Febrile Seizures

- Occurs in children 6m - 5 years
- Commonly seen first before 1-2 years of age
- Separated into simple febrile and complex partial seizures
- Simple: i) Only 1 in 24 hours 2) Generalized 3) < 15 minutes
- Complex: i) Recurrent (2 or more in 24 hours) 2) Focal 3) > 15 minutes

Febrile Seizures

- Presence of each factor which makes a febrile seizure complex increases risk of subsequent epilepsy in an additive manner BUT maxes out ~4-5% if all 3 factors present
- No daily preventive medication used, however Diastat sometimes used if prior seizures were prolonged
Seizures (Neonatal)

- Very common, especially among premature newborns
- Incidence of 57.5/1000 in birth weight less than 1500 g, 2.8/1000 in birth weight between 2500 and 3999 g

Seizures (Neonatal)

- Clonic seizures
  - Most classically associated with an EEG correlate
  - Rhythmic, slow compared to clonic seizures in older children (1-3 jerks/second)
  - Typically occur with focal pathology
  - Focal or multifocal (in latter, progress in a non-Jacksonian manner)

Seizures (Neonatal)

- Tonic seizures
  - May be generalized or focal (generalized >> focal)
  - May occur as tonic extension of both upper and lower extremities (similar appearance to decerebrate posturing) or tonic flexion of upper extremities with extension of lower extremities (as in decorticate posturing)

Seizures (Neonatal)

- Myoclonic seizures
  - Focal myoclonic seizures involving the flexor muscles of the upper extremities
- Subtle seizures
  - Fall outside of typical clonic, tonic, or myoclonic seizures
  - More common in premature infants than in term infants
  - Often involve ocular manifestations — sustained eye opening or horizontal movements
  - Mouth movements, apnea in the absence of bradycardia
Seizures (Neonatal)

- Common etiologies
  - Hypoxic-ischemic encephalopathy: 50-60% of cases
    - Begin within the first 24 hours of life, even within first 12 hours
  - Intracranial hemorrhage - 10% of cases
    - Intraventricular hemorrhage
    - Subarachnoid hemorrhage
  - Intracranial infections - 5-10% of cases

- Metabolic disturbances
  - Hypocalcemia/hypomagnesemia: 3% of seizures
  - Hypoglycemia: 3% of seizures
    - Frequently in SGA infants or infants of diabetic mothers
    - Seizures typically occur on 1st postnatal day

Seizures (Neonatal)

- Benign idiopathic neonatal convulsions
  - aka “Fifth Day Fits”
  - Typically multifocal clonic seizures with apnea
  - Occur around 5th day, cease by ~2 weeks
  - No known etiology
  - No metabolic disturbance/baby otherwise looks OK → no significant risk of lifelong epilepsy and no effect upon development

Seizures (Neonatal)

- Benign familial neonatal convulsions
  - Dominantly inherited mutation in the KCNQ2 and KCNQ3 genes (impairment K-dependent repolarization)
  - Chromosome 20 > 8
  - Occur on 2nd or 3rd day of life
  - Baby looks well between seizures
  - Repeated clonic or apneic seizures: 10-20/ day
  - Seizures stop by 1-6 mos of life
  - 10-20% of patients go on to develop long-term epilepsy
Seizures (Neonatal)

- Early myoclonic epilepsy/ early infantile epileptic encephalopathy (Ohtahara)
  - EME: myoclonic and clonic
  - EIEE: tonic
  - Burst-suppression pattern on EEG
  - Poor outcome

Pediatric Epilepsy Syndromes

- When considering the syndromes, keep in mind:
  - Age of onset
  - Age which seizures typically stop (if applicable)
  - Seizure types
  - Effect upon development, academic abilities
  - Potential co-morbidities
  - Genetic basis

Pediatric Epilepsy Syndromes (Focal)

- Benign Rolandic Epilepsy
  - aka Benign epilepsy with centrotemporal spikes (BECTS)
  - Most common epilepsy syndrome in childhood
  - Onset toward end of 1st decade of life: typically 5-9 years of age (range from 2-13 years)
  - Seizures usually stop by 13-15 years of age

Pediatric Epilepsy Syndromes (Focal)

- Benign Rolandic Epilepsy
  - Seizures are focal +/- secondary generalization: Classically unilateral sensory changes (tongue > lips and cheeks)
  - Speech arrest (motor aphasia) +/- clonic jerking of face and clonic jerking of ipsi arm -- often consciousness preserved
Pediatric Epilepsy Syndromes (Focal)

Benign Rolandic Epilepsy

- Predilection to night, but up to 1/3 of patients have seizures during day only
- Generally thought to be “benign” in that no impairment of development/academic skills, although subtle neuropsychological differences may be present, particularly in visuomotor skills, visuospatial memory, language and attention

- Genetic cause has not been identified, but family history may be present
- 20-40% of patients have +FH of epilepsy or centrotemporal spikes
- Large FH of centrotemporal spikes (with or without seizure: “benign rolandic trait”)
Pediatric Epilepsy Syndromes (Focal)

- Benign childhood epilepsy with occipital paroxysms
  - Two variants: infantile/young childhood and later (school-age/adolescent)
  - Infantile form known as Panayiotopoulos syndrome or early-onset childhood epilepsy with occipital spikes
  - Panayiotopoulos syndrome characterized by ictal emesis, head/eye deviation and prolonged periods of unresponsiveness

- Benign Childhood Epilepsy with Occipital Paroxysms
  - 2/3 of children with nocturnal seizures only
  - Autonomic sx: very common: especially nausea/ emesis, but also mydriasis, pallor, flushing/cyanosis, BP changes
  - ~50% of children with seizures > 30 minutes (for autonomic sx)

Pediatric Epilepsy Syndromes (Focal) (Later-onset)

- Commence with visual symptoms: 1. Narrowed vision or loss of vision, 2. Visual illusions (e.g. macro-/micropsia) 3. Formed basic or complex visual hallucinations
- Followed by hemiconvulsions --> often associated with migrainous headache thereafter
- Classically, EEG shows paroxysms of occipital or occipitotemporal spikes with eye closure

Pediatric Epilepsy Syndromes (Generalized)

- Childhood Absence Epilepsy
  - The “youngest” of the 3 major absence epilepsy syndromes
  - This syndrome is the “classic” absence epilepsy
  - Onset ~3-13 years of age, with peak at 7-8 years
  - More represented in girls: 60-80% of CAE in girls
Pediatric Epilepsy Syndromes (Generalized)

- Childhood Absence Epilepsy
  - Most children will become seizure-free (50-80%)
  - Of children who do not go into remission, about 1/2 will go on to juvenile myoclonic epilepsy pattern

- Childhood absence epilepsy
  - Low risk for convulsions... usually absences alone
  - Because of this, 1st line treatment with ethosuximide (Zarontin), followed by valproic acid (Depakote)
  - Absences thought to be generated by thalamocortical circuits... ethosuximide affects T-type Ca channels which are involved with thalamocortical relays

- Childhood Absence Epilepsy
  - Patients with up to 100’s of seizures per day: staring +/- automatism lasting 5-15 sec long
  - Variants
    - 1) Absences with staring alone
    - 2) Absences with eyelid myoclonia
    - 3) Absence with gradually lowering of head or body
    - 4) Absences with tonic components (eyerolling)
    - 5) Absences with automatisms or continued activity
    - 6) Absences with autonomic changes
Pediatric Epilepsy Syndrome (Generalized)

- Childhood Absence Epilepsy
  - FH of epilepsy present in 1/3 of patients
  - Therefore, presumed genetic etiology
  - Some genetic absence epilepsies:
    - ECA1 (c.some 8q24) - absences
    - ECA2 (c.some 5q31: mutation in GABRG2) - absence and febrile seizures
    - ECA3 (c.some 3q26: mutation in CLCN2 (Cl-channel) and CACNA1H (Ca channel))

- Juvenile Absence Epilepsy
  - The next “oldest” of the absence epilepsies
  - Onset is later than childhood absence -- usually 10-12 years of age
  - Absences are less frequent than in childhood absence (few per day), but seizures longer (usually 10-15 seconds) and children are at increased risk for generalized tonic-clonic seizures (80% of patients)
  - 10-15% of patients with myoclonic seizures

- 1st line treatment is valproic acid; other meds include levetiracetam, lamotrigine
Pediatric Epilepsy Syndromes (Generalized)

- Juvenile Absence Epilepsy
  - EEG still shows generalized spike-and-wave discharges, however may be faster than in childhood absence epilepsy (3.5-4 Hz)

- Juvenile myoclonic epilepsy
  - The “oldest” of the absence epilepsies
  - Onset in early adolescence: 10-13 years of age
  - Unfortunately, this tends to be a life-long condition
  - Characterized by the triad of (i) absences, (ii) myoclonic seizures and (iii) generalized tonic-clonic seizures
  - Absences may be infrequent/rare

- Seizures -- especially myoclonic seizures -- often occur 1st thing in the morning
- Think about the child sitting at the breakfast table and tossing his orange juice
- Seizures are also very photosensitive (especially “strobing” of the sun through the trees riding to school)
- Also exquisitely sensitive to alcohol and sleep deprivation
Pediatric Epilepsy Syndromes (Malignant)

West Syndrome/ Infantile Spasms
- Characterized by the triad of (i) infantile spasms (ii) hypsarrythmia on EEG and (iii) mental retardation
- Do not need all 3 to meet diagnosis
- Infantile spasms tend to start ~4-6 months of age; 90% by age 1
- Have a rapid progression

Episodes are brief (1-3 seconds), but occur in clusters, typically when patients awaken from sleep or upon going to sleep
- Consist of tonic spasms which are:
  - i. Extensor (abduction of arms at shoulder, extension of neck and trunk)
  - ii. Flexor (flexion of body at the waist, head and neck: “salaam attacks”)
  - iii. Mixed flexion and extension

Malignant syndrome because development begins to lag, regression occurs when spasms begin
- Frequently, parents will first complain of a lack of interactiveness -- poor eye contact, smiling/laughing less
- Examination: skin becomes important, particularly with Wood’s lamp to assess for ash leaf spots in the context of tuberous sclerosis
Pediatric Epilepsy Syndromes (Malignant)

- West Syndrome
  - Spasms classified as
    - i. Symptomatic -- Known etiology such as tuberous sclerosis, HIE or developmental malformation of brain
    - ii. Cryptogenic -- Genetic etiology suspected because of other anomalies, however diagnosis can not be made
    - iii. Idiopathic -- Etiology not at all clear - normal development prior to onset of spasms and no neuroradiological or metabolic abnormalities

- From the standpoint of prognosis, children with symptomatic spasms do worse, children with idiopathic spasms do best
- Only 15% of patients with symptomatic will have normal or near-normal development v. 30-50% in idiopathic group

- Best treatment is debatable, but is subject of 2004 CNS position paper
  - First-line treatment consists of IM ACTH: position paper described ACTH as “probably effective” for tx of spasms and resolution of hypsarrythmia
  - Prednisone/ prednisolone have been examined as tx: position paper found that no clear evidence to support use of these, however there is evidence to suggest that this is as good as low-dose ACTH (20-30 Units/ day)
Pediatric Epilepsy Syndromes (Malignant)

- West Syndrome
  - Vigabatrin is the treatment of choice for patients with tuberous sclerosis (obtained via Canada) -- in position paper listed as “possibly effective”
  - When compared to ACTH, patients did not do as well initially, but seizure-free rates @ 1 year were similar
  - Major toxicity is retinal, with peripheral field cuts -- warrants serial ophthalmologic examinations

- Other agents include
  - Benzodiazepines
  - Valproic acid
  - Topiramate
  - Zonisamide
Pediatric Epilepsy Syndromes (Malignant)

- Lennox-Gastaut Syndrome
  - Characterized by multiple seizure types: i) generalized tonic seizures ii) atypical absence seizures and iii) atonic/astatic seizures
  - Patients may also have focal, myoclonic, GTC seizures
  - Malignant in that the majority have patients have significant developmental delays or mental retardation

- Onset typically within 1st decade -- often patients with infantile spasms evolve into LGS pattern
- Seizures prove to be difficult to treat
- 1st line therapies: Valproic acid (+/- Lamotrigine, Felbamate, Rufinamide
- Vagal nerve stimulator
- Corpus callosotomy for “drops”

EEG shows generalized spike-and-wave activity at 1-2.5 Hz (“slow spike-and-wave”) with paroxysmal fast activity (especially during NREM sleep)
A 13 year old girl presents after having a generalized tonic-clonic seizure. She has noticed that, when she brushes her teeth or combs her hair in the morning, she occasionally experiences a brief, involuntary jerk in her upper extremities. Past medical history is otherwise unremarkable. There is no family history of seizures. Exam is normal. You obtain an EEG, which reveals occasional generalized bilateral polyspikes and spike wave complexes at 4Hz.

Of the following options, which agent is the best choice as a first-line monotherapy treatment?

A) Gabapentin
B) Oxcarbazepine
C) Valproate
D) Felbamate
E) No treatment is indicated

An 8 year old girl presents to your office accompanied by her parents. The parents state that on 2 occasions over the last several months, the girl has come into their room in the early morning, drooling and having difficulty talking, with a slight droop on the right side of her face. These symptoms resolved fairly quickly on both occasions. Then, this morning, she had a generalized tonic clonic seizure. There is no significant past medical history, and no family history of epilepsy. The patient had a normal birth history, and has consistently met her developmental milestones. Physical exam is normal.

What is the most likely course of this child's epilepsy?
A) Her seizures will become more frequent and more severe as she gets older
B) Her seizures are associated with focal epileptiform discharges from the medial frontal region on an EEG
C) Her seizures will persist for life and will be refractory to medical treatment
D) She will not have any more seizures
E) Her symptoms will remit eventually

**Nonepileptic Paroxysmal Disorders**

**Breath holding spells**

- Occurs in mid-infancy to ~5 years of age
- At the end/middle of the expiratory phase of crying (usually from pain or anger), apnea will occur with a loss of tone
- Broken down into pallid and cyanotic spells
Breath holding spells

- Cyanotic (more common than pallid)
  - As the name implies, associated with cyanosis and occurs with emotional disturbance (e.g. frustration, being yelled at)
  - Associated with LOC, opisthotonus and bradycardia; may have few clonic jerks (looks like sz)

- Pallid
  - Associated with pallor, more likely caused by pain than emotional disturbance
  - Associated with tonic seizure

LOC due to brief cerebral anoxia
Episode usually lasts <1 minute

Paroxysmal kinesigenic choreoathetosis

- Usually begins ~10-15 years of age (cases around ~2 years have been described)
- Consists of unilateral> bilateral dystonia and/or choreoathetosis occurring in the leg or arm
- May be associated with facial grimace, dysarthria
- Precipitated by a sudden movement -- e.g. rising from a chair, jumping from diving board

Imaging, electrophysiologic studies are normal
Presumed to be Na-channel abnormality as it responds to phenytoin, carbamazepine
Abates during late adolescence, early adulthood
Chorea

- Most commonly Sydenham’s chorea in the pediatric age group: e.g. rheumatic fever
- Thought to be immune-mediated attack of CNS (subthalamic n., caudate) by group-A strep
- Sydenham chorea additionally associated with hypotonia and moodiness (which may be the worst part)

Chorea

- Sydenham chorea
  - Unilateral or bilateral
  - Occurs in face, distal extremities
  - Worsened by stress, disappear in sleep
  - Characterized by
    - “Milkmaid’s grip”: Will relax and tighten handshake
    - “Choreic hand”: Spooning of outstretched fingers
    - “Darting tongue”: Tongue unable to be held protruded: darts in and out of mouth

Chorea

- Sydenham’s chorea
  - May persist for 6-24 months
  - Treated with antipsychotics (e.g. haldol) and/or depakote (may help with mood sxs)
  - Additionally, tx’d with PCN longterm -- does not shorten cause of disease, but helps with prevention of endocarditis from longterm effects of rheumatic fever

Chorea

- Huntington’s disease/ Westphal variant
  - In pediatric population (e.g. adolescents), often associated with myoclonus or generalized tonic-clonic seizures
  - Rigidity, dystonia occur more than the choreoathetosis that is seen in adults
  - Rapid course with death often occurring in 1 decade
Chorea

- Wilson’s disease
  - Onset in early to middle adolescence
  - Associated with psychiatric sx (may be more prominent than choreoathetosis): mood changes, psychosis
  - Additionally, there is an elevation of liver function tests
  - Occurs due to chromosome 13 mutation: abnormality in Cu transport and incorporation of copper into ceruloplasmin: therefore should see low serum ceruloplasmin on testing, high copper excretion in urine

Chorea

- Wilson’s disease
  - Liver disease ranges from asymptomatic hepatomegaly to failure
  - Movement disorder may also include dystonia, associated with dysarthria
  - Can look for Kayser-Fleischer ring on slit lamp exam (Cu deposits)

Chorea

- Wilson’s disease
  - Tx with restriction of copper intake (e.g. nuts, shellfish, chocolate)
  - Chelation with penicillamine: may be associated with worsening of neurologic symptoms or significant adverse effects

Kayser-Fleisher Rings

Source: http://organelle盥s.well.ox.ac.uk
Parasomnias

- Split into disorders that occur out of slow-wave sleep (partial-arousal disorders) and those out of REM
- Partial arousal disorders -- sleepwalking, sleep talking, sleep terrors -- cluster during 1st third of night, when patients have an increased concentration of slow-wave sleep
- REM disorders (e.g. nightmares) occur during last 3rd of night, when REM most concentrated

Parasomnias

- Partial-arousal parasomnias tend to occur more if patient is sleep-deprived
- Likewise REM parasomnias occur more if patient is in the midst of REM-rebound
- Partial-arousal disorders often associated with amnesia for the event

Parasomnias

- Sleepwalking:
  - May occur along with sleep talking
  - Often with complex movements (e.g. moving furniture, going outside): may be violent or dangerous
  - Often appear to be acting out a dream

Syncope

- Most commonly associated with vasovagal syncope in pediatric age range
- Episode of pain, fear, excitement causes bradycardia and relative cerebral ischemia
- Usually begins in adolescent age range, more common in girls than boys
- May be precipitated by tilt-table testing, treated with beta blockers
### Syncope
- Vasovagal syncope often preceded by nausea, diaphoresis, lightheadedness
- Episodes generally brief (<10 sec), though if patient remains or is put into an upright position, it may be longer
- May be associated with up-rolling of eyes and/or tonic stiffening, a few clonic jerks
- EEG during episodes shows generalized slowing, but not epileptiform discharges

### Prolonged QT syndrome
- Occurs in 1/10,000 patients: usually starting at end of 1st decade or adolescence
- Unlike syncope, occurs during exercise or emotional experience
- Patient will collapse suddenly, with LOC
- ECG will show arrhythmia during episode (often v-fib)
- While child may recover within minutes, this is a relatively common cause of sudden pediatric death during exercise

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### Prolonged QT syndrome
- Defined -- as name implies -- by a prolonged QT interval on ECG during rest or exercise: varies by age, but benchmark is >0.46 msec
- May occur in context of acquired disease (e.g. drug-induced, myocarditis) or due to congenital cause

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### Prolonged QT syndrome
- May occur in AR inheritance, associated with deafness (Jervell or Lang-Nielsen syndrome) or AD inheritance (Romano-Ward)
- Often associated with K-channelopathy
- Treatment with beta-blockers and/or implanted defibrillator (if refractory)
The End