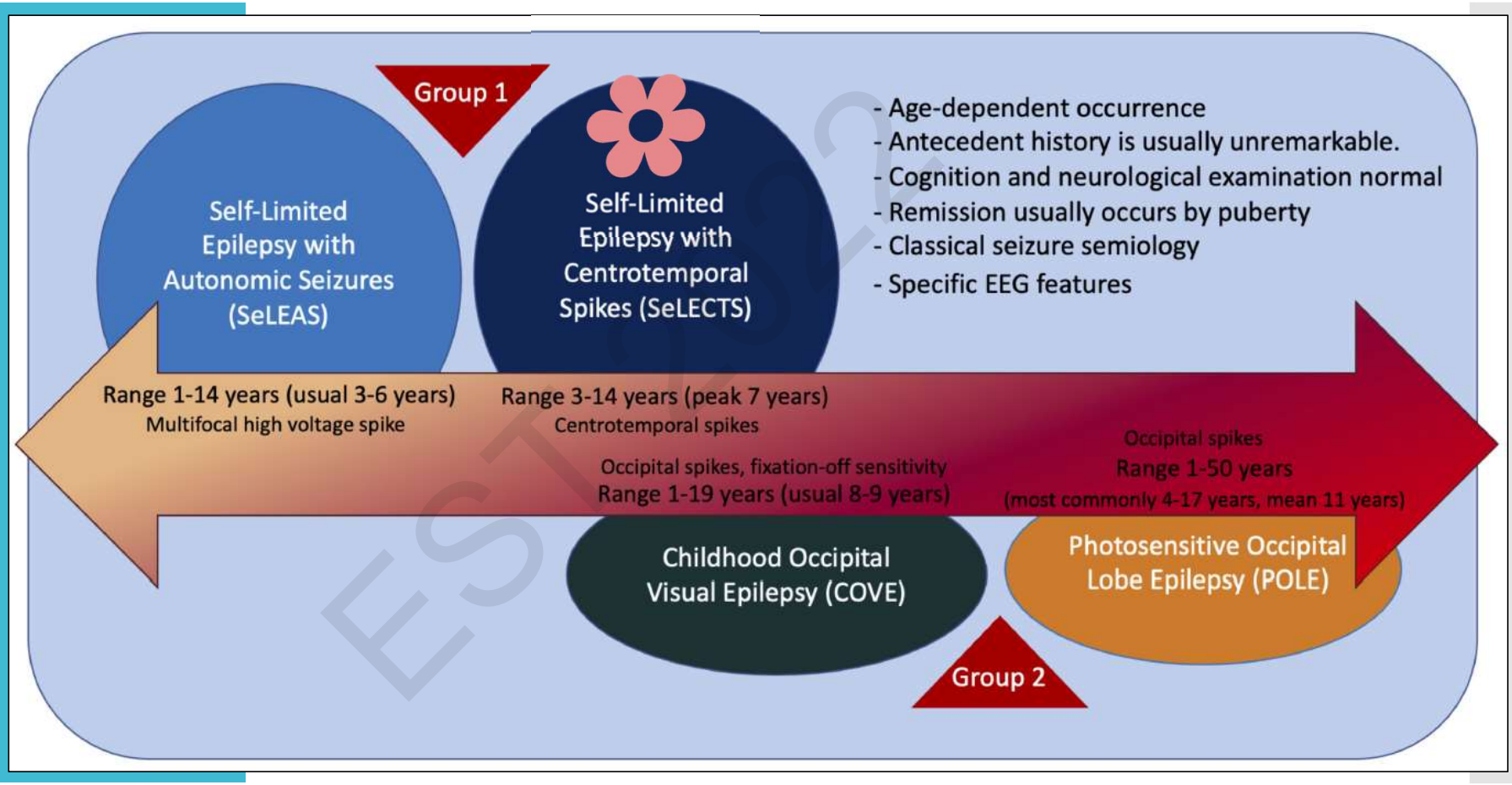
| Self-limited focal epilepsies (SeLFEs) | Generalized epilepsy syndromes | Developmental and/or epileptic encephalopathies (DEE) |
|---|---|---|
| 1. Self-limited epilepsy with centrotemporal spikes (SeLECTs)<br>2. Self-limited epilepsy with autonomic seizures (SeLEAs)<br>3. Childhood occipital visual epilepsy (COVE)<br>4. Photosensitive occipital lobe epilepsy (POLE) | 1. Childhood absence epilepsy (CAE)<br>2. Epilepsy with myoclonic absence (EMA)<br>3. Epilepsy with eyelid myoclonia (EEM) | 1. Epilepsy with myoclonic-atonic seizures (EMAtS)<br>2. LGS<br>3. DEE or EE with spike-and-wave activation in sleep<br>4. Hemiconvulsion-hemiplegia-epilepsy syndrome (HHE)<br>5. FIRES |

# Self-Limited Focal Epilepsies (SeLFEs) syndromes

1. Age-dependent occurrence, specific for each syndrome
2. No significant structural lesion of the brain.
3. Birth, neonatal and antecedent history is usually unremarkable.
4. Cognition and neurological examination are typically normal
5. Remission usually occurs by adolescence
6. Pharmaco-responsiveness if treated
7. Genetic predisposition for the EEG trait
8. Classical seizure semiology for each syndrome. Seizures are focal motor or sensory with or without impaired awareness and may evolve to bilateral T-C seizures.
9. Specific EEG features: epileptiform d/c with distinctive morphology and location (depending on the epilepsy syndrome), often activated with sleep. The EEG has a normal background.

# SeLFEs

25% in Ped



1

# Self-limited epilepsy with centrotemporal spikes (SeLECTs)

80-90% in sleep

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal seizures with dysarthria, sialorrhea, dysphasia, and unilateral clonic or tonic–clonic movement of mouth in wakefulness or sleep and/or nocturnal focal to bilateral tonic–clonic seizures in sleep only<br>If seizures occur during sleep, they are seen within 1 h of falling asleep or 1–2 h prior to awakening | Focal motor or generalized convulsive status epilepticus >30 min<br>Usual seizure frequency more than daily<br>Daytime seizures only | Generalized tonic–clonic seizures during wakefulness<br>Atypical absences<br>Seizures with gustatory hallucinations, fear, and autonomic features |
| EEG | High-amplitude, centrotemporal biphasic epileptiform abnormalities | Sustained focal slowing not limited to the postictal phase<br>Persistently unilateral centrotemporal abnormalities on serial EEGs<br>Lack of sleep activation of centrotemporal abnormalities | |
| Age at onset | | >12 years | <3 years or >14 years |
| Development at onset | | Moderate to profound intellectual disability | Neurocognitive regression with a continuous spike-and-wave pattern in sleep (suggests EE-SWAS) |
| | | | Causal lesion on brain MRI |
| Course of illness | Remission by mid to late adolescence<br>No developmental regression | | Neurocognitive regression with a continuous spike-and-wave pattern in sleep suggests evolution to EE-SWAS |
| An MRI is not required for diagnosis but should be strongly considered in cases with alerts.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, SeLECTs can be diagnosed without EEG and MRI in children without alerts who meet all other mandatory and exclusionary criteria. | | | |

Prior to epilepsy onset, ADHD and specific cognitive function deficits, mainly related to language and executive function, maybe seen.

2

# Self-limited epilepsy with autonomic seizures (SeLEAS)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal autonomic seizures, with or without impaired awareness<br>Autonomic symptoms often involve prominent retching and vomiting, but may also include malaise, pallor, flushing, abdominal pain, and pupillary or cardiorespiratory changes | Seizure frequency greater than monthly | |
| EEG | High-amplitude, focal or multifocal epileptiform abnormalities that increase in drowsiness and sleep | Sustained focal slowing not limited to the postictal phase<br>Unilateral focal abnormalities in a consistent focal area across serial EEGs | |
| Age at onset | | <3 years or >8 years | <1 year or >14 years |
| Development at onset | | Moderate to profound intellectual disability | Neurocognitive regression with a continuous spike-and-wave pattern in sleep (suggests EE-SWAS) |
| Neurological exam | | Hemiparesis or focal neurological findings, other than Todd paresis | |
| Imaging | | | Causal lesion on brain MRI |
| Course of illness | Remission by early to mid adolescence<br>No developmental regression | | Neurocognitive regression with a continuous spike-and-wave pattern in sleep suggests evolution to EE-SWAS |
| An MRI is not mandatory for diagnosis but should be done in the presence of any alerts.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, at a minimum, an interictal EEG is required to confidently diagnose this syndrome. | | | |

3

# Childhood occipital visual epilepsy (COVE)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal sensory visual seizures with elementary visual phenomena (multicolored circles), with or without impaired awareness, and with or without motor signs (deviation of the eyes or turning of the head)<br>Seizures arise predominantly or exclusively from wakefulness | Prolonged seizure lasting >15 min<br>GTCS during wakefulness | Drop (tonic or atonic) seizures<br>Atypical absences<br>Progressive myoclonus |
| EEG | Occipital spikes or spikes-and-wave abnormalities (awake or sleep) | Sustained focal slowing not limited to the postictal phase | |
| Age at onset | | <6 years >14 years | <1 year or >19 years |
| Development at onset | | Intellectual disability | Neurocognitive regression |
| Neurological exam | | Any significant neurological examination abnormality | Persistent visual field deficit |
| Imaging | | | Causal lesion on brain MRI<br>Cerebral occipital lobe calcifications |
| Course of illness | | | Neurocognitive regression<br>Development of myoclonic seizures, ataxia, spasticity |
| An MRI is required for diagnosis to exclude a causal lesion.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, at a minimum, an interictal EEG and MRI are required to confidently diagnose this syndrome. | | | |

4

# Photosensitive occipital lobe epilepsy (POLE)

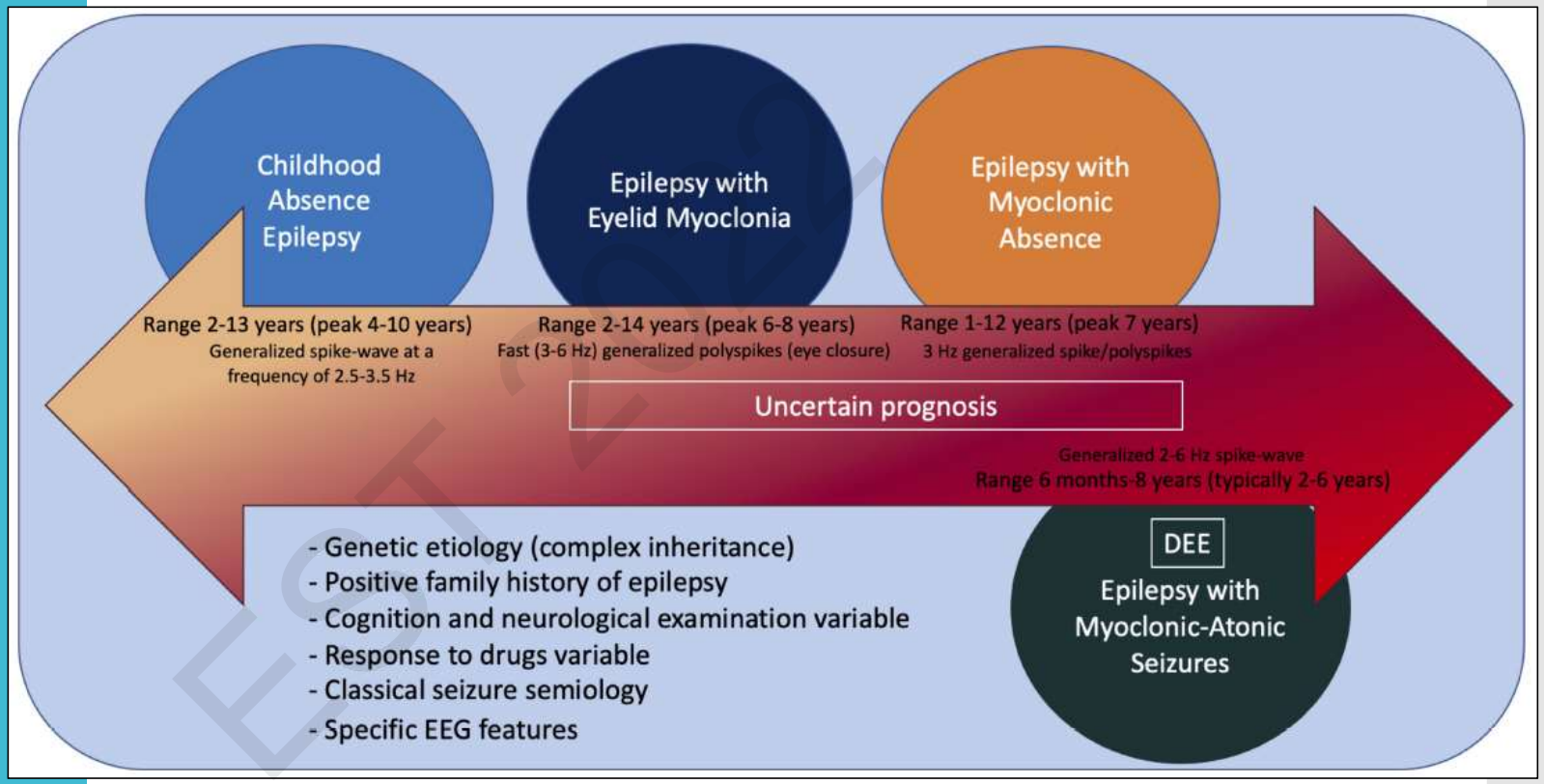
| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Focal sensory visual seizures (see text), which may evolve to bilateral tonic–clonic seizures<br>Seizures are triggered by photic stimuli, such as flickering sunlight | Prolonged seizures lasting >15 min | Eyelid myoclonia<br>Progressive myoclonus |
| EEG | Occipital epileptiform abnormalities facilitated by eye closure and IPS | Sustained focal slowing not limited to the postictal phase<br>Photoparoxysmal response at slow photic frequency (1–2 Hz; suggest CLN2 disease) | |
| Age at onset | | <4 years or >17 years | <1 year or >50 years |
| Development at onset | | Moderate to profound intellectual disability | Neurocognitive regression |
| Neurological exam | | Any significant neurological examination abnormality | Permanent visual field deficit |
| Imaging | | | Causal lesion on brain MRI |
| An MRI is required for diagnosis to exclude a causal lesion.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, at a minimum, an EEG and MRI are required to confidently diagnose this syndrome. | | | |

# Generalized epilepsy syndromes of childhood

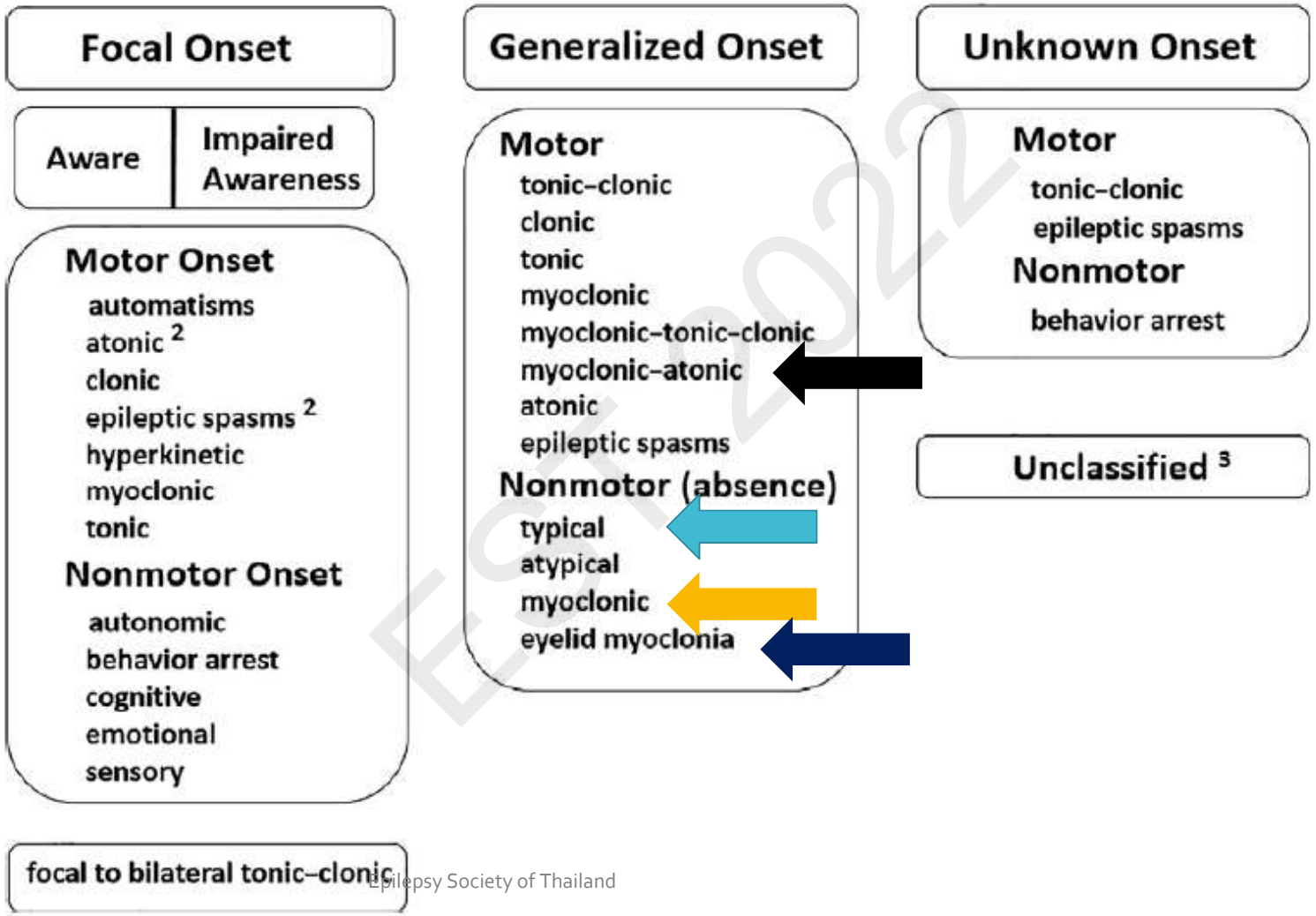
All generalized epilepsy syndromes that have onset in childhood have a

genetic etiology

# Generalized epilepsy syndromes of childhood



# ILAE 2017 Classification of Seizure Types Expanded Version [1]



5

# Epilepsy with eyelid myoclonia (EEM)

- Eyelid myoclonia, w or without absence
- Induced by eye closure/photic stimulation

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Eyelid myoclonia (see text) | Inability to induce eyelid myoclonia in the office by slow eye closure during exposure to bright light in ted patient rks affecting limbs—onsider JME | Any of the following seizure types:<br>• Myoclonic–absence seizures<br>• Focal seizures |
| EEG | Eye closure and intermittent photic stimulation elicits fast (3–6 Hz) generalized polyspikes or polyspike-and-wave complexes | | Focal slowing<br>Consistently unilateral focal spikes<br>Generalized slow spike-and-wave pattern at frequency < 2.5 Hz (unless it is at the end of a higher frequency burst)<br>Diffuse background slowing that is not limited to the postictal period<br>Lack of EEG correlate with typical clinical event |
| Age at onset | | | <2 years or >14 years |
| Neurological exam | | Focal neurological findings | |
| Imaging | | Potentially relevant abnormal neuroimaging, excluding incidental findings (see text) | Abnormal neuroimaging with causative lesion |
| Course of illness | | | Progressive cognitive decline over the course of the epilepsy |
| An MRI is not required for diagnosis.<br>An ictal EEG is not required for diagnosis, provided that eyelid myoclonia has been observed clinically by the diagnosing provider and the interictal study shows fast (3–6 Hz) generalized polyspikes or polyspike-and-wave complexes induced by eye closure or intermittent photic stimulation. However, most untreated patients will have recorded photoparoxysmal response with eyelid myoclonia on a routine EEG performed during intermittent light stimulation. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, epilepsy with eyelid myoclonia can be diagnosed in persons who meet all other mandatory and exclusionary clinical criteria if they have eyelid myoclonia witnessed by the examiner or captured on home video. | | | |

*Note:* Alert criteria are absent in the vast majority of cases, but rarely can be seen. Their presence should result in caution in diagnosing the syndrome and consideration of other conditions.

Abbreviations: EEG, electroencephalogram; JME, juvenile myoclonic epilepsy; MRI, magnetic resonance imaging.

6

# Epilepsy with myoclonic absences (EMA)

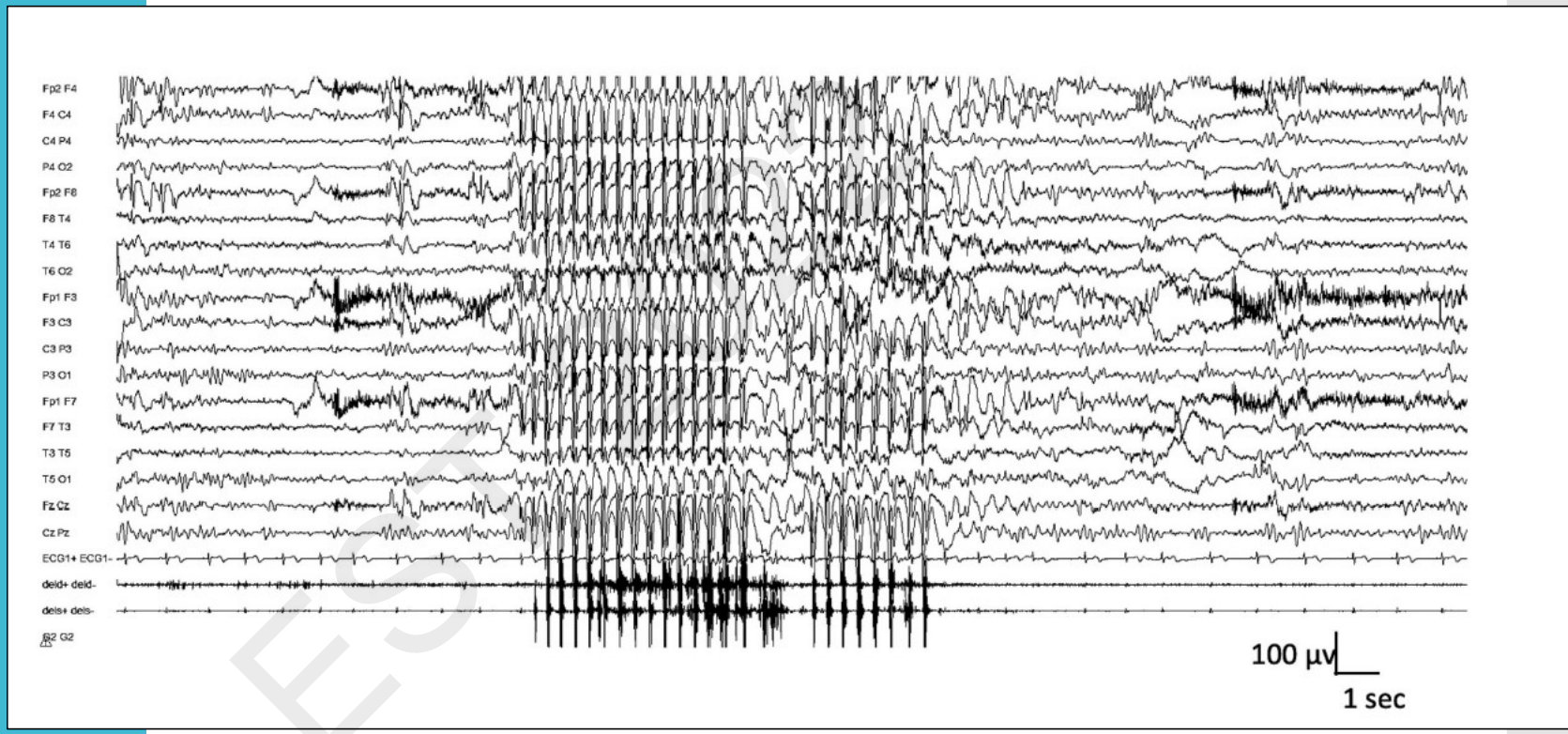
- Myoclonic absence seizure in 1/3
- Mixed type sz: GTC 45%, clonic,, atonic, typical absence

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Myoclonic absence seizures as predominant type (see text) | | Focal seizures<br>Atonic, myoclonic–atonic, or tonic seizures |
| EEG | Regular 3-Hz generalized spike-and-wave pattern time-locked with myoclonic jerks | | Focal slowing<br>Consistently unilateral focal spikes<br>Generalized slow spike-and-wave pattern at frequency < 2 Hz (unless it is at the end of a higher frequency burst)<br>Diffuse background slowing that is not limited to the postictal period |
| Age at onset | | | <1 year or >12 years |
| Neurological exam | | Moderate or greater intellectual disability<br>Focal neurological findings | |
| Imaging | | | Abnormal neuroimaging with causative lesion |
| Course of illness | | | Progressive cognitive decline over the course of epilepsy |
| An MRI should be considered to exclude other causes.<br>An ictal EEG is not required for diagnosis, provided that myoclonic absences have been observed clinically by the diagnosing provider and the interictal study shows regular 3-Hz generalized spike-and-wave complexes. However, most untreated patients will have recorded myoclonic absence seizure on routine EEG. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, epilepsy with myoclonic absences can be diagnosed in persons who meet all other mandatory and exclusionary clinical criteria if they have myoclonic absence seizures witnessed by the examiner or captured on home video. | | | |

*Note:* Alert criteria are absent in the vast majority of cases, but rarely can be seen. Their presence should result in caution in diagnosing the syndrome and consideration of other conditions.

Abbreviations: EEG, electroencephalogram; MRI, magnetic resonance imaging.

# EMA
## (Epilepsy with myoclonic absences)

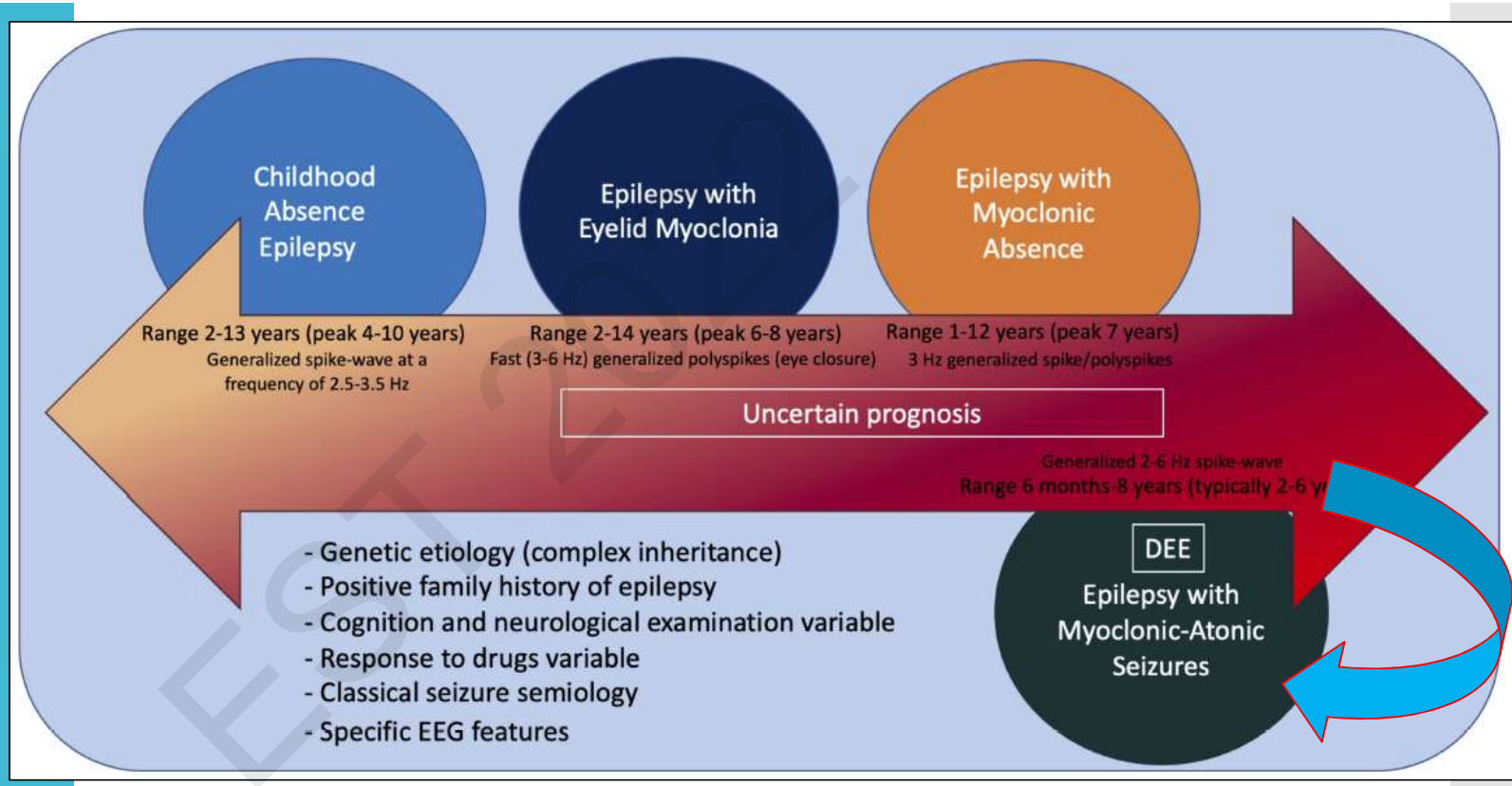







*Epilepsia. 2022;00:1–45*

# Generalized epilepsy syndromes of childhood



7

# Epilepsy with myoclonic atonic seizures (EMAtS)

- Myoclonic-atonic
- Pure atonic
- Myoclonic, absence, GTC
- Tonic- poor outcome
- Non-convulsive status

| Mandatory | | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Myoclonic–atonic seizures | Tonic seizures within 12 months of epilepsy onset | Epileptic spasms or IESS prior to diagnosis<br>Focal seizures |
| | | Generalized paroxysmal fast activity in sleep<br>Generalized slow spike-and-wave complexes of <2 Hz<br>Photoparoxysmal response at low frequencies (suggests *CLN2* disease) | Persistent focal abnormalities<br>Hypsarrhythmia |
| | | | <6 months or >8 years |
| Development at onset | | Moderate to severe developmental delay preceding seizure onset | |
| Neurological exam | | Focal neurological findings | |
| Imaging | | | Causal lesion on MRI |
| An MRI is not required for diagnosis but is typically done to exclude other causes.<br>An ictal EEG is not required for diagnosis. However, in a child with alerts or with clinical features that may suggest Lennox–Gastaut syndrome or infantile epileptic spasms, a video at least is essential and ideally an ictal EEG should be recorded.<br>Syndrome-in-evolution: Epilepsy with myoclonic atonic seizures should be suspected in the case of explosive onset of multiple generalized seizure types in an appropriately aged child without other alerts or exclusionary features. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, epilepsy with myoclonic atonic seizures can be presumptively diagnosed without EEG if the clinician has personally witnessed myoclonic atonic seizures, either directly by observing the patient, or on video provided by the family. However, an EEG is strongly recommended. | | | |

8

# LGS (Lennox-Gastaut syndrome)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Tonic seizures (see text)<br>In addition to tonic seizures, at least one additional seizure type must be present, which may include any of the following:<br>• Atypical absences<br>• Atonic<br>• Myoclonic<br>• Focal impaired awareness<br>• Generalized tonic–clonic<br>• Nonconvulsive status epilepticus<br>• Epileptic spasms | | |
| EEG | Generalized slow spike-and-wave complexes of <2.5 Hz (or history of this finding on prior EEG)<br>Generalized paroxysmal fast activity in sleep (or history of this finding on prior EEG) | Photoparoxysmal response at low frequencies (consider CLN2 disease) | Persistent focal abnormalities without generalized spike-and-wave pattern |
| Age at onset | <18 years | >8 years | |
| Long-term outcome | Drug-resistant epilepsy<br>Mild to profound intellectual disability | | |
| An MRI is not required for diagnosis but is usually performed to evaluate for underlying etiology.<br>An ictal EEG is not required for diagnosis. However, it should be strongly considered in a child with alerts or with clinical features that may suggest epilepsy with myoclonic atonic seizures syndrome.<br>Syndrome-in-evolution: Approximately 50% of infants with a severe DEE, e.g., IESS or early infantile DEE, evolve over time to Lennox–Gastaut syndrome. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, at a minimum, an interictal EEG showing characteristic generalized slow spike-and-wave pattern during wakefulness is required for diagnosis. | | | |

# DDx in LGS

DDx

1. Infantile epileptic spasms syndrome
2. EMAtS
3. Dravet syndrome
4. Other early onset DEEs with multiple seizures types
5. DEE-SWAS or EE-SWAS
6. Ring (20) syndrome
7. Frontal lobe epilepsy
8. Rare metabolic disorders may lead to LGS phenotype i.e. CLN2

**Developmental and/or epileptic encephalopathies (DEE)**

1. Epilepsy with myoclonic-atonic seizures (EMAtS)
2. LGS
3. DEE or EE with spike-and-wave activation in sleep
4. Hemiconvulsion-hemiplegia-epilepsy syndrome (HHE)
5. FIRES

# DEE-SWAS

# EE-SWAS

- Combinations of cognitive, language, behavioral and motor regression
- Marked spike-and-wave activation in sleep
- Regression is seen within weeks from the EEG pattern
- Previous term
  : EE w continuous spike-and-wave in sleep
  : atyp benign partial epilepsy (pseudo Lennox syndrome)

Previous term
- LKS

9,10

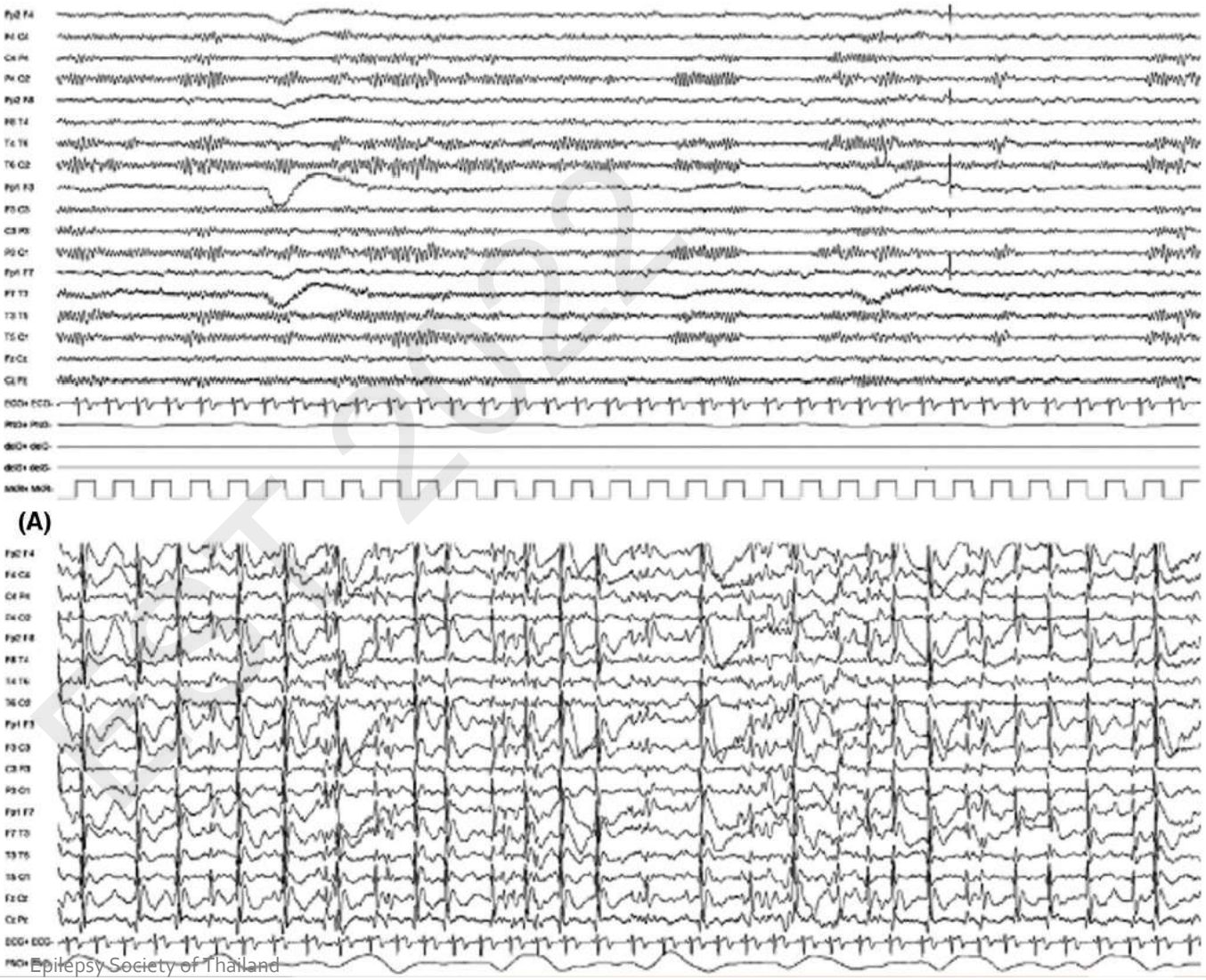
# DEE w SWAS
# EE w SWAS

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | | Tonic seizures during sleep | Epileptic spasms |
| EEG | Slow (1.5–2 Hz) spike-and-wave abnormalities in N-REM sleep<br>Abnormalities are markedly activated in sleep | Generalized paroxysmal fast activity in sleep (consider Lennox–Gastaut syndrome)<br>Generalized slow spike-and-wave complexes of <2.5 Hz in both awake and asleep states (consider Lennox–Gastaut syndrome) | |
| Age at onset | | >1 and <2 years | <1 year or >12 years |
| 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 | | |
| An MRI is not required for diagnosis but is often performed to evaluate for underlying etiology.<br>A sleep EEG is mandatory for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, this syndrome cannot be presumptively diagnosed without a sleep EEG. | | | |

*Note:* Alert criteria are absent in the vast majority of cases, but rarely can be seen. Their presence should result in caution in diagnosing the syndrome and consideration of other conditions.

Abbreviations: EEG, electroencephalogram; MRI, magnetic resonance imaging; N-REM, non-rapid eye movement; SWAS, spike-and-wave activation in sleep.

# DEE w SWAS
# EE w SWAS



11

# Febrile infection-related epilepsy syndrome (FIRES)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | History of nonspecific febrile illness in the 2 weeks preceding seizure onset<br>Focal and multifocal seizures that often evolve to bilateral tonic–clonic seizures<br>Seizures progress in frequency and severity to culminate in superrefractory status epilepticus typically within 2 weeks of onset | | History of epilepsy prior to onset of symptoms |
| EEG | Slowing of the background activity with multifocal epileptiform abnormalities and frequent, focal electrographic and electroclinical seizures | Unifocal seizures | |
| Age at onset | | <2 years | <1 year or >30 years |
| Development at onset | Acute encephalopathy with onset of frequent seizures | Intellectual disability prior to seizure onset | |
| Neurological exam | | Neurological exam abnormalities prior to onset of seizures | |
| Imaging | | | At presentation, MRI shows an epileptogenic lesion concordant with seizure onset (see text) |
| Other testing | | | Lumbar puncture showing evidence of central nervous system infection<br>Causal antibody on CSF or plasma autoimmune testing<br>Documented metabolic or genetic etiology<br>Documented toxic encephalopathy |
| Long-term outcome | | Lack of drug-resistant focal or multifocal epilepsy<br>Lack of learning difficulties or intellectual disability<br>Lack of variable degrees of cerebral atrophy on MRI | |
| An MRI is required for diagnosis to exclude a causal lesion.<br>An ictal EEG is required for diagnosis to confirm frequency and multifocality of seizures.<br>Syndrome without laboratory confirmation: In resource-limited regions, this syndrome cannot be presumptively diagnosed without EEG and MRI studies. | | | |

12

# Hemiconvulsion-hemiplegia-epilepsy syndrome (HHE)

| | Mandatory | Alerts | Exclusionary |
|---|---|---|---|
| Seizures | Diagnosis requires both a history of acute stage and chronic stage disease<br>Acute stage: Episode of febrile, hemiclonic status epilepticus, which is immediately followed by permanent hemiparesis<br>Chronic stage: After a variable time (usually <3 years after initial status epilepticus), unilateral focal motor or focal to bilateral tonic–clonic seizures appear | | Transient hemiparesis (Todd paresis)<br>Unilateral focal motor seizures that progress in a crescendo pattern over months to years, with late development of progressive hemiparesis (consider Rasmussen encephalitis) |
| EEG | Slowing of background activity over the affected hemisphere<br>Focal or multifocal epileptiform abnormalities over the affected hemisphere in the chronic phase | | |
| Age at onset | | >4 years | >6 years |
| Development at onset | | Intellectual disability prior to seizure onset | |
| Neurological exam | | Focal neurological abnormalities prior to initial episode of febrile status epilepticus<br>Facial angioma suggestive of Sturge–Weber syndrome | |
| Imaging | MRI immediately following febrile status epilepticus (acute stage) shows diffuse signal change with T2 hyperintensity and restricted diffusion of the subcortical region of the affected hemisphere, often with severe edema<br>Over time (chronic stage), there is atrophy of the affected hemisphere | | Other structural causes predisposing to focal status epilepticus |
| Other testing | | | Alternative cause of hemiparesis found such as acute ischemic stroke, intracranial infection, etc. |
| Long-term outcome | Drug-resistant epilepsy<br>Permanent focal motor deficit | | |

An MRI is required to diagnosis.

An ictal EEG is not required for diagnosis.

Syndrome-in-evolution: Children with acute permanent hemiparesis following an episode of focal convulsive febrile status epilepticus, with mandatory MRI findings, but who have not yet progressed to the chronic phase of the disease with recurrent, drug-resistant focal motor or focal to bilateral tonic–clonic seizures should be suspected of having emerging hemiconvulsion–hemiplegia–epilepsy syndrome.

Syndrome without laboratory confirmation: In resource-limited regions, hemiconvulsion–hemiplegia–epilepsy syndrome can be presumptively diagnosed without EEG in cases that meet all mandatory and exclusionary clinical criteria without alerts. However, an imaging study (CT or MRI) is required to exclude other causes.

# Epilepsy Syndromes 2022

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Epilepsia

SPECIAL REPORT

## ILAE definition of the Idiopathic Generalized Epilepsy Syndromes: Position statement by the ILAE Task Force on Nosology and Definitions

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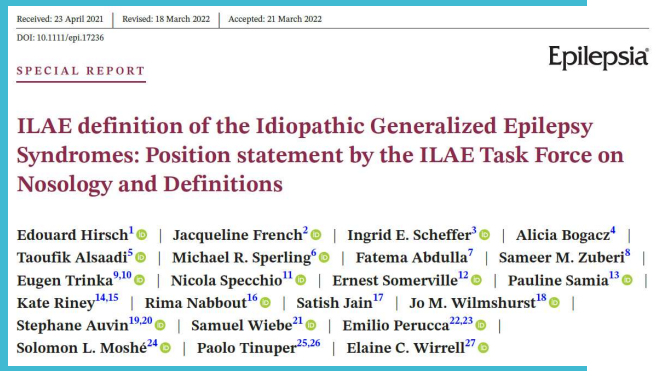
- **Genetic generalized epilepsy syndrome (GGE)**

# 2017 ILAE classification: GGEs

- **GGEs** = genetic generalized epilepsies
- Generalized epilepsy + EEG characters of generalized spike-wave
- Presumed genetic etiology
- GGEs and IGEs are overlapping, not synonymous
- **IGEs** = 4 syndromes
- Pts do not fulfill criteria 4 syndromes, but have one, or a combination, of gen seizure types: *absence, myoclonic, tonic-clonic and myoclonic-tonic-clonic seizures*, with 2.5-5.5 Hz generalized spike wave should be classified as having **GGE**

# Epilepsy Syndromes 2022



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Epilepsia

SPECIAL REPORT

**ILAE definition of the Idiopathic Generalized Epilepsy Syndromes: Position statement by the ILAE Task Force on Nosology and Definitions**

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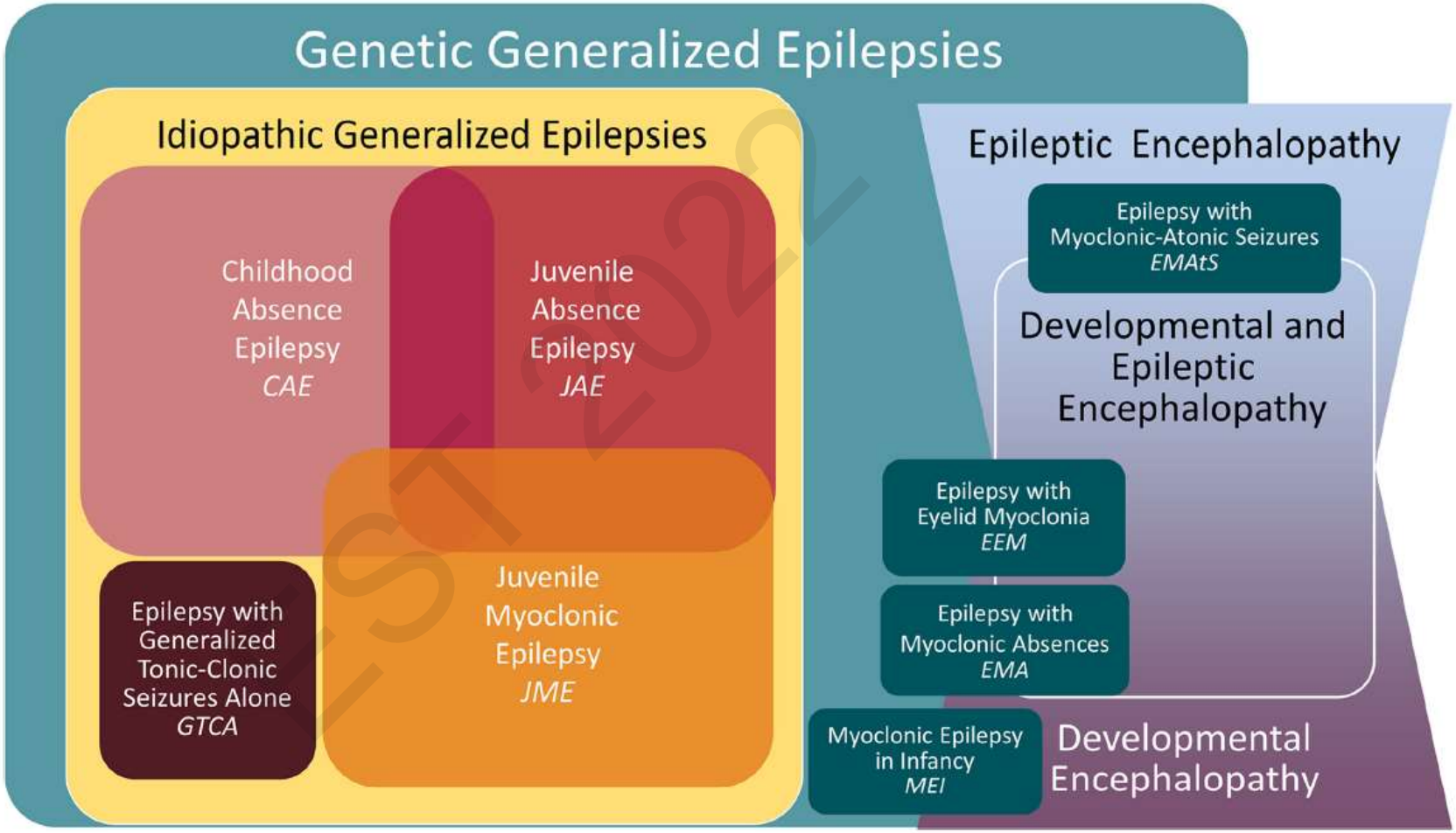
- **Genetic generalized epilepsy syndrome (GGE)**
- Idiopathic Generalized Epilepsies **(IGE)** ( Subgroup of GGE)
  - Good prognosis
  - Do not evolve to EE
  - Clinical overlap between CAE,JAE,JME
  - May evolve with age to another IGE syndrome
  - Some similar EEG findings (normal b/g, 2.5-6 Hz GSW or poly SW discharge, activated by HV, PS)

# GGE



# Idiopathic Generalized Epilepsy Syndromes

| | |
|---|---|
| Childhood Absence Epilepsy | • CAE<br>• Genetic study is not part of Ix: *GABRG2*, *GABRA1*, *SLC21A*, CNV 15p13.3 microdeletion |
| Juvenile Absence Epilepsy | • JAE<br>• Genetic study is not part of Ix: *GABRG2*, *GABRA1*, *CACNA1*, *SLC2A1* |
| Juvenile Myoclonic Epilepsy | • JME<br>• Genetic study is not part of Ix: *CACNB4*, *GABRA1*, *GABRD*, *EFHC1*, microdeletion 15q13.3, 15q11.2, 16p13.11 |
| Epilepsy with GTC seizure alone | • GTCA<br>• Previously: epilepsy with grand mal seizures on awakening |

1

# CAE

| | Mandatory | Alerts[a] | Exclusionary |
|---|---|---|---|
| Seizures | Typical absence seizures | GTCS prior to or during the period of frequent absence seizures<br>Staring spells with typical duration > 30 s or with postictal confusion or fatigue<br>Absences occurring <daily in an untreated patient | Any of the following seizure types:<br>• Prominent myoclonic seizures<br>• Prominent eyelid myoclonia<br>• Myoclonic–absence seizures<br>• Atonic seizures<br>• Tonic seizures<br>• Atypical absence seizures<br>• Focal impaired awareness seizures |
| EEG | Paroxysms of 3-Hz (range = 2.5–4 Hz) generalized spike-wave at the start of the absence (may have been obtained historically) | Consistently unilateral epileptiform discharges<br>Lack of HV-activated 2.5–4-Hz generalized spike-wave in untreated patient who performs HV well for 3 min or longer<br>Recording a typical staring spell without EEG correlate in a child with a history of 2.5–4-Hz generalized spike-wave<br>Persistent slowing of the EEG background in the absence of sedating medication | Diffuse background slowing |
| Age at onset | | 2–3 or 11–13 years | <2 or >13 years |
| Development at onset | | Mild intellectual disability | Moderate to profound intellectual disability |
| Neurological exam | | Potentially relevant neurological examination abnormalities, excluding incidental findings (see text) | |
| Comorbidities | | | Cognitive stagnation or decline |
| Imaging | | Potentially relevant abnormal neuroimaging, excluding incidental findings (see text) | |
| Other studies: genetics, etc. | | | Low CSF glucose and/or *SLC2A1* pathogenic variant (testing not needed in most cases but strongly recommended in children with onset at ≤3 years, microcephaly, and/or intellectual disability) |

An MRI is not required for diagnosis.

An ictal EEG is not required for diagnosis, provided the interictal study shows paroxysms of 2.5–4-Hz generalized spike-wave discharge during wakefulness. However, most untreated patients will have a recorded absence seizure on routine EEG.

Syndrome without laboratory confirmation: In resource-limited regions, CAE can be diagnosed in children without alerts who meet all other mandatory and exclusionary criteria, if they have a witnessed typical absence seizure with HV.

2

# JAE

| | Mandatory | Alerts[a] | Exclusionary |
|---|---|---|---|
| Seizures | Typical absence seizures | Staring spells with typical duration > 30 s or with postictal confusion or fatigue<br>Absence seizure frequency of >10 per day | Any of the following seizure types:<br>• Prominent myoclonic seizures<br>• Prominent eyelid myoclonia<br>• Myoclonic–absence seizures<br>• Atonic seizures<br>• Tonic seizures<br>• Atypical absence seizures<br>• Focal impaired awareness seizures |
| EEG | Paroxysms of 3–5.5-Hz generalized spike-wave (may have been obtained historically) | Lack of HV-activated 3–5.5-Hz generalized spike-wave in an untreated patient who performs HV well for 3 min or longer<br>Persistent EEG background slowing in the absence of a sedating medication | Consistently unilateral focal epileptiform discharges<br>Diffuse background slowing<br>Recorded typical staring spell without EEG correlate |
| Age at onset | | | <8 or >20 years |
| Development at onset | | Mild intellectual disability | Moderate to profound intellectual disability |
| Neurological exam | | Potentially relevant neurological examination abnormalities, excluding incidental findings (see text) | |
| Comorbidities | | | Cognitive stagnation or decline |
| Imaging | | Potentially relevant abnormal neuroimaging, excluding incidental findings (see text) | |
| Other studies: genetics, etc. | | | Low CSF glucose and/or *SLC2A1* pathogenic variant (testing not needed in most cases but strongly recommended in those with microcephaly and/or mild intellectual disability) |
| Course of illness | | Lack of GTCS over course of the epilepsy, in the absence of treatment with ASMs that are effective for GTCS | |
| An MRI is not required for diagnosis.<br>An ictal EEG is not required for diagnosis, provided the interictal study shows paroxysms of 3–5.5-Hz generalized spike-wave discharge during wakefulness. However, most untreated patients will have a recorded absence seizure on routine EEG. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, JAE can be diagnosed in persons without alerts who meet all other mandatory and exclusionary criteria, if they have a witnessed typical absence seizure with HV. | | | |

# CAE vs. JAE

| Feature | CAE | JAE |
|---|---|---|
| Age at onset | | |
| Usual | 4–10 years | 9–13 years |
| Range | 2–13; caution if diagnosing at <4 years of age | 8–20 years; exceptional cases may present in adulthood |
| Development | Typically normal, but may have learning difficulties or ADHD | Typically normal, but may have learning difficulties or ADHD |
| Absences | | |
| Frequency | At least daily to multiple per day but may be underrecognized by family | Less than daily |
| Duration | Typical duration = 3–20 s | Typical duration = 5–30 s |
| Impaired awareness | Severe loss of awareness | Less complete impairment of awareness |
| Other seizure types | | |
| Febrile | Occasional | Occasional |
| Generalized tonic–clonic seizure | Rarely precede or occur during period of frequent absences but may occur later with evolution to other IGE syndrome | May precede and commonly occur during the period of frequent absences |
| Myoclonic | Prominent myoclonus exclusionary | Prominent myoclonus exclusionary |
| EEG background | OIRDA in 21% | Normal |
| Interictal epileptiform discharge | | |
| Awake | 2.5–4-Hz generalized spike-wave | 3–5.5-Hz generalized spike-wave |
| Asleep | Polyspike and wave may be seen in drowsiness and sleep only | Polyspike and wave may be seen in drowsiness and sleep only |
| Irregular generalized spike-wave | Uncommon | More common than CAE<br>Discharges are more frequent than in CAE |
| Photoparoxysmal response | Rare<br>IPS triggers generalized spike-wave in 15%–21% but does not induce seizures | Rare<br>IPS triggers generalized spike-wave in 25% but does not induce seizures |
| Hyperventilation induction | 87% | 87% |
| Ictal EEG | Regular 3-Hz (range = 2.5–4 Hz) generalized spike-wave; 21% may have absences starting at 2.5-Hz spike-wave, and 43% may have absences starting at 4 Hz; if no generalized spike-wave is seen with hyperventilation for 3 min in an untreated patient, CAE can be excluded<br>Disorganized discharges[a] less frequent | Regular 3–5.5-Hz generalized spike-wave<br>If no generalized spike-wave is seen with hyperventilation for 3 min in an untreated patient, JAE can be excluded<br>Disorganized discharges[a] 8 times more frequent than CAE |

3

# JME

| | Mandatory | Alerts[a] | Exclusionary |
|---|---|---|---|
| Seizures | Myoclonic seizures (see text) | Generalized tonic–clonic status epilepticus<br>Consistent unifocal semiology (i.e., always affecting the same body part on the same side) at onset of generalized tonic–clonic seizures<br>Consistent unifocal myoclonus | • Myoclonic–absence seizures<br>• Atonic seizures<br>• Tonic seizures<br>• Atypical absence seizures<br>• Focal impaired awareness seizures<br>• Myoclonus predominantly or exclusively during sleep<br>• Myoclonic seizures that occur exclusively with reading<br>• Cortical tremor with myoclonus (see text) |
| EEG | 3–5.5-Hz generalized spike-wave or generalized polyspike-wave on EEG (may be obtained historically; see text) | | Habitual myoclonic event captured on EEG in the absence of polyspike and spike-wave discharge<br>Focal slowing<br>Consistently unilateral focal epileptiform abnormalities<br>Generalized slow spike-wave at frequency < 2.5 Hz (unless it is at the end of a higher frequency burst)<br>Diffuse background slowing that is not limited to the postictal period |
| Age at onset | | 8–9 years or 25–40 years | <8 years or >40 years (CAE may occasionally evolve to JME; in such cases, persons may have onset of absence seizures, but not GTCS or myoclonic seizures prior to age 8 years) |
| Development at onset | | Mild intellectual disability | Moderate to profound intellectual disability |
| Neurological exam | | Potentially relevant neurological examination abnormalities, excluding incidental findings (see text) | |
| Imaging | | Potentially relevant abnormal neuroimaging, excluding incidental findings (see text) | |
| Course of illness | | | Progressive cognitive decline<br>Progressive myoclonus with impaired fine motor function |
| An MRI is not required for diagnosis.<br>An ictal EEG is not required for diagnosis.<br>Syndrome without laboratory confirmation: In resource-limited regions, JME can be diagnosed in persons without alerts who meet all other mandatory and exclusionary clinical criteria. | | | |

4

# GTCA

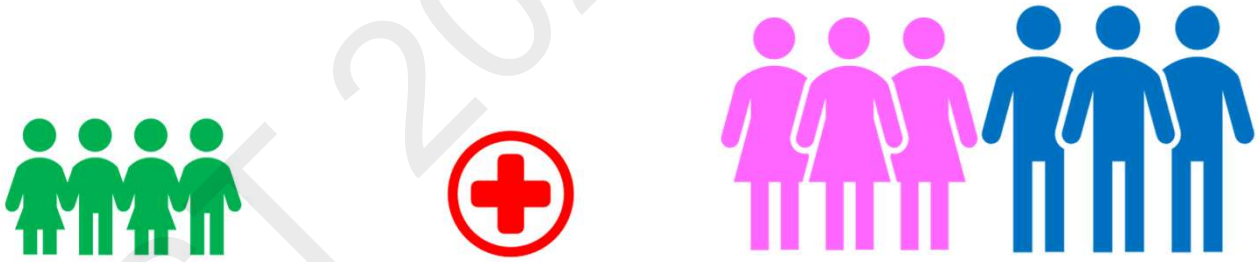
| | Mandatory | Alerts[a] | Exclusionary |
|---|---|---|---|
| Seizures | Generalized tonic–clonic seizures (see text) | Consistent unifocal semiology (i.e., always affecting the same body part on the same side) at seizure onset | Generalized myoclonic–tonic–clonic seizures (suggest JME)<br>Any other seizure type |
| EEG | 3–5.5-Hz generalized spike-wave or polyspike-wave on EEG (may be obtained historically) | | Focal slowing<br>Consistently unilateral focal epileptiform discharges<br>Generalized slow spike-wave at frequency < 2.5 Hz (unless it is at the end of a higher frequency burst)<br>Diffuse background slowing that is not limited to the postictal period |
| Age at onset | | 5–9 or 26–40 years | <5 or >40 years |
| Development at onset | | Mild intellectual disability | Moderate to profound intellectual disability |
| Neurological exam | | Potentially relevant neurological examination abnormalities, excluding incidental findings (see text) | |
| Comorbidities | | | |
| Imaging | | Potentially relevant abnormal neuroimaging, excluding incidental findings (see text) | Abnormal neuroimaging with causative lesion |
| Course of illness | | | Progressive cognitive decline |
| An MRI is not required in every case but should be considered with alerts or if clinical concern for a possible structural lesion exists.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, GTCA cannot be diagnosed without interictal EEG showing generalized spike-wave, as one cannot exclude focal onset without EEG. | | | |

# JME vs. GTCA

| Feature | JME | GTCA |
|---|---|---|
| Age at onset | | |
| Usual | 10–24 years | 10–25 years |
| Range | 8–40 years | 5–40 years |
| Development | Typically normal but may have learning disorder or ADHD | Typically normal but may have learning disorder or ADHD |
| Main seizure type | Myoclonic seizures, seen predominantly on awakening | Generalized tonic–clonic seizures typically within 2 h of awakening |
| Other seizure types | | |
| Febrile seizures | May occur in approximately 4%–5%<br>Generalized tonic–clonic seizures in >90%, which are often preceded by myoclonic jerks (myoclonic–tonic–clonic), and often occur on awakening<br>Absence seizures in 33%, typically brief (3–8 s), infrequent (<daily), and with variable impairment of awareness | May occur in approximately 15%<br>Absence or myoclonic seizures are not present |
| Triggers | Sleep deprivation<br>Photic stimulation | Sleep deprivation |
| EEG background | Normal | Normal |
| Epileptiform discharges | Irregular, generalized 3–5.5-Hz spike-wave and polyspike-wave seen in all states<br>May fragment in sleep | Generalized 3–5.5-Hz spike-wave or polyspike-wave, which may be seen only in sleep<br>May fragment in sleep |
| Photoparoxsmal response | Seen in 30%–90% and may trigger myoclonic jerks or generalized myoclonic–tonic–clonic seizures | May be seen |
| Hypeventilation induction | 33% have hyperventilation-induced generalized spike-wave discharge but rarely induces absence seizures | May be seen |
| Ictal EEG | Disorganized discharges significantly more common with absences in JME than CAE<br>Generalized polyspike-wave with myoclonic jerks<br>3.5–6-Hz generalized spike-wave or polyspike-wave with absences<br>Generalized spikes with tonic phase of generalized tonic–clonic seizure followed by spike-wave during clonic phase, but often obscured by muscle artifact | Generalized spikes with tonic phase followed by spike-wave during clonic phase, but often obscured by muscle artifact |

# Epilepsy Syndromes 2022

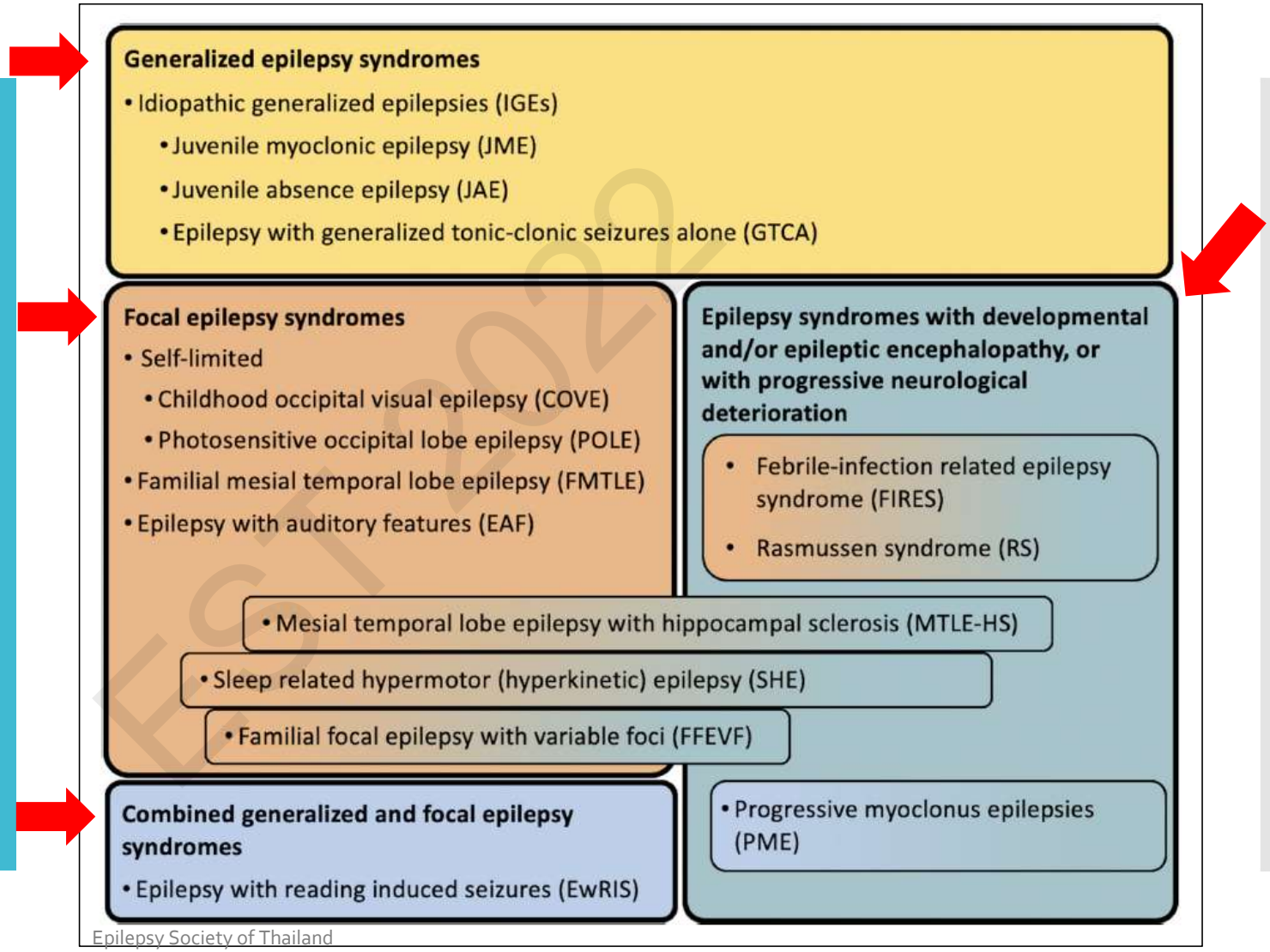
## Variable Age Onset (children and adult)





*Riney K et al. Epilepsia. 2022;00:1–32*

# Epilepsy syndromes with variable age onset



# Distinguishing features of SHE, FMTLE, FFEVF and EAF

| Syndrome | Onset (usual) | Clinical | Interictal EEG | Imaging |
|---|---|---|---|---|
| SHE | Second decade of life | From sleep, brief hyperkinetic or asymmetric tonic/dystonic motor seizures | Background interictal EEG is usually normal; focal (usually frontal) epileptiform abnormality can be seen | Normal, FCD, or acquired structural abnormality |
| FMTLE | Adolescence or adulthood | Typically, focal aware seizures with intense déjà vu and associated features, e.g., dreamy perceptions, fear or panic, slow motion, visual or auditory illusions, and autonomic manifestations | Background interictal EEG is usually normal or may show mild temporal slowing; temporal epileptiform abnormality can occasionally be seen | Normal, rarely hippocampal atrophy or increased T2 signal |
| FFEVF | First or second decade of life | Focal seizures, semiology dependent on focal cortical area involved in an individual, but constant in that individual | Background interictal EEG is usually normal; focal epileptiform abnormality can be seen | Normal or FCD |
| EAF | Second or third decade of life | Sensory seizures (auditory), cognitive seizures with receptive aphasia | Background interictal EEG is usually normal; focal (usually temporal) epileptiform abnormality can be seen | Usually normal, although posterior temporal FCD reported |

Abbreviations: EAF, epilepsy with auditory features; EEG, electroencephalogram; FCD, focal cortical dysplasia; FFEVF, familial focal epilepsy with variable foci; FMTLE, familial mesial temporal lobe epilepsy; SHE, sleep-related hypermotor (hyperkinetic) epilepsy.

| Focal epilepsy syndrome | Related genes |
|---|---|
| SHE | *CHRNA4, CHRNA2, CHRNB2, DEPDC5, KCNT1, NPRL2, NPRL3, PRIMA1* |
| FMTLE | *DEPDC5* (Mendelian inheritance is rare, FMTLE typically displays complex inheritance) |
| FFEVF | *TSC1, TSC2, DEPDC5, NPRL2, NPRL3* |
| EAF | *LGI1, RELN, MICAL1* |

1

# SHE

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Brief focal motor seizures with hyperkinetic or asymmetric tonic/dystonic features occurring predominantly from sleep | Seizures predominantly from the awake state | Seizures only during wakefulness<br>Generalized onset seizures |
| EEG | | Frequent epileptiform abnormality outside of the frontal regions<br>Generalized epileptiform abnormality | |
| Age at onset | | <10 or >20 years | <2 months or >64 years |
| Development at onset | | Moderate to severe intellectual disability | |
| Neurological exam | | Focal neurological examination abnormalities | |
| An MRI is not required for diagnosis but should be done to evaluate for underlying etiology.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, SHE can be diagnosed if other mandatory and exclusionary criteria are met, and the patient has witnessed or video-recorded hyperkinetic seizures during sleep. | | | |

2

# Familial mesial temporal lobe epilepsy (FMTLE)

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Focal cognitive (particularly déjà vu), sensory, or autonomic seizures | | Generalized onset seizures |
| EEG | | Generalized epileptiform abnormality | |
| Development at onset | | Intellectual disability | |
| Neurological exam | | Focal abnormalities on neurological examination | |
| Imaging | Normal or hippocampal atrophy/ sclerosis | | |
| Other studies: genetics, etc. | Family history of individuals with focal seizures that arise from the mesial temporal lobe | | |
| An MRI is required for diagnosis to exclude other causes.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, MRI is required to exclude other structural etiologies. | | | |

3

# Familial focal epilepsy with variable foci (FFEVF)

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Focal onset seizures | | Generalized onset seizures |
| EEG | | Generalized epileptiform abnormality | |
| Age at onset | | Neonatal onset | |
| Development at onset | | | Moderate to profound intellectual disability |
| Neurological exam | | Focal neurological examination abnormalities | |
| Imaging | Normal or focal cortical dysplasia | | |
| Other studies: genetics, etc. | Family history of individuals with focal seizures that arise from cortical regions that differ between family members | | Family history of focal seizures that occur exclusively before 20 months of age |
| An MRI is required for diagnosis. Family history of focal seizures might be incidental, due to an acquired cause. An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, FFEVF can be diagnosed without EEG in a patient if other mandatory and exclusionary criteria are met. However, an MRI or CT is required to exclude other structural etiologies. | | | |

4

# Epilepsy with auditory features (EAF)

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Focal sensory auditory seizures and/or focal cognitive seizures with receptive aphasia | | Generalized onset seizures<br>Other focal onset seizures |
| EEG | | Generalized epileptiform abnormality | |
| Development at onset | | | Moderate or severe intellectual disability |
| Neurological exam | | Focal neurological examination abnormalities | |
| Imaging | Normal or focal cortical dysplasia | | |
| An MRI is required for diagnosis to exclude other causes.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, MRI is required to exclude other structural etiology. | | | |

5

# Mesial temporal lobe epilepsy w hippocampal sclerosis (MTLE-HS)

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Focal aware or impaired awareness seizures with initial semiology referable to medial temporal lobe networks (see text) | Initial semiology referable to networks other than mesial temporal (e.g., throat discomfort, clonic or dystonic movements, somatic sensory symptoms, hyperkinetic activity, visual symptoms, auditory symptoms, laughter) | Generalized onset seizures |
| EEG | | Consistent lack of temporal epileptiform abnormality, despite repeated EEGs<br>Generalized epileptiform abnormality<br>High-amplitude, centrotemporal spikes with horizontal dipole<br>Interictal epileptiform abnormality or focal slowing outside of the temporal regions or over the posterior temporal region | Recorded seizures with generalized onset<br>EEG seizures recorded with onset in regions outside the temporal lobe |
| Age at onset | | <2 years | |
| Development at onset | | Moderate to severe intellectual disability | |
| Neurological exam | | Focal neurological findings such as hemiparesis (excluding facial asymmetry) | |
| Imaging | Hippocampal sclerosis (unilateral or bilateral) on MRI | | |
| An MRI documenting hippocampal sclerosis is required for diagnosis.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, an MRI is required for confirmation of diagnosis. | | | |

6

# Rasmussen syndrome

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Focal/hemispheric seizures that often increase in frequency over weeks to months | Focal onset independently in both hemispheres (only 2% of RS is bilateral) | Generalized onset seizures |
| EEG | Hemispheric slowing and epileptiform abnormality | Generalized spike-and-wave | |
| Age at onset | | Adolescence or adulthood | |
| Development at onset | | Abnormal development prior to seizure onset | |
| Neurological exam | | | Hemiparesis present at onset (if permanent hemiparesis is present immediately following status epilepticus, consider HHE) |
| Imaging | Progressive hemiatrophy (early insula and head of caudate atrophy; see text) | Lack of hyperintense signal and/or atrophy of the ipsilateral caudate head, and/or lack of T2/FLAIR hyperintense signal of gray or white matter | Imaging shows Sturge–Weber syndrome |
| Other studies: genetics, etc. | | | Metabolic cause of epilepsia partialis continua<br>Condition is due to specific antibody-mediated encephalitis |
| Long-term outcome | Drug-resistant epilepsy<br>Progressive neurological deficits | | |
| An MRI is required for diagnosis.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome in evolution: Children with drug-resistant, focal hemispheric seizures that progressively increase in frequency, with progressive neurological deficits, but whose MRI remains normal, and where other metabolic and autoimmune etiologies have been excluded, should be highly suspected of having emerging RS. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, RS can be diagnosed without EEG in a patient with focal/hemispheric onset seizures, who shows the typical clinical evolution, who meets all other mandatory and no exclusionary clinical criteria, and has no alerts. However, imaging (CT or MRI) is required to exclude other causes. | | | |

# Rasmussen syndrome

| Stage | Duration | Characters |
|---|---|---|
| 1. Prodromal phase | Months to years | • Infrequent seizures<br>• Mild hemiparesis |
| 2. Acute phase | Months to years | • Frequent seizures, epilepsia partialis continua<br>• Progressive hemiparesis, hemianopia, cognitive and language deterioration |
| 3. Chronic phase | | • Continued seizures (less frequent )<br>• Permanent hemiparesis and other disabilities |

7

# Epilepsy with reading-induced seizures (EwRIS)

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Reflex myoclonic seizures affecting orofacial muscles triggered by reading/language-related tasks | Prominent myoclonic jerks affecting the upper limbs | All other seizure types, except generalized tonic–clonic seizures |
| EEG | | | Background slowing on EEG, excluding in the postictal phase of a generalized tonic–clonic seizure |
| Age at onset | | >20 years | |
| Development at onset | Normal | | |
| Neurological exam | Normal | | |
| Imaging | Normal | | |
| An MRI is required for diagnosis to exclude a structural cause.<br>An ictal EEG is not required; however, observation during reading (either directly or by video) is highly recommended, as it shows the characteristic myoclonus affecting orofacial muscles. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, this syndrome can be diagnosed in children and adults who meet all mandatory criteria and have no exclusionary seizure types. | | | |

8

# Progressive myoclonus epilepsies (PME)

| | Mandatory | Alert[a] | Exclusionary |
|---|---|---|---|
| Seizures | Myoclonic seizures | | |
| EEG | Generalized spike/polyspike-and-wave | | Persistent focal epileptiform abnormality, other than occipital |
| Age at onset | 2–50 years | >20 years | |
| Development | Normal at onset | | |
| Neurological exam | Normal at onset | | |
| Comorbidities | Progressive neurocognitive deterioration (in some cases observation over time is necessary to distinguish PME from JME) | | |
| Imaging | Normal at onset | | |
| Course of illness | Progressive worsening of myoclonus, myoclonic and generalized tonic–clonic seizures, cognitive decline, progressive cerebellar signs<br>EEG deterioration with progressive background slowing and/or increased epileptiform abnormality | | |
| An MRI is not required for diagnosis but is often done to evaluate for underlying etiology.<br>An ictal EEG is not required for diagnosis. | | | |
| Syndrome without laboratory confirmation: In resource-limited regions, PME can be suspected in persons who meet mandatory and no exclusionary criteria, without alerts, and who show a progressive worsening of myoclonic seizures and neurological and cognitive function. | | | |

# Progressive myoclonus epilepsies (PME)

| PME type | Age at onset | Progression | Diagnosis |
|---|---|---|---|
| ULD | 7–13 years | Slow cognitive and motor deterioration with stabilization in adulthood | Cystatin B (*EMP1*) expansion variations account for ~90% of cases worldwide |
| LD | 6–19 years | Early rapid cognitive, vision, and motor deterioration; fatal approximately a decade after onset; focal seizures with visual symptoms are an early feature | Laforin (*EMP2A*) pathogenic gene variant in 70%, malin (*EMP2B*) pathogenic gene variant in 27%, no pathogenic variant found in 3%; Lafora bodies are seen in sweat duct cells or other tissues |
| CLN2 | 2–4 years | Initial speech delay and seizures, subsequently deterioration in cognition and motor skills, and then vision loss emerges at 4–6 years of age | *CLN2/TPP1* pathogenic gene variants; TPP1 enzyme activity is reduced; EEG can show a photoparoxysmal response at low (1–3 Hz) frequency; curvilinear bodies profile of lipofuscin accumulation in tissues (e.g., skin) or lymphocytes |
| CLN3 | 4–10 years | Rapidly progressing vision loss, with macular degeneration, optic atrophy ± retinitis pigmentosa; survival: late teens–30 years | *CLN3* pathogenic gene variants; fingerprint profile of lipofuscin accumulation in tissue (e.g., skin) or lymphocytes; lymphocytes are vacuolated |
| Adult onset NCL (type A) | 11–50 years | Slow development of dementia and ataxia; visual impairment is not expected | *CLN6* pathogenic gene variants (pathogenic variants in *CTSD*, *PPT1*, *CLN3*, *CLN5*, *CTSF*, and *GRN* also reported); mixed type inclusions (fingerprint, curvilinear, rectilinear) in tissue (e.g., skin) or lymphocytes |

Abbreviations: TPP1, tripeptidyl-peptidase 1; PME, progressive myoclonus epilepsies; MRI, magnetic resonance imaging; ULD, Unverricht–Lundborg disease; LD, Lafora disease; CLN, ceroid lipofuscinosis; NCL, neuronal ceroid lipofuscinosis; EEG, electroencephalogram.

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Epilepsia

SPECIAL REPORT

# 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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Epilepsia

SPECIAL REPORT

# ILAE definition of the Idiopathic Generalized Epilepsy Syndromes: Position statement by the ILAE Task Force on Nosology and Definitions

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Epilepsia

SPECIAL REPORT

# 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

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Epilepsia

SPECIAL REPORT

# International League Against Epilepsy classification and definition of epilepsy syndromes with onset at a variable age: position statement by the ILAE Task Force on Nosology and Definitions

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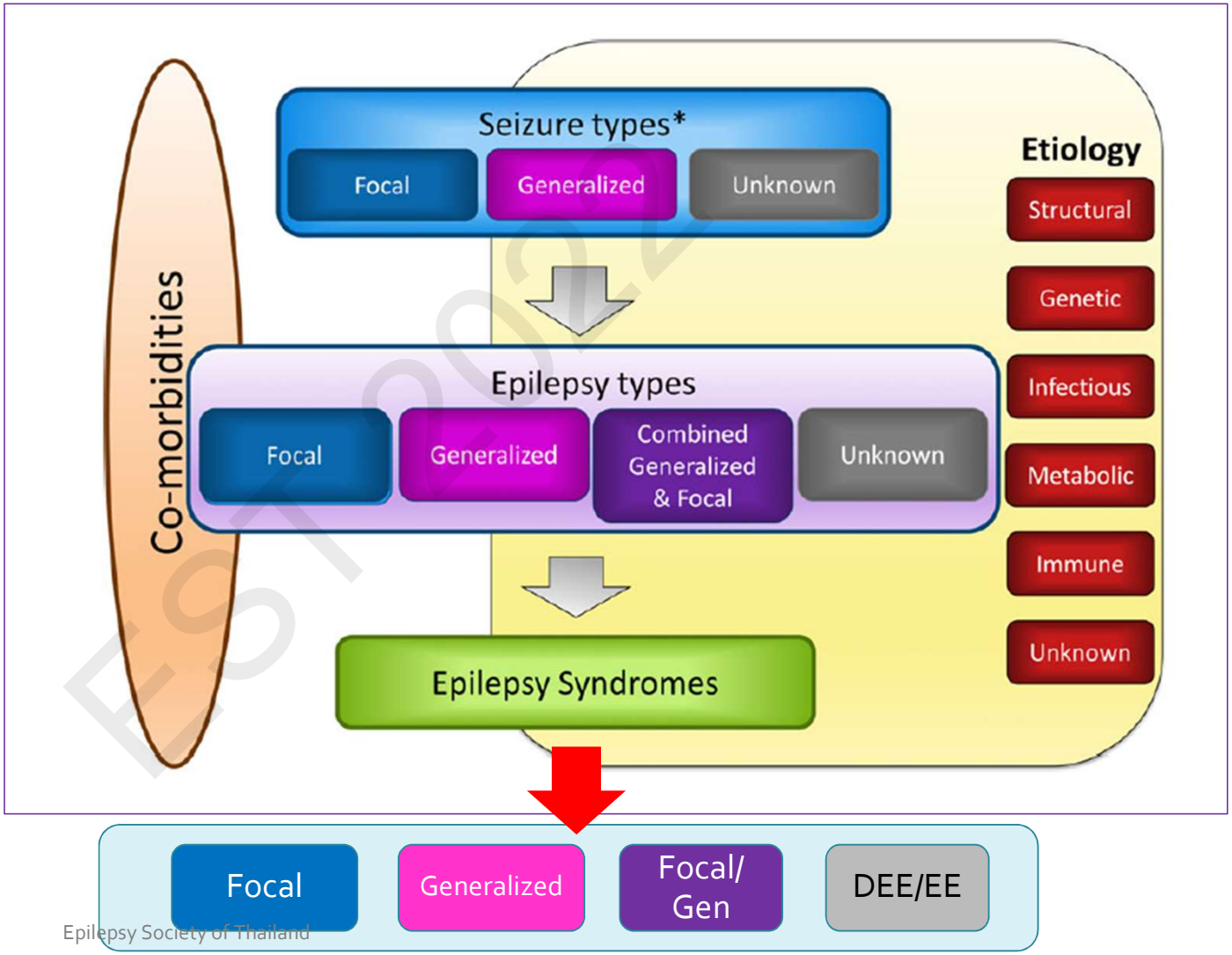
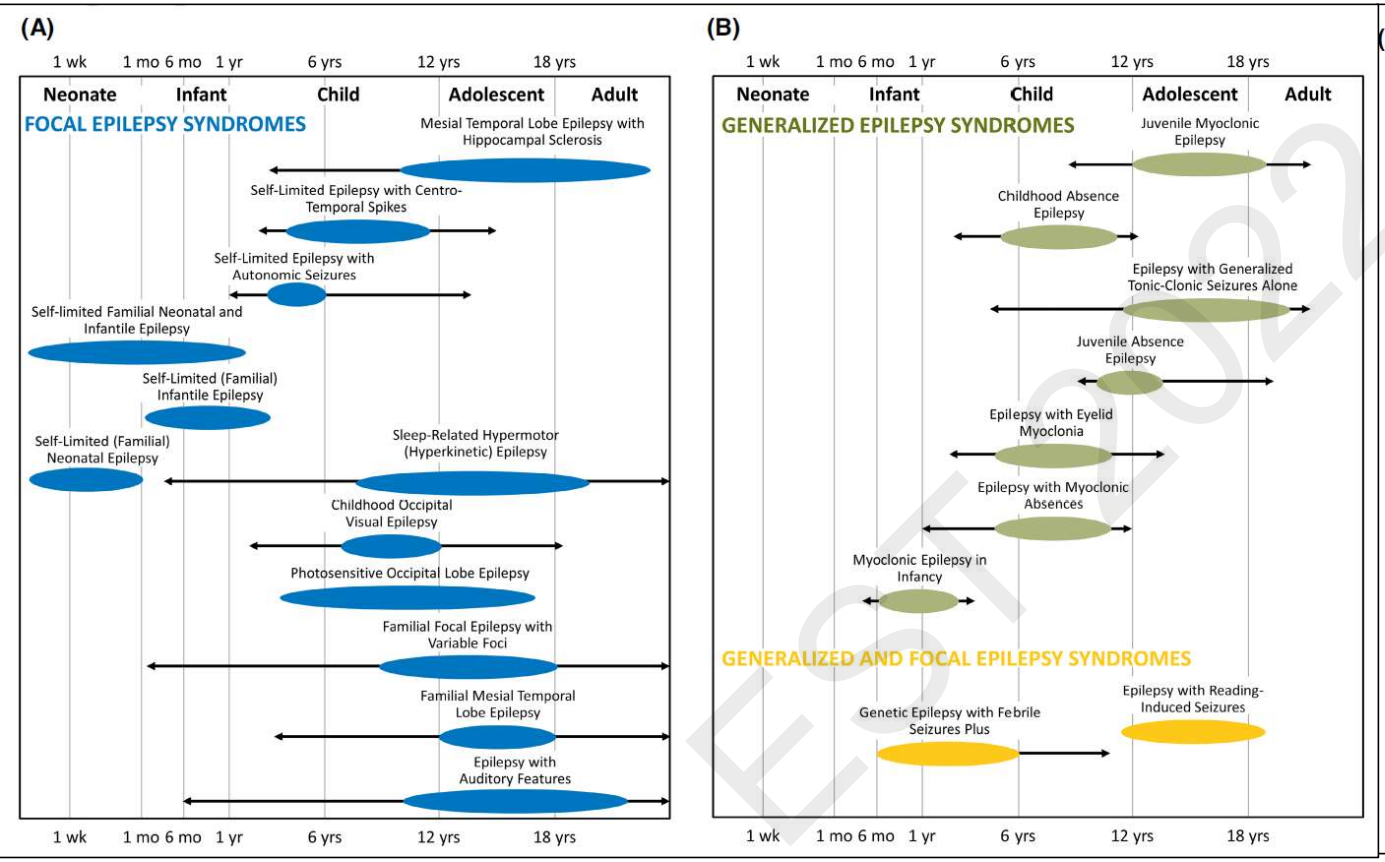
# Epilepsy Classification 2017 + Epilepsy syndromes 2022




(A)
1 wk
1 mo 6 mo
1 yr
6 yrs
12 yrs
18 yrs
Neonate
Infant
Child
Adolescent
Adult
FOCAL EPILEPSY SYNDROMES
Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis
Self-Limited Epilepsy with Centro-Temporal Spikes
Self-Limited Epilepsy with Autonomic Seizures
Self-limited Familial Neonatal and Infantile Epilepsy
Self-Limited (Familial) Infantile Epilepsy
Self-Limited (Familial) Neonatal Epilepsy
Sleep-Related Hypermotor (Hyperkinetic) Epilepsy
Childhood Occipital Visual Epilepsy
Photosensitive Occipital Lobe Epilepsy
Familial Focal Epilepsy with Variable Foci
Familial Mesial Temporal Lobe Epilepsy
Epilepsy with Auditory Features
(B)
GENERALIZED EPILEPSY SYNDROMES
Juvenile Myoclonic Epilepsy
Childhood Absence Epilepsy
Epilepsy with Generalized Tonic-Clonic Seizures Alone
Juvenile Absence Epilepsy
Epilepsy with Eyelid Myoclonia
Epilepsy with Myoclonic Absences
Myoclonic Epilepsy in Infancy
GENERALIZED AND FOCAL EPILEPSY SYNDROMES
Genetic Epilepsy with Febrile Seizures Plus
Epilepsy with Reading-Induced Seizures
(C)
Syndromes with Developmental and Epileptic Encephalopathy and Syndromes with Progressive Neurological Deterioration
Infantile Epileptic Spasm Syndrome
Early Infantile Developmental and Epileptic Encephalopathy
Developmental and/or Epileptic Encephalopathy with Spike-Wave Activation in Sleep
Lennox Gastaut Syndrome
Epilepsy with Myoclonic-Atonic Seizures
Dravet
Epilepsy in Infancy with Migrating Focal Seizures
Rasmussen Syndrome
Febrile Infection-Related Epilepsy Syndrome
Progressive Myoclonus Epilepsy
Gelastic Seizures with Hypothalamic Hamartoma
Hemiconvulsion-Hemiplegia-Epilepsy