Pediatric Epilepsy

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Spell
(or event or attack)

• is a noncommittal (honest) term used when the nature of an attack is uncertain.
• Is it a seizure or a seizure equivalent?
• Is the seizure really a generalized or a focal brain disturbance?
• Unless the nature of concurrent brain electrical activity is known with certainty, medically precise terms like “petit mal seizure” should not be applied to an attack of stereotyped behavior.
Seizure

• is a paroxysmal disturbance of brain electrical activity. Seizure types are classified based on both EEG and behavioral changes during a seizure.

• 8-10% of the population will have a seizure by age 80, 4-5% by age 20
Epilepsy

- is recurrent unprovoked seizures.
- Prevalence (or percent of the population actively experiencing recurring seizures) varies from 0.2 - 1%, usually 0.7%.
- In other words, most seizures do not recur, and those that do often do not persist.
Epilepsy Syndrome

- is a characteristic clinical constellation of one or more seizure types, plus certain EEG, genetic, pathological or prognostic features.

- Unlike disease, it may not have uniform etiology and prognosis.

- CAT scans, MRI scans, PET scans, interictal EEGs, psychological tests, etc. cannot determine whether or not a certain behavior is a seizure. They may help define the seizure type and syndrome and therefore the treatment and prognosis.
## Nonepileptic Seizure "Equivalents"

<table>
<thead>
<tr>
<th>Childhood</th>
<th>Adolescents and adults</th>
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<tbody>
<tr>
<td>* Migraine</td>
<td>* Pseudoseizures</td>
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<td>* Gastroesophageal reflux</td>
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<td>* Benign paroxysmal vertigo</td>
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<td>Shudders and Startles</td>
<td>Syncope</td>
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<td>Transient global amnesia</td>
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<td>Breath-holding spells, pallid infantile syncope</td>
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<td>Sleep disorders (somnambulism, night terrors)</td>
<td>Automatic behavior syndrome</td>
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<td>Cyclic vomiting, recurrent abdominal pain</td>
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* May not always be associated with impairment of consciousness
Psychogenic Nonepileptic Seizures

• PNES are commonly misdiagnosed as epilepsy.
• It is by far the most frequent nonepileptic condition seen in epilepsy centers, where they represent 20-30% of referrals.
• About 50-70% of patients become seizure-free after diagnosis, and about 15% also have epilepsy.
• Like most manifestations of conversion and other somatoform disorders, PNES occur more frequently in women (approximately 70% of cases) than in men.
• Frontal lobe seizures can be mistaken for PNES.
• **Recurrence, frequency and risk** determine the need for medication.

• **Seizure type** determines the type of medication

• **Epilepsy syndrome** determines etiology (and need for scans), age limited features (and prognosis for remission), as well as such issues as potential surgical interventions and developmental liabilities.
Classification of epilepsy

- Based on underlying etiology
- Based on EEG
Symptomatic vs idiopathic epilepsy

• Symptomatic: caused by an identifiable injury to the brain

• Idiopathic: no obvious cause
Some Causes of Symptomatic Localization-Related Epilepsy

• Vascular:
  – Stroke
  – Infantile hemiplegia
  – AVM
  – Sturge-Weber syndrome
  – Aneurysms
  – Venous thrombosis
  – Hypertensive encephalopathy
  – Blood dyscrasias (sickle cell disease)

• Tumors:
  – Meningiomas
  – Gliomas
  – Hamartomas
  – Metastatic tumors

• Infectious:
  – Abscess
  – Meningitis and encephalitis
  – Toxo
  – Rubella
  – Rasmussen’s syndrome
  – Cysticercosis

• Degeneratives:
  – Alzheimer’s
  – MS

• Congenital:
  – Heterotopias
  – Cortical dysplasia

• Traumatic:
  – Prenatal and perinatal injuries
  – Head injuries
Focal vs Generalized Epilepsy

- Focal and generalized EEG discharges define partial and generalized seizures, respectively.
OUTLINE OF THE INTERNATIONAL CLASSIFICATION OF EPILEPTIC SEIZURES

• Partial seizures (seizures with focal onset)
  – Simple partial seizures (consciousness unimpaired)
    • With motor signs
    • With somatosensory or special sensory symptoms
    • With autonomic symptoms or signs
    • With psychic symptoms (higher cerebral functions)
  – Complex partial seizures (consciousness impaired)
    • Starting as simple partial seizures
      – Without automatisms
      – With automatisms
    • With impairment of consciousness at onset
      – Without automatisms
      – With automatisms
  – Partial seizures evolving into secondarily generalized seizures

• Generalized seizures
  – Absence seizures: Brief lapse in awareness without postictal impairment (Atypical absence seizures may have the following: Mild clonic, atonic, tonic, automatism, or autonomic components.)
  – Myoclonic seizures: Brief, repetitive, symmetric muscle contractions (loss of tone)
  – Clonic seizures: Rhythmic jerking; flexor spasm of extremities
  – Tonic seizures: Sustained muscle contraction
  – Tonic-clonic seizures
  – Atonic seizures: Abrupt loss of muscle tone

• Unclassified epileptic seizures

* From Committee on Classification and Terminology of the International League Against Epilepsy, Epilepsia 1996; 38(11):1051-1059.
Generalized Epilepsy
• **Common semantic confusion:**

• “*Secondarily generalized seizures*” are partial-onset seizures that spread and generalize. They may be seen in either benign partial or common potentially lesional partial epilepsies.

• “*Primary generalized epilepsy*” is a constellation of any number of generalized-onset seizure types.
Focal Epilepsy
Left Temporal, FT9 maximal, Sharps

Bipolar (double banana,s) Montage
# Clinical seizure type

- **Focal or partial seizures** originate in a focus or part of the brain. *They may or may not spread to other parts or the whole brain.*

  - **SPS** Focal seizures which do not spread are called simple partial seizures. They are often associated with auras ("a breeze", or momentary disturbance of function).

  - **CPS** Focal seizures which spread bilaterally are called complex partial seizures. They are associated with loss of awareness and inability to correctly respond to the environment.

  - **GTCS** Focal seizures which spread to the entire brain are called secondarily generalized partial seizures (SGTCS). They are associated with convulsions.

- **Generalized seizures** originate uniformly in the entire brain. *There is no focus. There is no aura.*

  - **GTCS** Nonfocal (primary generalized) tonic stiffening alternating with rhythmic clonus.

  - **Tonic** Pure bilateral stiffening.

  - **Clonic** Pure rhythmic bilateral flexion and extension.

  - **Absences** Brief behavioral arrest with unresponsiveness only, or with very simple ocular or oral automatisms.

  - **Atypical Absence** Longer absence, complicated automatisms, poorer response to medications, <3 / see spike wave.

  - **Myoclonic** Lightening fast single bilateral jerk, may repeat.

  - **Atonic** Sudden generalized loss of tone, uncommon.

  - **Astatic** Drop attacks due to tonic, myoclonic, or atonic seizures.

### “Best” Medications

- CBZ (Tegretol / carbamazepine)
- PHT (Dilantin / phenytoin)
- PB (phenobarbital)
- LEV (Keppra / levetiracetam)
- LTG (Lamictal / lamotrigine)
- OCBZ (Trileptal / oxcarbazepine)
- TGB (Gabitril / tiagabine)
- TPM (Topamax / topiramate)
- VPA (Depakote / valproic acid)
- ZNS (Zonegran / zonisamide)

*Note: (VPA, LTG, and ZNS may have efficacy for all seizure types)*

- VPA / LTG / TPM / ZNS / PHT / PB / CBZ / most AEDs
- VPA / LTG / ZNS / ESM (Zarontin / ethosuximide) / CZP (Klonopin / clonazepam)
- VPA / LTG / ZNS / CZP
The Major Epilepsy Syndromes

Symptomatic / Cryptogenic / Lesional

Adult

Idiopathic / Benign / Primary

Child
Pediatric epilepsy syndromes by age of onset

• Newborns
  – Benign idiopathic neonatal convulsions (fifth-day fits)
  – Benign familial neonatal convulsions
  – Early myoclonic encephalopathy
  – Severe idiopathic status epilepticus
  – Early infantile epileptic encephalopathy with suppression-burst
Pediatric epilepsy syndromes by age of onset

• Infants
  – Febrile convulsions
  – West’s syndrome
  – Benign myoclonic epilepsy in infants
  – Severe myoclonic epilepsy in infants
  – Myoclonic epilepsy in nonprogressive encephalopathies
  – Myoclonic-astatic epilepsy of early childhood
  – Lennox-Gastaut syndrome
Pediatric epilepsy syndromes by age of onset

• Children
  – Childhood absence epilepsy
  – Epilepsy with myoclonic absences
  – Epilepsy with generalized convulsive seizures
  – Benign partial epilepsy
  – Benign epilepsy with centrotemporal spikes (Rolandic)
  – Benign psychomotor epilepsy
  – Benign epilepsy with occipital spike-waves (BEOSW)
  – Other benign partial epilepsies
  – Benign partial epilepsy with extreme somatosensory evoked potentials
  – Landau-Kleffner syndrome
  – Epilepsy with continuous spikes and waves during sleep
  – Epilepsy with photosensitivity
  – Eyelid myoclonia absence
  – Self-induced epilepsy
Pediatric epilepsy syndromes by age of onset

• Older children and adolescents
  – Juvenile absence epilepsy
  – Juvenile myoclonic epilepsy (JME)
  – Epilepsy with grand mal on awakening (GME)
  – Benign partial seizures of adolescence
  – Kojewnikoff’s syndrome
  – Progressive myoclonus epilepsies
    • Juvenile Gaucher’s
    • Juvenile neuronal ceroid lipofuscinosis (NCL)
    • Lafora’s body disease
  – Unverricht-Lundborg disease
    • Cherry-red spot myoclonus
    • Dyssynergia cerebellaris myoclonica (Ramsay Hunt Syndrome)
    • Mitochondrial encephalopathy
Special pediatric seizures and epilepsy syndromes
Neonatal Seizures

- are never generalized, due to the incomplete myelination.
- They often appear fragmentary or multifocal.
- Pre and perinatal injury and metabolic causes are most common.
- Neonatal ictal behaviors usually change within a few months.
Neonatal Seizures

• Benign familial neonatal convulsions: BFNC

• Benign idiopathic neonatal convulsions (fifth day fits): BINC
Neonatal Seizures

**Benign familial neonatal convulsions:**
- Seizures occur in otherwise **healthy neonates**.
- In 80% of patients, onset is on **day 2 or 3 of life**. However, seizures can occur any time in the neonatal period through age 3 months.
- Seizure types: **clonic** or **apneic**
- BFNC have been proven to be epileptic by electroclinical correlation
- No specific EEG criteria
- BFNC is **inherited** as an **autosomal-dominant** disorder
- Phenobarbital is the most commonly used drug for treatment of BFNC
- Approximately **14%** of these patients later develop epilepsy
Neonatal Seizures

Benign idiopathic neonatal convulsions: "fifth day fits"

- They have no known cause or concomitant metabolic disturbances
- Seizures occur around the fifth day of life
- Normal neurologic state before and between seizures
- Clonic and/or apneic seizures
- Normal biological and radiological examinations
- Interictal EEG often shows alternating sharp theta waves
- There is no recurrence of seizures, and the psychomotor development is not affected
Febrile seizures

- Febrile seizures are common. is the most common human convulsive event.
  - 2-5% in north America and Europe
  - 7-14% in Japan and Pacific islands

- Typical age range between 6months – 5years.

- FS is benign even though 1/3 of the children will have recurrent febrile seizures.
Febrile seizures

• They are classified separately:

  – **Simple febrile seizures**
    (1) brief
    (2) do not recur within 24 hours
    (3) generalized

  – **Complex febrile seizures** 30% of FS is distinguished as complex FS.
    (1) longer than 15 minutes
    (2) 2 or more seizures in 24 hours
    (3) focal
Febrile seizures

• Simple febrile seizures do not increase the risk of epilepsy or developmental problems, and are often not treated unless they are frequently recurrent.

• Complex febrile seizures may increase the risk of epilepsy slightly (to 3-10%), but are usually not treated unless problematic or associated with other risks.
FS → Epilepsy

• Characteristics that can predict non-benign long-term outcomes:
  – Neurodevelopmental abnormalities
  – FH of epilepsy
  – Recurrent FS
  – Brief duration of fever before FS
  – Complex FS
Febrile seizures

• Daily phenobarbitol (or valproate) or intermittent Valium with fever are the only effective preventative treatments.
Febrile seizures

- Retrospective studies of patients with epilepsy: 10-15% had previous FS. The association differs as a function of the type of epilepsy:
  - 11% in idiopathic generalized epilepsy
  - 25% in temporal lobe epilepsy (TLE)
  - 5-6% in partial epilepsy other than TLE
FS and MTLE

• Whether complex FS is the cause of hippocampal sclerosis and MTLE is one of the most controversial issues in epilepsy research.
FS and MTLE

• The high frequency of antecedent (and often complex) FS observed in patients with MTLE seems to contradict epidemiological studies that show no increase in the incidence of TLE or of hippocampal sclerosis after FS or complex FS, including febrile status epilepticus.

The Lancet Neurology vol 3 July 2004
Is there genetic component in the etiology of FS?

• GEFS+: Generalized epilepsy with febrile seizure plus

• Mutations in genes for subunits of the voltage-gated sodium channel and the $\gamma_2$ subunit of the ligand-gated GABA$_A$ receptor.
Familial forms of FS

- FEB1 on chromosome 8q13-21
- FEB2 on chromosome 19p13.3
- FEB3 on chromosome 2q23-24
- FEB4 on chromosome 5q14-15
- FEB5 on chromosome 6q22-24
The Major Benign Partial Syndromes
Benign Rolandoic Epilepsy (BRE, Benign Partial Epilepsy with Centro-Temporal Spikes of Childhood)

- **Frequency** 15 - 20%
- **Genetic** predisposition 40%
- **Male** preponderance 60%
- **Onset** 2 - 13 years (peak: 9-10 years)
- **EEG** Blunt, high voltage centro-temporal (Rolandic sulcus) spikes, often followed by slow waves, activated by sleep and tending to shift from side to side.
- **Seizures:** Older children- Brief, hemifacial motor, with frequent associated somatosensory symptoms, usually nocturnal. Younger children- Hemiclonic or GTCS (especially at night).
- **Rx:** None if seizures are mild and rare. Most AEDs very effective.
- **Evolution:** Recovery before 15 - 16 years.
Benign Occipital Epilepsy (BOE, Benign Partial Epilepsy of Childhood with Occipital Paroxysms)

- **Frequency** rare
- **Genetic** 37%, migraine 17%
- **Male = female**
- **Onset** 2 - 17 years (peak: 7 - 8 years)
- **EEG** Paroxysms of high amplitude spike-waves, recurring more or less rhythmically on the occipital and posterotemporal areas of one or both hemisphere, and occurring when the eyes are closed (“fixation off response”).
- **Seizures:** Initial visual symptoms, often followed by a hemiclonic seizure or by automatisms when the occipital discharge spreads anteriorly. **Postictal** migrainous cephalgia in a quarter of the cases.
- **Rx:** Most AEDs with control in 60%.
- **Evolution:** Recovery by end of adolescence.
- **Caution:** Lesional cases may have identical features.
The Major Primary Generalized Syndromes
Childhood Absence Epilepsy (CAE, True Petit Mal Epilepsy)

- **Frequency** 8%
- **Genetic predisposition**- strong 20%
- **Female** preponderance 75%
- **Onset** 3 - 12 years (peak: 6 - 7 years)
- **EEG**: bilateral, synchronous, symmetrical 3 / sec spike wave, normal background.
- **Seizures**: Very frequent simple absences.
- **Rx**: VPA or ESM with control in 70 - 80%.
- **Evolution**: Remission- 95%. Rare persistence of absences only- 6%. GTCS during adolescence or later- 40%.
Childhood Absence Epilepsy
Juvenile Myoclonic Epilepsy (JME)

- **Frequency** 5%
- **Genetic** predisposition- strong >25%
- **Male = female**
- **Onset** 8-26 (peak: 16 - 17)
- **EEG:** Rapid 4 - 5 / sec spike or polyspike-wave ictally and interictally; often photosensitive.
- **Seizures:** Myoclonus on waking or after sleep deprivation. GTCS often also occur, occasional absence.
- **Rx:** VPA with control in 60 - 100%
- **Evolution:** Rarely remits (<10%)
Grand Mall on Awakening (GMA)

- **Frequency**: ?%
- **Genetic predisposition**: strong >10%
- **Male > female**
- **Onset**: 6-24 (peak: puberty)
- **EEG**: One of the patterns of generalized epilepsy; often photosensitive.
- **Seizures**: GTS exclusively or predominate (90%) on after awakening, or evening leisure, worse with sleep deprivation. Myoclonic or absence may occur.
- **Rx**: VPA with control in 60 - 100%
- **Evolution**: Rarely remits (<20%)
The Major Secondary Generalized Syndromes
Infantile Spasms (West Syndrome)

- **Frequency** rare
- **Genetic** predisposition - no
- **Male** preponderance
- **Onset** < 1 year (peak: 3 - 7 months)
- **EEG**: Hypsarrythmia.
- **Seizures**: Very brief, frequent flexion (and/or extension), often in clusters.
- **Rx**: ACTH or prednisone with control in >50%; CZP and VPA may be used.
- **Evolution**: Often evolves to LGS or other secondary generalized epilepsy; the spasms always stop by age 5.
- **Poor prognosis in most cases (<5% develop normally).**
Lennox Gastaut Syndrome (LGS)

- **Frequency**: 3 - 10%
- **Genetic predisposition**: no
- **Male preponderance**
- **Onset**: 1 - 8 years (peak: 3 - 5 years)
- **Evolution**: Often frequent seizures wax and wan, becoming less common and more "temporal" over decades.
- **Poor prognosis in most cases (<10% develop normally).**
- **EEG**: Abnormal background, slow generalized spike-wave (<2.5 / sec), generalized fast paroxysms.
- **Seizures**: Tonic, atypical absence, drop attacks, other generalized or partial seizures.
- **Rx**: VPA, often with other drugs appropriate for seizure types, rarely with complete control.
- **Evolution**: Cognitive slowing, persisting seizures.
• **Q:** “Will my child outgrow the seizures?”
• **A:** Only in the *benign* partial or generalized epilepsies excepting juvenile myoclonic epilepsy. On the other hand, most patients with nonbenign partial epilepsy do not continue to forever seize, while most with secondary generalized epilepsies do.
Points to take home:

• Description is most helpful in suggesting an event was or was not a seizure, but not whether it originates focally or is generalized in onset, unless there is a typical aura or focal motor component.

• Syncope or apnea are most unlikely to be seizures.

• Odds of a seizure being generalized vs. partial are 50:50 in childhood, 20:80 in adults.
Points to take home:

- "Staring spells" may be CPS or absences, but should be easily distinguished.
- GTC seizures may be focal "secondarily generalized" or "primarily generalized".
- EEG when abnormal can suggest the nature of the seizure tendency as focal or generalized, but does not determine whether or not a spell was a seizure or whether or not to treat, therefore help in drug selection, the value of a scan, and the prognosis.
Points to take home:

• 50% of patients with partial seizures show focal spikes (or slowing), up to 75% after repeat studies or sleep deprivation.

• 90% of patients with generalized seizures show generalized spikes, more with sleep deprivation, hyperventilation, or photic stimulation.

• A normal EEG would favor partial onset seizures in a pediatric patient with epilepsy.
Points to take home:

• 1-2% of nonepileptics have spikes on their EEGs.
• 20% of patients with spikes on the EEG do not have epilepsy.
• There is no “perfect medication” (yet) that treats all seizure types.
Points to take home:

• Most AEDs treat partial seizures or convulsions (whether focal or generalized in onset), but there is a great deal of individual variation among patients.
• VPA, LTG and ZNS are the only drugs effective for all types of generalized seizures.
• CBZ, GBP (Neurontin) and TGB may worsen or cause generalized seizures (absence or myoclonus).
• LTG is not recommended as first choice in children, especially if on VPA, because of frequent serious rashes.
REFERENCES

General Points

- Etiology and Incidence

Genetics


Seizure equivalents/Nonepileptic paroxysmal events


Initial evaluation

- EEG

Classification of Seizures


Status epilepticus