Children and Youth with Epilepsy

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Definitions

• Seizure: A sudden stereotyped episode with change in motor activity, sensation, behavior, and/or consciousness
  – Due to an abnormal electrical discharge in the brain
  – **Provoked seizure**: seizure with an acute antecedent cause, such as fever, a CNS infection, trauma, metabolic abnormality.
  – **Unprovoked seizure**: no provoking factor
Epilepsy is the condition of recurrent unprovoked seizures

- 1 in 26

- Approximately 1% of children have epilepsy
  (Russ SA et al Pediatrics. 2012; 129; 256-264)
Types of seizures

- Generalized
- Focal (partial)
  - Focal with retained awareness
    - Simple partial
  - Focal with dyscognitive features
    - Complex partial
  - Secondarily generalized
- Unclassified
Differential diagnosis

- Not all paroxysmal events are seizures
- Important to remember imitators of seizures
- Several physiological processes can mimic seizures
Common non-epileptic events

- Gastroesophageal reflux
- Breath-holding spells
- Night terrors
- Parasomnias
- Benign sleep myoclonus
- Benign neonatal myoclonus
- Syncope / convulsive syncope
- Panic attacks / Anxiety episodes
- Conversion disorder
- Etc.
Classification of epilepsies

Importance of classification:
– Framework for diagnosis
– Define appropriate work-up
  • Avoid neuroimaging in certain epilepsies
– Select appropriate treatment
  • Choice of anti-seizure medication
  • Consideration of non pharmacologic treatment(s)
– Better understand prognosis
Classification (ILAE 1989)

1. Localization Related
2. Generalized epilepsies and Syndromes
3. Undetermined whether focal or generalized
4. Special syndromes

Etiology: Idiopathic, Symptomatic, Cryptogenic (presumed symptomatic)
New organization (2010)

• Advances in neuroscience have improved the understanding and etiology of some epilepsies
  – Genetics (CMA, Epilepsy gene panels, WES)
  – Neuroimaging (FCD)
  – Immunology (autoimmune epilepsies)
New system

• Terms no longer used
  – Simple partial
  – Complex partial
  – Secondarily generalized
• Replaced by
  – With or without impairment of consciousness/awareness
  – Dyscognitive
  – Evolving to a convulsive seizure
New organization of epilepsies


*†Anne T. Berg, †Samuel F. Berkovic, §§Martin J. Brodie, ¶¶Jeffrey Buchhalter, #***J. Helen Cross, ††Walter van Emde Boas, †‡Jerome Engel, §§§Jacqueline French, ¶¶¶Tracy A. Glauser, ###Gary W. Mathern, ***Solomon L. Moshé, †Douglas Nordli, †‡‡Perrine Plouin, and ‡Ingrid E. Scheffer
New system

• Emphasizes electroclinical syndromes
  – complex of clinical features, signs and symptoms that together define a distinctive, recognizable clinical disorder

Berg et al, Epilepsia 2010.
Acute evaluation

• Was really a seizure?
  – Detailed description of event
  – Patient’s medical history
  – Determine if truly “first” seizure
  – Was it a non-epileptic paroxysmal event?
    • Often difficult to tell
    • No reliable test to differentiate
    • Sometimes interictal EEG is helpful
Acute evaluation:
Determine the cause

- Head Trauma
- CNS infection
- Metabolic abnormality
  - Electrolyte abnormality
  - Renal or hepatic disease
- Toxic ingestion
  - Recreational drugs
  - Other toxins
- Epilepsy?
Acute diagnostic workup

• Routine Labs:
  – Yield is low in the absence of clinical signs/symptoms
  – Ordered on a case-by-case basis
  – Common tests:
    • Glucose
    • Electrolytes
    • Serum Alcohol level
    • Toxicology drug screen
Acute diagnostic workup

- Lumbar puncture not recommended routinely following a single unprovoked seizure.
- Lumbar puncture should be considered if:
  - Clinical suspicion of CNS infection
  - Young child (<6 months), and/or persistent altered mental status, or failure to return to baseline

Diagnostic work-up: EEG

- Optimal timing not clear.
  - Usually ok to do as outpatient

- EEG within 24-48 hours after a seizure more likely to be abnormal.
  - Some abnormalities, like postictal slowing, may be transient and should be interpreted cautiously.
Diagnostic work-up: EEG

- Single outpatient EEG abnormal in 70%.
- ↑Yield with ↑ sampling.
- EEG can be useful for diagnosis of seizure vs. non-seizure event.
  - *BUT normal EEG does not r/o seizure.*
Neuroimaging

- **Emergent imaging**
  - Goal: Detect serious abnormality with immediate treatment implications (e.g. hemorrhage) → head CT
  - Incidence of lesions requiring acute intervention in children presenting with a first seizure is ~2%

- **Non-urgent imaging**
  - To detect abnormalities that might affect prognosis, define epilepsy syndrome (therefore treatment decisions) → brain MRI
  - Most common MRI abnormalities: encephalomalacia and cerebral dysgenesis

O’Dell, Epilepsia 1997;38(S8):184.
To treat or not to treat?

First unprovoked afebrile seizure: Don’t start the child on medicine

Risk of seizure recurrence after a first unprovoked afebrile seizure

- Prospective study of 407 children (Shinnar 1996)
- Median time to recurrence 5.7 months
- 53% recurrences within 6 months, 69% within 1 year, 88% within 2 years
To treat or not to treat

- Risk factors for seizure recurrence
  - Remote symptomatic etiology
  - Abnormal EEG
  - Seizure occurring while asleep
  - History of prior febrile seizures
  - Todd’s paresis

- Late recurrence (>2 years)
  - Etiology, abnormal EEG, febrile seizures
The Ideal Medicine

• Effective
• Safe
• Few side effects
• Easily absorbed
• Single daily dose
• No drug interactions
• Inexpensive
Making the pieces fit

Type of Epilepsy

Co-morbidities

Age

AED Pharmacology
Monotherapy or polytherapy?

• The most effective Rx is with a single drug, chosen on the basis of epilepsy syndrome diagnosis (and type of seizure) and titrated to the seizure control or side effects

• Problems with polytherapy
  – Additive side effects
  – Drug interactions

• Drugs with different mechanisms of action: “rational” polytherapy/synergism
Choice of AEDs

• Based on seizure type/epilepsy syndrome

• Age:
  – Valproate not the preferred drug <2 years
  – Phenobarbital still the drug of choice in neonatal seizures

• Co-existing conditions
  – Weight, feeding, other medical conditions
  – Other medications
Choice of AEDs

- AED pharmacology
  - Rapidity of titration
  - Side effect profile

- Most important parameters:
  - Efficacy
  - Safety
Choice of AEDs

Efficacy

Safety
Choice of AEDs

- Based on seizure type/epilepsy syndrome
- Common choices
  - Generalized epilepsy:
    - ethosuximide, valproate, lamotrigine, topiramate, zonisamide, levetiracetam.
    - Carbamazepine/oxcarbazepine not preferred in generalized epilepsies for risk of absence status
Choice of AEDs

- Rolandic Epilepsy (BECTS), other focal epilepsies
  - Carbamazepine, oxcarbazepine
  - Gabapentin (Bougeois et al)
- Absence Epilepsy: ethosuximide > valproate > lamotrigine
- Juvenile Myoclonic Epilepsy: Valproic acid
  - also levetiracetam, lamotrigine, zonisamide
- Symptomatic Generalized Epilepsy (Lennox Gestaut Syndrome)
  - Valproate, lamotrigine, topiramate, felbamate
Management of Epilepsy

Treatment of seizures
(just the tip of the iceberg)
Management of Epilepsy: the bigger picture

- Treatment of seizures
- Safety incl driving
- Bone and Reproductive Health
- Education and Learning
- Family Issues

University of Michigan
C.S. Mott Children’s Hospital
Comprehensive Management

- Epilepsy is a complex disorder:
  - Recurrent unprovoked seizures
  - Mental health
  - Learning
  - Behavior
  - Physical health comorbidities
- Epilepsy care is about more than just seizures
Learning differences

- Risk for ↓ academic achievement, memory, behavior scores.
  - Despite seizure control
  - Despite “normal range” IQ

- Learning problems predate seizures.

- Not solely attributable to AEDs or seizures.
Learning differences

• ADHD: 38% of children with epilepsy.
• Independent risk factor for trouble.
  – school, injuries, drug use, car accidents...
• Stimulants are NOT contraindicated.
  – Methylphenidate = safe and effective.
  – Atomoxetine, Guanfacine = alternative.

School and Learning

- Useful to ask about school performance
- Can request an Individualized Education Plan (IEP) and special services if necessary
- Consider referral for neuropsychological testing
Driving

- **Driving is not permitted when seizures are not controlled**
- State laws differ as to when an individual with epilepsy can drive.
- Know your state’s laws about:
  - Driving with epilepsy
  - Physician reporting (PA, CA, DL, NV, NJ, OR)
  - Good resource: www.epilepsyfoundation.org
- If a parent of child with epilepsy has epilepsy, check if the parent is driving
• Epilepsy = risk for poor bone mineralization.

• Seizures = risk for falls & fractures.
Bone Health & Epilepsy

• Complex problem
  – Vitamin D
  – Calcium
  – Anticonvulsants
  – Co-morbid neuromotor dysfunction
  – Lack of physical exercise
Vitamin D

• Vitamin D insufficiency is common.
  – 25-hydroxyvitamin D <32ng/mL
  – ~60% of all US children
  – ~75% of Michigan children with epilepsy

• Risk factors: female sex, obesity

• All anticonvulsants implicated.

• All epilepsy syndromes implicated.

Typical scenario

- Assess nutritional status:
  - Drinks no/very little milk, eats cheese 2x/week
  - Not taking any supplemental vitamins

<table>
<thead>
<tr>
<th>25-OHD (ng/mL)</th>
<th>Supplement</th>
<th>Recheck</th>
<th>Additional studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥30</td>
<td>400 IU daily</td>
<td>Yearly</td>
<td></td>
</tr>
<tr>
<td>15-29</td>
<td>1000 IU BID</td>
<td>Every 4 weeks until normal</td>
<td>Ca, Mg, PO₄</td>
</tr>
<tr>
<td>&lt;15</td>
<td>2000-4000 IU per day in divided doses</td>
<td>Every 3-4 weeks until normal</td>
<td>PTH, Ca, Mg, PO₄, and consider Dexa</td>
</tr>
</tbody>
</table>

• Teens with epilepsy are at high risk for unplanned pregnancy.
• AEDs can make hormonal contraceptives less effective.

Neural Tube Defects

- Valproic Acid 1-2%
- Carbamazepine 0.5%
Reproductive Health

• AEDs are teratogenic
  – Valproate = classic treatment for JME
  – Valproate = highest risk for teratogenicity
  – Consider levetiracetam or lamotrigine.
• Recommend folic acid daily
  – 5 mg per day
• Get adolescents used to taking folic acid, (prenatal vitamins at least)
When AEDs don’t work

• Medically Refractory epilepsy
  – failure of 2 AEDs (appropriately chosen) to control seizures, when the AED is used at an appropriate/maximum tolerated dose

• Seizure control with AEDs
  – 1\textsuperscript{st} AED 47%
  – 2\textsuperscript{nd} AED 13%
  – 3\textsuperscript{rd} or subsequent AED 4%

Kwan and Brodie NEJM 2000
Beyond AEDs

- Epilepsy surgery
  - Resective surgery of the epileptogenic zone
  - Hemispherectomy
  - Corpus callosotomy
  - Multiple subpial transections
- Ketogenic diet or other dietary treatments
- Brain stimulation
  - VNS
  - Responsive stimulation

Joshi et al Arch Pediatr Adolesc Med 2012
Who follows these kids?

Neurologist?

Epilpetologist?
Neurologist vs Epileptologist

**Neurologist**
- Residency in Neurology
- Child neurology residency includes 1-2 years of general pediatrics
- BE/BC by ABPN

**Epileptologist**
- Fellowship trained after Neurology/Child Neurology residency
- Specific training for expertise in EEG interpretation, diagnosis and management of complex epilepsy
- Advanced treatments for complex epilepsy
- BE/BC for Epilepsy by ABPN
Epilepsy Center

- National Association of Epilepsy Centers (NAEC)
- Established criteria for Level 3 and Level 4 Epilepsy centers
- Formal evaluation and certification process for Level 3 and 4 Epilepsy centers
<table>
<thead>
<tr>
<th>SERVICES PROVIDED</th>
<th>PERSONNEL</th>
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<tbody>
<tr>
<td>Electrodiagnostic EEG services including long term</td>
<td>Neurologists (Adult and/or Pediatric) with special expertise in epilepsy</td>
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<tr>
<td>monitoring</td>
<td>EEG technologists and related personnel</td>
</tr>
<tr>
<td>Epilepsy Surgery including VNS (routine lesional</td>
<td>Neurosurgeon(s) with special expertise in epilepsy</td>
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<tr>
<td>surgeries and those not requiring invasive monitoring)</td>
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<tr>
<td>Neuroimaging</td>
<td>Neuroradiologist</td>
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<tr>
<td>Neuropsychological and psychological services</td>
<td>Neuropsychologist/neuropsychometrist</td>
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<td></td>
<td>Psychosocial personnel including clinical psychologist, social worker,</td>
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<td></td>
<td>school services for children</td>
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<tr>
<td>Pharmacological expertise</td>
<td>Access to consultation with Clinical Pharmacist</td>
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<tr>
<td>Nursing support (specific to epilepsy)</td>
<td>Nurse specialist</td>
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<tr>
<td>Rehabilitation (in patient and outpatient)</td>
<td>Rehabilitation service personnel</td>
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<tr>
<td>including physical, occupational and speech therapy</td>
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<tr>
<td>Consultative expertise in multiple fields: neurosurgery</td>
<td>Interdisciplinary clinical services available</td>
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<tr>
<td>psychiatry, internal medicine, pediatrics, general</td>
<td></td>
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<tr>
<td>surgery, obstetrics/gynecology</td>
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<tr>
<td>Other</td>
<td>Biomedical engineer and IT support</td>
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</table>
# Level 4 Epilepsy Center

## Table 3. Features distinguishing Level 4 centers

<table>
<thead>
<tr>
<th>Feature</th>
<th>Details</th>
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<tbody>
<tr>
<td>Functional cortical mapping by stimulation of subdural electrodes</td>
<td>either extra-operatively or intraoperatively.</td>
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<tr>
<td>Evoked potential recording capable of being used safely with</td>
<td>intracranial electrodes.</td>
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<tr>
<td>Electrocorticography.</td>
<td></td>
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<tr>
<td>Placement of intracranial electrodes.</td>
<td></td>
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<tr>
<td>Resection of epileptogenic tissue in the absence of structural lesions.</td>
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<tr>
<td>Adequate clinical experience by both the neurosurgeon and neurologist/</td>
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<tr>
<td>epileptologist.</td>
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<tr>
<td>Specialized neuroimaging either on site or by established arrangement</td>
<td>including interictal positron emission tomography (PET) and/or ictal</td>
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<tr>
<td></td>
<td>single photon emission computed tomography (SPECT).</td>
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</table>
Access to care

• Average wait times to see a Neurologist are about 53 days
• Access to care is a bigger challenge in rural and medically underserved areas
• Inclement weather, caregivers’ work, travel (distance) can all be barriers to accessing care
• 8 year old boy with cerebral palsy and intractable epilepsy
• Treated with multiple anti-seizure medications, and the ketogenic diet
• Partially G-tube fed, wheelchair bound
• Attends a school for children with special needs
• Parents have full time jobs
• Visits to Child Neurologist needed every 3-4 months for medication adjustment and ketogenic diet monitoring
• Drive to specialty clinic ~100 miles one way
• Typical day for a Neurology appointment involves both parents missing a day of work, and the child missing school
• Seeing a pediatric neurologist often requires children and youth with epilepsy to travel long distances, resulting in missed school time, loss of work days and extra expenses for travel and lodging.
Telemedicine

- Defined as “the use of medical information exchanged from one site to another via electronic communications to improve a patient’s clinical health condition” (ATA)
- Usually used in the context when direct patient care is delivered
Telemedicine

- Easier access to specialty care
- Impact on cost?
  - Reduction in cost for travel
  - Reduction in missed work days
  - Reduction in utilization of tertiary care services
Telemedicine

• Advantages:
  – Avoids /minimizes travel for families
  – Avoids /minimizes missing work and school
  – Care co-ordination between patient, primary care physician and neurologist, especially telemedicine is medical home based.
Telemedicine in MI (2013)

Telemedicine Sites
Dickinson
Alcona
Saginaw – 2 sites
Tawas
Grand Rapids
Holland
Thunder Bay
East Jordan
Emmet
Baldwin

Specialist Sites
University of Michigan,
Ann Arbor, MI

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