Summer Lecture Series

Childhood Epilepsy Syndromes

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Preamble

- Epilepsy is the second most common neurological disorder affecting approximately 1% of the population worldwide.

- Incidence of epilepsy is highest at the extremes of age with 60% of epilepsy beginning before the age of 16 years.

Hauser et al., 1996
Approach to Seizure in Child

**Preamble**

**Approach to Seizure in Child**

**Provoked**  
- Febrile seizures  
- Electrolyte abnormalities  
- CNS Infection (meningitis)  
- Vascular  
- Trauma  
- Toxic ingestion  
- Inflammatory  
- Inborn error of metabolism  
- CNS tumour  

**Unprovoked**

- History  
- Exam  
- Investigations: lytes (Glc, Ca, P, Mg); CBC; LP; tox screen, etc)  
- Neuroimaging
History

- Antenatal History
- Birth history
- Developmental history
- Family history
- PMHx (CNS infections)
- Head trauma
- Seizure description (aura, trigger, eyewitness description)

Serologies/TORCH
Preeclampsia/GDM/Infections
Substance abuse/meds
Antenatal U/S
Fetal distress
Apgars, Cord pH
Need for postnatal resuscitation
Normal vs delayed vs regressed
Consanguinity, hx of febrile seizures, epilepsy, developmental delay, recurrent miscarriages, SIDs, IEM
Physical Exam

• Dysmorphism

• Stigmata of Neurocutaneous disorders

• Neurological exam including
  • HC
  • developmental

• Liver, heart involvement (IEM)
Physical Exam

- Dysmorphism
- Stigmata of Neurocutaneous disorders
- Neurological exam including
  - HC
  - Developmental
- Liver, heart involvement (IEM)

- Hypopigmented macule (Tuberous sclerosis)
- Shagreen patch (Tuber Sclerosis)
- Café-au-lait macule (Neurofibromatosis)
- Port Wine Stain (Sturge-Weber)
Physical Exam

• Dysmorphism

• Stigmata of Neurocutaneous disorders

• Neurological exam including
  • HC
    • developmental

• Liver, heart involvement (IEM)
**Preamble**

**Approach to Seizure in Child**

**Provoked**
- Febrile seizures
- Electrolyte abnormalities
- Infection (meningitis)
- Vascular
- Trauma
- Toxic ingestion
- Inflammatory
- Inborn error of metabolism
- CNS tumour

**Unprovoked**

**Does it fit any of the Childhood Epilepsy Syndromes?**
- Semiology of seizures
- Age of onset
- EEG features
- Clinical features/progression
- Response to Rx
- Prognosis
What is an Epilepsy Syndrome:

Clinical entity with relatively consistent clinical features that is defined by seizure semiology, etiology, EEG signature, neurologic status, prognosis and in some cases response to specific anticonvulsants.
Outline

- **Childhood Epilepsy Syndromes**
  - Neonate (<28days)
  - Infancy (<2yrs)
  - Childhood (2yrs – adolescence)
  - Adolescence/early adulthood

Table 3. Electroclinical syndromes and other epilepsies

<table>
<thead>
<tr>
<th>Electroclinical syndromes arranged by age at onset(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal period</td>
</tr>
<tr>
<td>Benign familial neonatal epilepsy (BFNE)</td>
</tr>
<tr>
<td>Early myoclonic encephalopathy (EME)</td>
</tr>
<tr>
<td>Ohtahara syndrome</td>
</tr>
<tr>
<td>Infancy</td>
</tr>
<tr>
<td>Epilepsy of infancy with migrating focal seizures</td>
</tr>
<tr>
<td>West syndrome</td>
</tr>
<tr>
<td>Myoclonic epilepsy in infancy (MEI)</td>
</tr>
<tr>
<td>Benign infantile epilepsy</td>
</tr>
<tr>
<td>Benign familial infantile epilepsy</td>
</tr>
<tr>
<td>Dravet syndrome</td>
</tr>
<tr>
<td>Myoclonic encephalopathy in nonprogressive disorders</td>
</tr>
<tr>
<td>Childhood</td>
</tr>
<tr>
<td>Febrile seizures plus (FS+) (can start in infancy)</td>
</tr>
<tr>
<td>Panayiotopoulos syndrome</td>
</tr>
<tr>
<td>Epilepsy with myoclonic atonic (previously astatic) seizures</td>
</tr>
<tr>
<td>Benign epilepsy with centrotemporal spikes (BECTS)</td>
</tr>
<tr>
<td>Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)</td>
</tr>
<tr>
<td>Late onset childhood occipital epilepsy (Gastaut type)</td>
</tr>
<tr>
<td>Epilepsy with myoclonic absences</td>
</tr>
<tr>
<td>Lennox-Gastaut syndrome</td>
</tr>
<tr>
<td>Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)(^b)</td>
</tr>
<tr>
<td>Landau-Kleffner syndrome (LKS)</td>
</tr>
<tr>
<td>Childhood absence epilepsy (CAE)</td>
</tr>
<tr>
<td>Adolescence – Adult</td>
</tr>
<tr>
<td>Juvenile absence epilepsy (JAE)</td>
</tr>
<tr>
<td>Juvenile myoclonic epilepsy (JME)</td>
</tr>
<tr>
<td>Epilepsy with generalized tonic–clonic seizures alone</td>
</tr>
<tr>
<td>Progressive myoclonus epilepsies (PME)</td>
</tr>
<tr>
<td>Autosomal dominant epilepsy with auditory features (ADEAF)</td>
</tr>
<tr>
<td>Other familial temporal lobe epilepsies</td>
</tr>
</tbody>
</table>
Neonatal Seizures

*Neonatal Period* (<28 days)

- Seizures in newborns are often difficult to distinguish from normal activity
- Most commonly occur within the first week of life
  - 2/3 of neonatal seizures are due to Hypoxic-ischemic encephalopathy (HIE)
  - Other causes: infection, electrolyte abnormalities, inborn errors of metabolism, structural, vascular
- The clinical and electroencephalographic features of neonatal seizures differ considerably from those in older children and adults.
  - Some seizures can be quite subtle making diagnosis difficult
  - Important to note that in neonates 50%-80% of prolonged epileptiform discharges on EEG are not associated with visible clinical changes
  - This electroclinical dissociation is due to the incomplete myelination of white matter tracts and immaturity of regional brain interconnectivity
  - Leads to only modest behavioural manifestations of seizures and explains why unlikely to get tonic-clonic seizures in newborns

⭐️ When in doubt, request an EEG! ⭐️
# Neonatal Seizures

## Subtle Seizures:
- Random and roving eye movements
- Sucking
- Chewing
- Tongue protrusion
- Rowing
- Swimming
- Bicycling movements of lower limbs

## TABLE 1-2
Seizure Patterns in Newborns

<table>
<thead>
<tr>
<th>Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea with tonic stiffening of body</td>
</tr>
<tr>
<td>Focal clonic movements of one limb or both limbs on one side</td>
</tr>
<tr>
<td>Multifocal clonic limb movements</td>
</tr>
<tr>
<td>Myoclonic jerking</td>
</tr>
<tr>
<td>Paroxysmal laughing</td>
</tr>
<tr>
<td>Tonic deviation of the eyes upward or to one side</td>
</tr>
<tr>
<td>Tonic stiffening of the body</td>
</tr>
</tbody>
</table>

## TABLE 1-1
Movements That Resemble Neonatal Seizures

<table>
<thead>
<tr>
<th>Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign nocturnal myoclonus</td>
</tr>
<tr>
<td>Jitteriness</td>
</tr>
<tr>
<td>Nonconvulsive apnea</td>
</tr>
<tr>
<td>Normal movement</td>
</tr>
<tr>
<td>Opisthotonos</td>
</tr>
<tr>
<td>Pathological myoclonus</td>
</tr>
</tbody>
</table>
Neonatal Seizures

**EEG Features of Neonatal Seizures**

- Ictal rhythmic discharges of a clear epileptic nature
- Ictal discharges can be highly polymorphic
  - Repetitive sharp waves/spikes
  - Abnormal paroxysmal rhythms including beta, gamma, theta, delta that remain focal or involve only one hemisphere
- Unrelated discharges of various shapes or rhythms that occur independently in both hemispheres
- Bilateral symmetrical discharges are rare except in Benign Familial Neonatal Seizures
- For discharges to be called ictal, they need to be at least 10 secs in duration
- Can have paroxysmal clinical events (tonic/subtle) that have no changes on EEG and these tend to be release phenomena

*Despite this, it is often difficult and may be impossible to accurately differentiate epileptic from non-epileptic events in neonates*
Case 1:

Called from NICU to assess a term baby girl on body cooling. Unremarkable pregnancy. Mom in healthy G1P0A0. Spontaneous ROM at 39 weeks. During labour, fetal decelerations noted. Stat C/S performed. Evidence of placental abruption. Apgars, 2, 4, 6 at 1, 5 and 10 min respectively. Cord pH 6.8, HCO3 13, BE -20. BB intubated at 10 minutes of life. Suspicion of seizures at 2 hours of life and loaded with Phenobarbital. BB transferred to MCH for cooling protocol. On exam, there is evidence of axial hypotonia, appendicular hypertonia, increased reflexes.
Case 2:

Called from NICU to assess a term baby girl with onset of seizures at DOL3.
Unremarkable pregnancy and delivery. BB born at 38 weeks, SVD. Apgars 8, 9 and 9.
Doing well in first few days of life. At DOL3 started having abnormal jerking
movements. Family history remarkable for a number of relatives with neonatal
seizures but family history of epilepsy as adults. On exam, baby is reactive and has a
completely normal neurological exam. In between seizures, she continues to feed well
and there is no evidence of encephalopathy. Neuroimaging as well as basic
bloodwork is normal.
Pediatric Epilepsy Syndromes with Onset in the NEONATAL PERIOD

- **Benign**
  - Benign Familial Neonatal Convulsions
  - Benign Idiopathic Neonatal Convulsions

- **Epileptic encephalopathies**
  - Early infantile epileptic encephalopathy (Ohtahara syndrome)
  - Early Myoclonic encephalopathy (EME)
Pediatric Epilepsy Syndromes with Onset in the NEONATAL PERIOD

- **Benign**
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**Benign Familial Neonatal Convulsions (BFNC)**

- First reported in 1964
- Incidence estimated at 14.4 per 100,000 live births

**Clinical presentation:**
- Normal pregnancy and antenatal period
- Seizures start on day 2-3 of life in 80% of cases
  - Brief, generalized or focal tonic-clonic
- Except for the seizures, babies are not encephalopathic (i.e. Normal in between seizures, feed well)
- Neurologic exam normal
- EEG is normal or mildly abnormal
- Normal psychomotor development
- Seizures remit by 1 month but in 10-15% of patients may develop epilepsy later in life

**Diagnosis:**
- Clinical presentation
- Family history of neonatal seizures without severe epilepsy in family members
- Genetic testing
**Benign Familial Neonatal Convulsions (BFNC)**

- **EEG:**
  - Interictally: normal, discontinuous, focal/multifocal abnormalities or theta pointu alternant pattern (never a pattern that suggests poor prognosis: paroxysmal, inactive or burst suppression pattern)
  - Ictally: seizures start with generalized flattening of background activity (lasting between 5-19secs) followed by localized or generalized spikes or slow waves lasting as long as the clinical event
  - Seizures can last 59-155secs and are usually generalized

- **Genetics:**
  - Autosomal dominant with up to 85% penetrance
  - **KCNQ2** (aka Kv7.2): chromosome 20q13.3
    - encodes voltage-gate potassium subunit, major locus for BFNS, accounts for 60% of families with BFNS
  - **KCNQ3** (aka Kv7.3): chromosome 8q24
    - represents minor locus for BFNS, accounts for 5% of families with BFNS
  - Unclear why these mutations causes seizures in early life and then remit
  - GABA(A) receptors in the neonatal period are depolarizing, possibility that inhibition primarily dependent on K channel activity
**Benign Idiopathic Neonatal Convulsions (BINC)**

- **Clinical presentation:**
  - No Family History
  - Normal pregnancy and antenatal period
  - Accounts for 2-7% of neonatal seizures, male > females
  - Seizures start on day 4-7 of life
    - Clonic type, partial, apnea, rarely generalized
    - Last 1-3min
  - Except for the seizures, babies are not encephalopathic (ie. Normal in between seizures, feed well)
  - Neurologic exam normal
  - Normal psychomotor development
  - Seizures remit by 1month but 0.5% of patients may develop epilepsy later in life

- **Diagnosis:**
  - Clinical presentation
  - Diagnosis of exclusion (etiology unknown, ?low Zinc in CSF but unproven hypothesis)

- **EEG:**
  - Interictally similar to BFNC, except seizures tend to be more focal whereas in BFNC they are generalized
Pediatric Epilepsy Syndromes with Onset in the NEONATAL PERIOD

- **Benign**
  - Benign Familial Neonatal Convulsions
  - Benign Idiopathic Neonatal Convulsions

- **Epileptic encephalopathies**
  - Early infantile epileptic encephalopathy (Ohtahara syndrome)
  - Early Myoclonic encephalopathy (EME)
Neonatal Epileptic Encephalopathies

- Represent a group of disorders characterized by recurrent and intractable seizures and result in significant global delay and intellectual disability (encephalopathy)
- Final common pathway that results from a heterogeneous group of disorders with underlying genetic, metabolic, or structural pathologies.

### Early Myoclonic Encephalopathy
- Onset always in the neonatal period
- Erratic/fragmentary myoclonus that typically is not associated with an EEG correlate
- EEG shows burst suppression pattern
- Usually normal MRI findings
- Etiology: Inborn errors of metabolism ex. Nonketotic hyperglycinemia, Menkes disease, propionic acidemia, etc

### Ohtahara Syndrome
- Early onset within few months of life
- Frequent extensor tonic spasms
- EEG shows burst suppression pattern both during wakefulness and sleep
- Etiology: Structural (cerebral dysgenesis: lissencephaly, focal cortical dysplasia, etc)
- Medically intractable seizures that can evolve to West syndrome and eventually Lennox-Gastaut
- Poor prognosis: early death

Chapman and Rho
Neonatal Epileptic Encephalopathies – Ohtahara syndrome
<table>
<thead>
<tr>
<th>Condition</th>
<th>Gene mutation</th>
<th>Clinical features (abbreviations defined within text)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIEE1</td>
<td>$ARX$</td>
<td>Lissencephaly, infantile spasms, intellectual disability, myoclonic epilepsy</td>
</tr>
<tr>
<td>EIEE2</td>
<td>$CDKL5$</td>
<td>Atypical Rett, infantile spasms, tonic or myoclonic epilepsy</td>
</tr>
<tr>
<td>EIEE3</td>
<td>$SLC25A22$</td>
<td>Severe neonatal myoclonic epilepsy, hypotonia</td>
</tr>
<tr>
<td>EIEE4</td>
<td>$STXBPI$</td>
<td>Infantile spasms, non-syndromic intellectual disability without epilepsy</td>
</tr>
<tr>
<td>EIEE5</td>
<td>$SPTAN1$</td>
<td>Infantile spasms, central hypomyelination, intellectual disability</td>
</tr>
<tr>
<td>EIEE6</td>
<td>$SCN1A$</td>
<td>Dravet syndrome, GEFS+</td>
</tr>
<tr>
<td>EIEE7</td>
<td>$KCNQ2$</td>
<td>BFNC (benign clinical course), or early seizures, hypotonia, dystonia, basal ganglia and thalamic hyperintensities</td>
</tr>
<tr>
<td>EIEE8</td>
<td>$ARHGEF9$</td>
<td>Refractory epilepsy, hyperekplexia, intellectual disability, sleep disturbance, brain imaging abnormalities</td>
</tr>
<tr>
<td>EIEE9</td>
<td>$PCDH19$</td>
<td>EFMR, FIRES</td>
</tr>
<tr>
<td>EIEE10</td>
<td>$PNKP$</td>
<td>Microcephaly, early-onset intractable epilepsy, developmental delay, behavioral abnormalities</td>
</tr>
<tr>
<td>EIEE11</td>
<td>$SCN2A$</td>
<td>Dravet, BFNIS, GEFS+</td>
</tr>
<tr>
<td>EIEE12</td>
<td>$PLCβ1$</td>
<td>Tonic seizures, infantile spasms</td>
</tr>
<tr>
<td>SRGAP2</td>
<td></td>
<td>Tonic spasms and hypsarrhythmia</td>
</tr>
<tr>
<td>MEF2C</td>
<td></td>
<td>Evolving epilepsy picture with hypsarrhythmia, severe intellectual disability, stereotypic movements, cerebral malformations</td>
</tr>
</tbody>
</table>

*Genetics of Neonatal Epileptic Encephalopathies*

*Asher and Scaglia* (2012)
**Neonatal Seizures**

*Neonatal Epileptic Encephalopathies*

- **Burst Suppression**: complex burst of spikes, sharp waves and slow waves separated by episodes of flattening
  - Bursts duration: 1-5 secs
  - Flat periods: 3-10 secs

- **Pathophysiology**
  - Burst suppression is the normal EEG pattern in premature infants <30 weeks
  - Believed to reflect a diffuse structural/functional disturbance of grey matter connectivity

*FIGURE 1. Burst-suppression pattern in a 1-month-old boy: The burst is strictly correlated with the appearance of brief tonic seizures recorded over both the deltoids.*
EEG/Video
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

- **Benign**
  - Febrile seizures
  - Benign Partial Epilepsies of Infancy
  - Benign familial infantile epilepsy
  - Benign myoclonic epilepsy of Infancy

- **Epileptic encephalopathies**
  - Infantile spasms and West syndrome
  - Dravet Syndrome
Case 1:

14mo bb girl, history of irritability and lethargy for 3 days. Brought to ER by parents because of sudden episode of body stiffening followed by limpness and fine shaking of all extremities for 1 min. In ER, BP=75/50; HR=150/min; RR=40/min; T=38.6°C rectal; O2 sat=98% RA.

Case 2:

14mo bb girl, history of irritability and lethargy for 3 days. Brought to ER by parents because of sudden episode of body stiffening followed by limpness and fine shaking of right arm and leg lasting 20 min. In ER, BP=75/50; HR=150/min; RR=40/min; T=38.6°C rectal; O2 sat=98% RA.

Case 3:

14mo bb girl, ex-34 weeker, known seizure disorder, on Frisium, history of irritability and lethargy for 3 days. Brought to ER by parents because of sudden episode of body stiffening followed by limpness and fine shaking of all extremities for 1 min. In ER, BP=75/50; HR=150/min; RR=40/min; T=38.6°C rectal; O2 sat=98% RA.
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

*Febrile Seizures*

- Febrile seizures are defined as seizures that occur in association with fever, in the absence of CNS infection (meningitis, encephalitis) and in patients with no history of previous afebrile seizures.

- Occur in 3-4% of children between 3 months – 6 years (peak age 18-24 months).

- High recurrence (30-40%)
  - 10% of children experience $\geq$ 3 febrile seizures.
  - Factors that increase risk of recurrence include:
    - Young age at time of first febrile seizure (<18 months).
    - Family history of in first degree relative.
    - Low degree of fever while in the emergency department.
    - Brief duration between onset of fever and the first seizure.

- Etiology – genetic predisposition
  - 40% concordance rate for monozygotic twins versus 7% for dizygotic twins.
  - 8% if sibling with febrile seizures, 22% if sibling + parent.
  - Mode of inheritance: polygenic vs autosomal dominant with variable penetrance.
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

Classification of Febrile Seizures

Simple (typical)
• Generalized
• <15min in duration
• No recurrence in a 24hr period
• Normal neurological status before seizure

Complex (atypical)
• Focal
• >15min in duration (status epilepticus)
• Multiple episodes in a 24hr period
• Abnormal preexisting neurological status before seizure

• Risk of developing epilepsy in general population: ~ 1%
• Not increased with simple febrile seizures except might be mildly increased if multiple episodes, FHx of epilepsy, and age <12months at first seizure
• Increased to 2.4% with atypical febrile seizures
  • Risk of epilepsy increased with the presence of each atypical feature:
    • One atypical feature – 3%
    • Two atypical features – 6%
    • Three atypical features – 9%
    • Four atypical features – 12-15%
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

**Febrile Seizures**

- Treatment of febrile seizures and prevention of recurrences does not alter risk of later possible epilepsy - ∴ routine use of AEDs not recommended.
- Parents can be advised to use anti-pyretics for comfort care, but there is no evidence that it prevents recurrence of febrile seizures.
- Intermittent benzodiazepine can be used when recurrence is expected; excessive parental anxiety
  - Nitrazepam (Mogadon)
    - < 2years 1.25mg TID
    - >2years 2.5mg TID (Minimum 3days or until fever subsides)

- What investigations are necessary:
  - Simple febrile seizures: nothing
  - Complex febrile seizures: EEG ± neuroimaging

- What do parents want to know:
  - Is this harmful
  - Will it happen again
  - Can I prevent it?
  - Will my child develop epilepsy
  - Will it go away?
CONCLUSIONS

Clinicians evaluating infants or young children after a simple febrile seizure should direct their attention toward identifying the cause of the child’s fever. Meningitis should be considered in the differential diagnosis for any febrile child, and lumbar puncture should be performed if the child is ill-appearing or if there are clinical signs or symptoms of concern. A lumbar puncture is an option in a child 6 to 12 months of age who is deficient in Hib and S. pneumoniae immunizations or for whom immunization status is unknown. A lumbar puncture is an option in children who have been pretreated with antibiotics. In general, a simple febrile seizure does not usually require further evaluation, specifically EEGs, blood studies, or neuroimaging.
Approach to Febrile Seizures

**TREATMENT**

- Treatment of febrile seizures and prevention of recurrences does not in any way modify the later risk of possible epilepsy.
- Aside from the situation of febrile status epilepticus, there is no medical reason to treat febrile seizures on an ongoing basis.

**INVESTIGATION**

- Clinical suspicion of CNS infection?
  - Yes
  - Lumbar puncture
  - Atypical febrile seizure
  - Typical febrile seizure then
  - NO investigation needed

**FOCALITY of the SEIZURE type or fociality on EXAMINATION**

- Managed as per status epilepticus guideline
  - EEG and Neuroimaging
    - If abnormal EEG and/or neuroimaging
      - Neurology consultation (ED)

**Exception to the rule**

- Frequent recurrences
  - At least 2 FS in a child with expected recurrence(s)
    - (ex: age < 18 months, atypical FS)
  - Parental anxiety
  - Consider treatment with intermittent benzodiazepine
    - Nitrazepam (Mogedon)
      - Under the age of 2y: 1.25mg tid
      - Over the age of 2y: 2.5mg tid
    - If fever < 3 days: give for 3 days
    - If fever > 3 days: give until fever subsides

**Division of Pediatric Neurology**

Michael Shevell MD CM, FRCPC Director
Elisabeth Simard Tremblay MD

Approved by the divisions of Neurology and Emergency
February 2010
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

**Benign Partial Epilepsies of Infancy**

- Benign Partial Epilepsy with complex partial Seizures
- Benign Partial Epilepsy with secondary generalized seizures

<table>
<thead>
<tr>
<th></th>
<th>BPE with CPS</th>
<th>BPE with SGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>Normal development and exam</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No underlying neurological conditions</td>
<td></td>
</tr>
<tr>
<td>Onset</td>
<td>Within first year of life</td>
<td>Within first year of life (3-20months)</td>
</tr>
<tr>
<td>Seizures</td>
<td>Complex partial occurring in clusters</td>
<td>Partial (blank stare, crying) with secondary generalization</td>
</tr>
<tr>
<td>EEG</td>
<td>Normal interictal</td>
<td>Normal interictal</td>
</tr>
<tr>
<td></td>
<td>Ictal: temporal focus</td>
<td>Ictal: centroparietal focus</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Excellent response to Rx</td>
<td>Good neurodevelopmental outcome</td>
</tr>
</tbody>
</table>
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

**Benign Familial Infantile Convulsions**

**Table 2 Clinical and electroencephalographic characteristics of benign familial infantile seizures**

- Family history of seizures (similar age at onset, autosomal-dominant trait)
- Normal development before onset
- No underlying disorders or neurologic abnormalities
- Onset between 4 and 8 mo of age
- Seizures in clusters
- Partial seizures localized in the occipitoparietal areas
- Semiology: psychomotor arrest, cyanosis, head/eye deviation to one side (variable), tonic contraction, bilateral clonic jerks
- Normal interictal electroencephalogram
- Ictal electroencephalogram: fast activity originating in the occipitoparietal area
- Postictal electroencephalogram: lateralized occipitoparietal delta waves and spikes
- Normal developmental outcome
- Benign course

**Genetics: SCN2A**
Case:

15mo bb boy, developmentally normal, presents to ER with 3 weeks history intermittent sudden jerky movements of the head and upper extremities, lasting 1-2secs, worsening over the course of the past 3 weeks. Multiple episodes a day, sometimes in clusters. Resumes activity right after jerk with no apparent alteration. No other unusual movements. Unremarkable perinatal history. No FHx of epilepsy or other seizure disorders. Exam normal except for myoclonic jerks noted. Video-EEG normal, with no associated changes during myoclonic episodes.
Seizures in Infancy (<2yrs)

Infancy (<2yrs)

Girl aged 3 years with a 6 weeks history of frequent massive jerks of head and shoulders

Benign Myoclonic Epilepsy
Infant (<2yrs)

Case:

15mo bb boy, developmentally normal, presents to ER with 3 weeks history intermittent sudden jerky movements of the head and upper extremities, lasting 1-2secs, worsening over the course of the past 3 weeks. Multiple episodes a day, sometimes in clusters. Resumes activity right after jerk with no apparent alteration. No other unusual movements. Unremarkable perinatal history. No FHx of epilepsy or other seizure disorders. Exam normal except for myoclonic jerks noted. Video-EEG shows normal background, however myoclonic episodes are associated with epileptiform activity.
Infant (<2yrs)

Case 5:

6mo bb girl presents to ER with episodes of stiffening of upper extremities and abduction of arms. Multiple episodes a day, sometimes in clusters lasting 5-10min since 4months of age. Unremarkable pregnancy. Parents brought bb to ER at DOL3 for abnormal eye movements but were reassured and sent back home. BB’s development remarkable for left handedness. Neurological exam demonstrates decreased right arm movements and hyperreflexia and increased tone.
Case 5:

Here’s what her imaging looked like:
## Myoclonus in Infancy:

<table>
<thead>
<tr>
<th></th>
<th>Age of onset</th>
<th>Seizures</th>
<th>EEG pattern</th>
<th>Clinical features</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign myoclonus of infancy</td>
<td>4 to 7 months</td>
<td>Similar to infantile spasms Occur in clusters usually around mealtime Worsen over course of next weeks/months then stop spontaneously</td>
<td>Normal</td>
<td>Normal exam</td>
<td>None required</td>
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<td></td>
<td>Normal development</td>
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<td></td>
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<td></td>
<td>Resolves by age 2yrs</td>
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<tr>
<td>Benign myoclonic epilepsy</td>
<td>4months-2yrs</td>
<td>Myoclonic jerks (head nodding→severe enough to throw child onto floor)</td>
<td>Spike &amp; wave (3cps)</td>
<td>Normal exam</td>
<td>VPA</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Polyspike &amp; wave (3cps)</td>
<td>Normal development</td>
<td>Levetiracetam</td>
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<td></td>
<td></td>
<td></td>
<td>Resolves by age 2yrs</td>
<td></td>
</tr>
<tr>
<td>Infantile spasms</td>
<td>4 to 7 months</td>
<td>Brief symmetric contractions of neck, trunk, extremities (flexor, extensor, mixed)</td>
<td>Hysarrhythmia Slow spike &amp; wave Burst-suppression</td>
<td>Abnormal exam</td>
<td>ACTH</td>
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<td>Abnormal development</td>
<td>Vigabatrin</td>
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<td>Abnormal development</td>
<td>Rivotril</td>
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<td>*Tuberous sclerosis</td>
<td></td>
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</tbody>
</table>
Infantile spasms

- Bilateral (symmetrical or asymmetric), brief clusters of myoclonic extensor or flexor spasms, sometimes associated with a cry, typically are observed shortly after a sleep-wake transition.

- Peak age of onset: 4-7 months

- Constitute about 25% of all childhood epilepsies beginning in the first year of life

- Pathophysiology unclear

- Classified into:
  - Symptomatic (75%)
    - Structural lesion
    - Cerebral dysgenesis
    - Preexisting injury secondary to ischemic insult, infection
    - Neurocutaneous disorders (TS)
    - Down syndrome (T21)
    - IEM
  - Cryptogenic – non-identifiable hidden cause
  - Idiopathic – developmentally normal at seizure onset

- Prognosis depends on underlying etiology
  - Idiopathic IS tend to have a better outcome
Infantile spasms

- West syndrome
  - Triad of infantile spasms, hypsarrhythmia on EEG, and developmental arrest/regression

FIGURE 2. Five-month-old girl with Down syndrome and infantile spasms. Typical and symmetrical hypsarrhythmia that is interrupted after a spasm (arrow) initiating a cluster of spasms (not shown). Note rapid rebuilding of hypsarrhythmia after the spasm.
Case

3 year old boy, with history of 5 febrile seizures in the past. First febrile seizure was atypical, at age of 7 months. Subsequent seizures have different semiology (atonic, myoclonic). Was meeting developmental milestones until ~1.5 years ago when he began to deteriorate with regression in development. Myoclonic jerks at age 18 months.
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

- **Benign**
  - Febrile seizures
  - Benign Partial Epilepsies of Infancy
  - Benign familial infantile epilepsy
  - Benign myoclonic epilepsy of Infancy

- **Epileptic encephalopathies**
  - Infantile spasms and West syndrome
  - Dravet Syndrome (Severe myoclonic epilepsy of Infancy)
Epileptic Encephalopathies of Infancy

**Severe Myoclonic Epilepsy of Infancy (SMEI, aka Dravet Syndrome)**

- Intractable epilepsy
- Begins in first year of life usually with prolonged hemiclonic febrile seizures
- Over time seizures evolve into febrile/afebrile generalized seizure types (myoclonic, atypical absence and partial complex) which rapidly become refractory to AEDs
- Myoclonic jerks between 12-36 months
- Prior to onset of seizures child is developmentally normal → ataxia, psychomotor regression, mental retardation
- EEG initially normal → generalized spike wave abnormalities
- 70-80% have mutation in SCN1A
  - >500 mutations associated with Dravet syndrome
  - Unlike GEFS+ where SCN1A mutations segregate with families, most mutations in Dravet syndrome are de novo (but familial SCN1A mutations also occur)
Pediatric Epilepsy Syndromes with Onset in INFANCY (< 2yrs)

- **Benign**
  - Febrile seizures
  - Benign Partial Epilepsies of Infancy
  - Benign familial infantile epilepsy
  - Benign myoclonic epilepsy of Infancy

- **Epileptic encephalopathies**
  - Infantile spasms and West syndrome
  - Dravet Syndrome
EEG/Video
Case:

Healthy 7 year old boy, brought to ER because parents noticed unusual event after patient went to bed. Heard gurgling noises from his room, found him sitting in bed with right lower face jerking, excessive drooling and unable to speak. Lasted 2min and was completely back to baseline. Developmentally normal. Exam normal. EEG shows ...
Pediatric Epilepsy Syndromes with Onset in Childhood (2yrs - Adolescences)

- **Benign**
  - Benign epilepsy with centrotemporal spikes (BECTS)
  - Generalized epilepsy with febrile seizures plus (GEFS+)
  - Panayatopoulous syndrome
  - Childhood absence epilepsy
  - Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE)

- **Epileptic encephalopathies**
  - Lennox-Gastaut
  - Epileptic encephalopathy with continuous spikes during slow wave sleep (ESES)
  - Landau-Kleffner
  - Epilepsy with myoclonic-atonic (astatic) seizures
Benign Epilepsy with Centrotemporal spikes (BECTS/Rolandic epilepsy)

• Most common form of idiopathic epilepsy in childhood

• Peak age of onset: 5-10 years (range 3yrs-13yrs)

• Developmentally & intellectually normal

• Strong genetic predisposition

• **Seizures:**
  • brief (1-2min)
  • infrequent
    - 10% of children will only have one seizure → Majority (70%) will seize 2-6x
  • Majority have nocturnal seizures only
  • Hemifacial clonic movements, speech arrest, dysarthria and excessive drooling
  • Preceding paresthesias in mouth, gum, cheeks or lips may occur
  • May have involvement of ipsilateral limbs or even generalization
Benign Epilepsy with Centrotemporal spikes (BECTS/Rolandic epilepsy)

• EEG
  • Normal background in awake and sleep
  • Epileptiform discharges: focal, diphasic spike-and-slow-wave discharges over rolandic/centrotemporal regions; unilaterally or independently bilaterally
  • Horizontal dipole with maximum spike negativity over central/temporal regions and maximum positivity over frontal region.

• Rx:
  • Often not necessary unless frequent and disruptive to child’s life
  • Carbamazepine, Clobazam, Trileptal

• Spontaneous resolution by adulthood (18yrs)

• Neuroimaging if EEG findings are focal
Case:

Healthy 6year old girl, brought to ER because parents noticed unusual event. Patient hurt herself whilst playing outside. Came indoors to mom, crying +++ then suddenly she stopped crying, eyes staring ahead, some blinking movements. Lasted 5secs then she snapped out of it and continued crying. Developmentally normal except parents report she is often “dans la lune”. Also, teachers complain that her grades have dropped during this academic year and that she continuously “stares off into space”. Exam completely normal.
Childhood (2yrs-adolescence)

*Childhood Absence Epilepsy*

- Idiopathic generalized epilepsy syndrome

**Age of onset**: 4yr to 10 yrs (peak 5-7yrs)
  - Onset before age 3yrs associated with an increased likelihood of neurodevelopmental abnormalities & probably represents another epilepsy syndrome

**Clinical Presentation**:
  - More frequent in girls
  - Developmentally and intellectually normal children

**Seizures** are brief (4-20secs) abrupt onset of impaired consciousness and unresponsiveness
  - Typically sudden onset and interruption of activity with blank stare
  - Abrupt end and child continues ongoing activity unaware that a seizure occurred
  - If other seizure types present (myoclonic, atonic, tonic-clonic) then not CAE!
  - Frequent (up to 100s/day)
  - Provoked by hyperventilation in 90% of children
Childhood Absence Epilepsy

• EEG: ictal events show generalized symmetric 3HZ spike-wave discharges

• Prognosis – excellent
  • Complete remission 2-6yrs after onset
  • Rx: Ethosuximide, VPA, Lamotrigine

• However,
  • Up to 30% can continue into adulthood, and these have a greater chance (40%) to get generalized tonic-clonic seizures
  • CAE can precede juvenile myoclonic epilepsy in 11-18% of cases

• Must be differentiated from Juvenile Absence Epilepsy (JAE)
  • Older age of onset: 10yrs to 16yrs
  • Infrequent absences with longer duration (>20secs)
  • More likely to experience generalized tonic-clonic seizures
  • EEG: 3.5Hz to 4Hz generalized spike-wave discharges
  • Good response to Rx, but usually lifelong
Case:

Healthy 6 year old boy, brought to ER because of recurrent events of sudden onset of nausea and protracted vomiting lasting up to 20-30min. Sometimes accompanied by eye deviation. Sometimes accompanied by headaches. Diagnosed with migraines on several occasions. No FHx of migraines or car sickness. Exam completely normal.
Benign Childhood Occipital Epilepsy (Panayiotopoulos Syndrome)

• Most common of the benign focal epilepsies of childhood after BECTS

• **Age of onset**: 1-14 years (peak 4 – 5 years)

• **Clinical manifestations**:
  • Autonomic changes at seizure onset
    • seizures usually begin with emetic symptoms (nausea, retching, vomiting)
    • Other autonomic features: pallor, mydriasis
    • May have loss of consciousness
    • May have headache
  • Eye or head deviations
  • Convulsions (20% hemiconvulsions, 20% generalized tonic-clonic seizures) at end of seizure

• **EEG**: normal background, multifocal spike wave discharges with posterior predominance (may occur anteriorly)

• **DDx**: migraine, gastroenteritis

• **Rx**: carbamazepine, Valproic acid

• Good prognosis
Benign Childhood Occipital Epilepsy (Panayiotopoulos Syndrome)

EEG variability in Panayiotopoulos syndrome in 6 children with autonomic seizures

Laplacian montage

Panayiotopoulos CP 2005
**Generalized Epilepsy with Febrile Seizures Plus (GEFS+)**

- Recently renamed “Genetic epilepsy with Febrile Seizures Plus”
- Incidence unknown due to the absence of epidemiological studies
- GEFS+ describes a spectrum of epilepsy phenotypes that can be seen in different members within the same family
- These phenotypes can range from:

  - **MILD**
    - Classical Febrile Seizures
    - Febrile Seizures Plus
  - **SEVERE**
    - Dravet syndrome
    - Myoclonic-Astatic epilepsy
Seizures in Childhood (2yrs-Adolescence)

Generalized Epilepsy with Febrile Seizures Plus (GEFS+)

- Types of Epilepsy seen in individuals with GEFS+

  - **Classical Febrile seizures:**
    - Occur in up to 5% of children, commonly between age of 6 months – 6 years
    - Seizures occur in the context of fever (T > 38°C)
    - EEG: Normal

  - **Febrile Seizures Plus:**
    - Febrile seizures occur outside the normal age range (continue past 6 years) or
    - Febrile and afebrile seizures occurring between 6 months – 6 years, or
    - Febrile seizures stop by age 6 years and afebrile seizures continue, or
    - Febrile seizures stop by age 6 years and afebrile seizures start.
    - EEG: Normal or may show irregular spike-wave discharges.

- **Myoclonic-astatic epilepsy (Doose syndrome):**
  - Characterized by drop attacks due to myoclonic-atonic seizures
  - Children can experience independent myoclonic and atonic seizures
  - About 1/3 of patients with Doose syndrome have febrile seizures at the onset of their seizure disorder
  - Variable developmental outcome: normal intellect ➔ significant intellectual disability
  - EEG: Fast generalized spike-wave activity

- **Dravet syndrome (Severe myoclonic epilepsy of infancy)**
Seizures in Childhood (2yrs-Adolescence)

**Generalized Epilepsy with Febrile Seizures Plus (GEFS+)**

- 4 genes implicated in GEFS+:
  - **SCN1A**: α-subunit of voltage-gated sodium channel
  - **SCN1B**: β-subunit of voltage-gated sodium channel
  - **GABRG2**: γ2-subunit of GABA(A) receptor
  - **GABRD**: δ-subunit of GABA(A) receptor

- Clinical testing:
  - Sequence analysis: detects 73-92% of mutations
  - Deletion analysis: detects 8-27% of mutations

- Overall, these ion-channels subunits have only been found in 10-20% of GEFS+ families studied

- Inheritance is autosomal dominant with 60% penetrance
  - Unclear what contributes to the phenotypic variability seen in these families
  - Suggestive of complex inheritance with interactions of various as of yet unidentified genes ± environmental interactions

- Findings in a family that have some specificity for SCN1A-related seizure disorders include the following:
  - One or more family members with epilepsy, especially of more than one type
  - Febrile seizures before age one year
  - Febrile seizures after age six years
  - Febrile seizures with unusual severity (including status epilepticus)
  - Febrile seizures that precede unprovoked (i.e., afebrile) seizures
Seizures in Childhood (2yrs-Adolescence)

**Severe Myoclonic Epilepsy of Infancy (SMEI, aka Dravet Syndrome)**

- What explains the phenotypic variability between GEFS+ and Dravet syndrome?
  - GEFS+ mostly missense mutations that occur outside the pore-forming region
  - DS mutations usually involve the pore-forming region of the channel
  - Missense mutations in GEFS+ often alter the function of the channel but do not completely abolish it whereas in DS, most mutations cause truncation and loss of function of the channel
  - Remember that these Sodium channels are found predominantly on interneurons – therefore complete loss of function will result in disinhibition
Case:

Healthy 5-year-old boy, with previous diagnosis of night terrors, admitted to telemetry for investigation of frequent episodes that occur in clusters mostly at night but sometimes during the day during which he becomes agitated, has a scared look on his face, last a few seconds. FHx: epilepsy in grandfather, uncle with parasomnias.
Childhood (2yrs-adolescence)

Autosomal Dominant Nocturnal Frontal Lobe Epilepsy

- Characterized by clusters of nocturnal motor seizures
  - Hyperkinetic body movements involving limbs, head or trunk
  - Complex, often violent behaviour
  - Dystonic-dyskinetic component
  - Cycling, rocking or repetitive movements
  - Patient may vocalize, scream or swear
  - Expression of fear
  - Brief (5 seconds to 5 minutes)
  - Occur during non-REM sleep
  - May have daytime seizures

- Patients may also have paroxysmal arousals
  - Sudden arousal
  - Opening of eyes
  - Sitting up in bed
  - Frightened expression

- May also present with epileptic wandering
  - Mimicks sleepwalking with semi-purposeful ambulatory behaviour

- Family History often present
  - Patients with ADNFLE often have normal intelligence but some families with intellectual disability have been recently reported
**Childhood (2yrs-adolescence)**

*Autosomal Dominant Nocturnal Frontal Lobe Epilepsy*

- **EEG:**
  - Interictal EEG is usually normal with epileptiform activity seen only in 33% of individuals during wakefulness and 45% during sleep
  - Ictal EEG demonstrates no epileptic activity in 50% of cases (in 10% may see focal fast activity and in another 10% slow spike-and-wave activity)

- The **diagnostic clinical features** of autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE):
  - Cluster of seizures with a frontal semiology
  - Occurrence of seizures dominantly during sleep
  - Absence of neurologic deficits
  - Normal findings on neuroimaging
  - Ictal EEG that may be normal or obscured by movement artifact
  - Interictal EEG that shows infrequent epileptiform discharges
  - Presence of the same disorder in other family members with evidence of an autosomal dominant mode of inheritance

- **Genetic basis:**
  - Autosomal dominant with 70% penetrance
  - Four genes implicated, but these account for only 15% of patients with ADNFLE
    - **CHRNA2** (chromosome 8p21)
    - **CHRNA4** (chromosome 20q13.2)
    - **CHRNB2** (chromosome 1q21)
Case 9b: Structural FLE
Pediatric Epilepsy Syndromes with Onset in Childhood (2yrs - Adolescences)

- **Benign**
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  - Childhood absence epilepsy
  - Panayatopoulous syndrome
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- **Epileptic encephalopathies**
  - Epilepsy with myoclonic-atonic (astatic) seizures
  - Lennox-Gastaut
  - Epileptic encephalopathy with continuous spikes during slow wave sleep (ESES)
  - Landau-Kleffner
  - Rasmussen’s encephalitis/syndrome
Epilepsy with Myoclonic-Atonic (Astatic) Seizures (Doose Syndrome)

- Idiopathic generalized epilepsy

- **Age of onset**: 7 months – 6 years (peak 2-4 years)

- **Clinical manifestations**:
  - Normal development and exam prior to onset of seizures
  - May have a history of febrile seizures or afebrile generalized seizures a few months prior to onset of myoclonic-astatic seizures in 2/3 of children

- **Seizures**
  - Myoclonic-astatic (myoclonic-atonic) seizures: myoclonus → loss of postural tone
  - Atonic seizures: sudden, brief and severe loss of postural tone involving the whole body or just the head
  - Myoclonic jerks
  - Brief absence seizures (>50% cases)
  - Myoclonic-atonic status lasting hours or days

- **Etiology**:
  - Presumed multifactorial/polygenic with variable penetrance (1/3 have FHx of IGE)
  - GLUT1 mild mutations

Panayiotopoulos CP 2005
Epilepsy with Myoclonic-Atonic (Astatic) Seizures (Doose Syndrome)

• EEG:
  • Interictal EEG:
    • Initially may be normal with possible rhythmic theta activity in the parasagittal regions
    • Subsequently, when myoclonic-atonic seizures appear: frequent clusters of 2–3 Hz GSWD interrupted by high amplitude slow waves in cases with predominant atonic or myoclonic-atonic seizures. In children with predominantly myoclonic seizures, paroxysms of irregular spikes or polyspike–wave complexes prevail.
  • Ictal:
    • Myoclonic & atonic seizures: Discharges of irregular spike–wave or polyspike–wave complexes at a frequency of 2.5–3 Hz or more
    • Atonia: slow wave of a single or multiple spike–wave complex and the intensity of the atonia is proportional to the amplitude of the slow wave. Drop attacks are associated with diffuse EMG paucity indicating their true atonic nature.

• DDx: BME, Lennox-Gastaut, Dravet syndrome, late onset West syndrome

• Prognosis is variable:
  • 50% may achieve seizure-free state and normal development
  • 50% may have developmental regression and seizure disorder
Childhood (2yrs-adolescence)

Irregular polyspike-wave complexes

Myoclonic Astatic Epilepsy
Lennox-Gastaut syndrome

- Intractable pediatric epilepsy

- **Onset:** 2 to 8yrs (peak 3 to 5years)
  - Male predominance
  - 2/3 of cases are symptomatic i.e. have pre-existing brain abnormalities
    - 1/3 of cases have history of infantile spasms
    - 1/3 are cryptogenic affecting children who are initially developmentally & neurologically normal

- **Classic triad:**
  - Multiple generalized seizure types (tonic, atonic, myoclonic, atypical absence)
  - **EEG:**
    - Abnormal background
    - generalized burst of 2-2.5Hz spike-wave complexes during atypical absence/atonic seizures
  - Cognitive dysfunction (which may not be present at onset)

- Poor response to AEDs (VPA, lamotrigine, topiramate)
  - Ketogenic diet: significant reduction in seizures in 50% of patients

- **Prognosis:** poor with mental handicap in 80% of cases
Childhood (2yrs-adolescence)

**Lennox-Gastaut syndrome**

Boy aged 11 years with severe learning difficulties and frequent multiformal seizures of Lennox-Gastaut

Panayiotopoulos CP 2005
Electrical Status Epilepticus in slow sleep (ESES):

- ESES was first described in 1971

- Comprises of 2 clinically related syndromes:
  - Continuous spike-wave in sleep (CSWS)
  - Landau Kleffner syndrome (Acquired epileptic aphasia)

- ESES used synonymously with CSWS

- **Age of onset**: 3 to 8 years

- Usually history of normal development with regression in preschool years
  - CSWS: global regression, decreased intellectual level, poor memory, hyperkinesis, motor impairment, psychosis
  - LKS: acquired auditory agnosia

- **EEG**:
  - CSWS: frontal and multifocal sharp waves that become continuous during sleep
  - LKS: centrotemporal sharp waves that increase during sleep (50% or more of NREM sleep)
**Electrical Status Epilepticus in slow sleep (ESES):**

- Occurs in children with
  - benign partial epilepsies (ex BECRS, BOE),
  - epileptic encephalopathies (LGS)
  - structural pathologies (CP, hydrocephalus, etc)

- Prognosis related to duration of ESES
  - The longer the duration, the higher the chance for residual intellectual deficits even when seizures are controlled.
  - Therapeutic window 12-18months

- **Rx:** oral steroids and high dose diazepam, high dose VPA, ESM and clobazam

*Kramer et al., 2009*
Childhood (2yrs-adolescence)

**Rasmussen syndrome**

- Syndrome characterized by intractable, partial motor seizures with progressive deterioration in motor and cognitive function, hemiparesis and unilateral cortical atrophy
- Restricted to one hemisphere
- Pathophysiology: autoimmune process
- Seizures often refractory to medication
- Ultimate Rx: hemispherectomy to improve seizure control and prevent further cognitive and behavioural deterioration
Figure 2. Serial MRI and histopathologic findings of a girl with onset of the disease at 1.7 years of age.

EEG/Video
Case:

15 year old girl, previously healthy and developmentally normal, experienced a 2 minute generalized tonic-clonic seizure in the morning while on vacation with parents. Admitted to staying up later than usual. Denied alcohol/substance abuse. Mom reports that for the past couple of years, has had episodes when she would drop her dishes. Also reported early morning limb jerks. Otherwise, developmentally normal. Exam normal.
Pediatric Epilepsy Syndromes with Onset in ADOLESCENTS

- **Benign**
  - Juvenile Absence Epilepsy (JAE)
  - Juvenile Myoclonic Epilepsy (JME)

- **Epileptic encephalopathies**
  - Progressive Myoclonic Epilepsies (PME)
Juvenile Myoclonic Epilepsy (JME)

• Most common form of idiopathic generalized epilepsy

• **Age of onset**: 12 to 18 years (peak 15 yrs)

• **Clinical Presentation**: Neurological and developmentally normal

• **Seizures**:
  - Typically first seizures noted are early morning generalized tonic-clonic seizures precipitated by sleep deprivation
  - Often there is a preceding history of: Myoclonic jerks and absence seizures
  - Triggers: Sleep deprivation; Alcohol consumption; Menstruation

• **EEG**: 4Hz to 6Hz generalized atypical spike and polyspike-and-wave discharges with normal background
  - Photosensitivity in 30-90% of cases

• **Prognosis**: excellent response to AEDs (VPA) but lifelong Rx necessary
  - Avoid carbamazepine, phenytoin and gabapentin as these exacerbate myoclonus
Progressive Myoclonic Epilepsies

- Represents a group of disorders characterized by myoclonic seizures, tonic-clonic seizures, and progressive neurological deterioration typically with cerebellar signs and dementia.

- Myoclonus in PME is typically:
  - Fragmentary and multifocal
  - Precipitated by posture, action or external stimuli (light, sound, touch)

- Five main causes of PME include:
  1. Unverricht-Lundborg disease: CSTB gene
  2. Sialodosis: Neuraminidase deficiency
  3. Neuronal ceroid lipofuscinosis (NCL): TPP1, CLN3, CLN5
  4. Myoclonic epilepsy with ragged red fibers (MERRF): MTTK
  5. Lafora disease: EPM2A
  6. Dentatorubral-pallidoluysian atrophy (DRPLA): CAG repeats
EEG/Video
Interesting Videos

Case 11:

6-year-old girl, previously healthy and developmentally normal, presenting with episodes of hysterical inappropriate laughing. Otherwise, developmentally normal. Exam normal.
Case 11:

6 year old girl, previously healthy and developmentally normal, presenting with episodes of hysterical inappropriate laughing. Otherwise, developmentally normal. Exam normal.
Case 12:

Case 13:

2day old bb girl in NICU presenting with “seizures”. Unremarkable pregnancy except mom often noticed episodes of prolonged repetitive baby movements lasting a few minutes which she attributed to hiccups. In NICU baby had frequent seizures. Started on anticonvulsants. No improvement despite 2 meds (Phenobarbital, Topamax). Normal MRI. Normal exam. No FHx of seizures. No consanguinity.
**Hyperekplexia**

- Syndrome of exaggerated response to tactile, auditory, or other stimuli

**Clinical presentation:**
- Can present early in the neonatal period with episodes of stiffening that can be so severe to cause apnea and death
- With age, these episodes are replaced by startle responses consisting of stiffening and falls.

**Genetics:**
- Autosomal recessive, Autosomal dominant or sporadic
- Mutations in glycine receptor gene (GLRA1, GLRB), glycine transporter gene (SCL6A5), glycine clustering molecule gene (GPHN) and collybistin gene (ARHGEF9)

**Treatment:**
- Clonazepam
- “Counteract the hypertonia”: flex the head and neck towards the trunk during an attack

**Prognosis:**
- In severe cases, death secondary to apnea and cardiac arrest
- Feeding difficulties in some patients
- Normal development
Summary

• Childhood epilepsy syndromes are a group of developmental epilepsies defined by their clinical presentation, age of onset, EEG signature, seizure semiology, response to treatment and prognosis

• EEG plays an integral role in making diagnosis of an epilepsy syndrome and thus in dictating management
References


○ Stafstrom CE. (2009) Severe epilepsy syndromes of early childhood: the link between genetics and pathophysiology with a focus on SCN1A mutations. J Child Neurol. 2009 Aug;24(8 Suppl):15S-23S.


