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

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Epilepsy

- 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)

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Types of seizures

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

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Differential diagnosis

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

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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.

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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

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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)

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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)

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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

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New organization of epilepsies

Epilepsia, 51(4):676–685, 2010
doi: 10.1111/j.1528-1167.2010.02522.x

SPECIAL REPORT

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

*†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

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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.

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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

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Acute evaluation: Determine the cause

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

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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

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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

Practice parameter. Neurology. 2000;55:616-623

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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.

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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.*

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Neuroimaging

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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.
Berg, Ann Neurol 1999;45:618.

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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

- Prosepective 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

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To treat or not to treat

- Risk factors for seizure recurrence
  - Remote symptomatic etiology
  - Abnormal EEG
  - Seizure occuring while asleep
  - History of prior febrile seizures
  - Todd's paresis
- Late recurrence (>2 years)
  - Etiology, abnormal EEG, febrile seizures

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The Ideal Medicine

- Effective
- Safe
- Few side effects
- Easily absorbed
- Single daily dose
- No drug interactions
- Inexpensive

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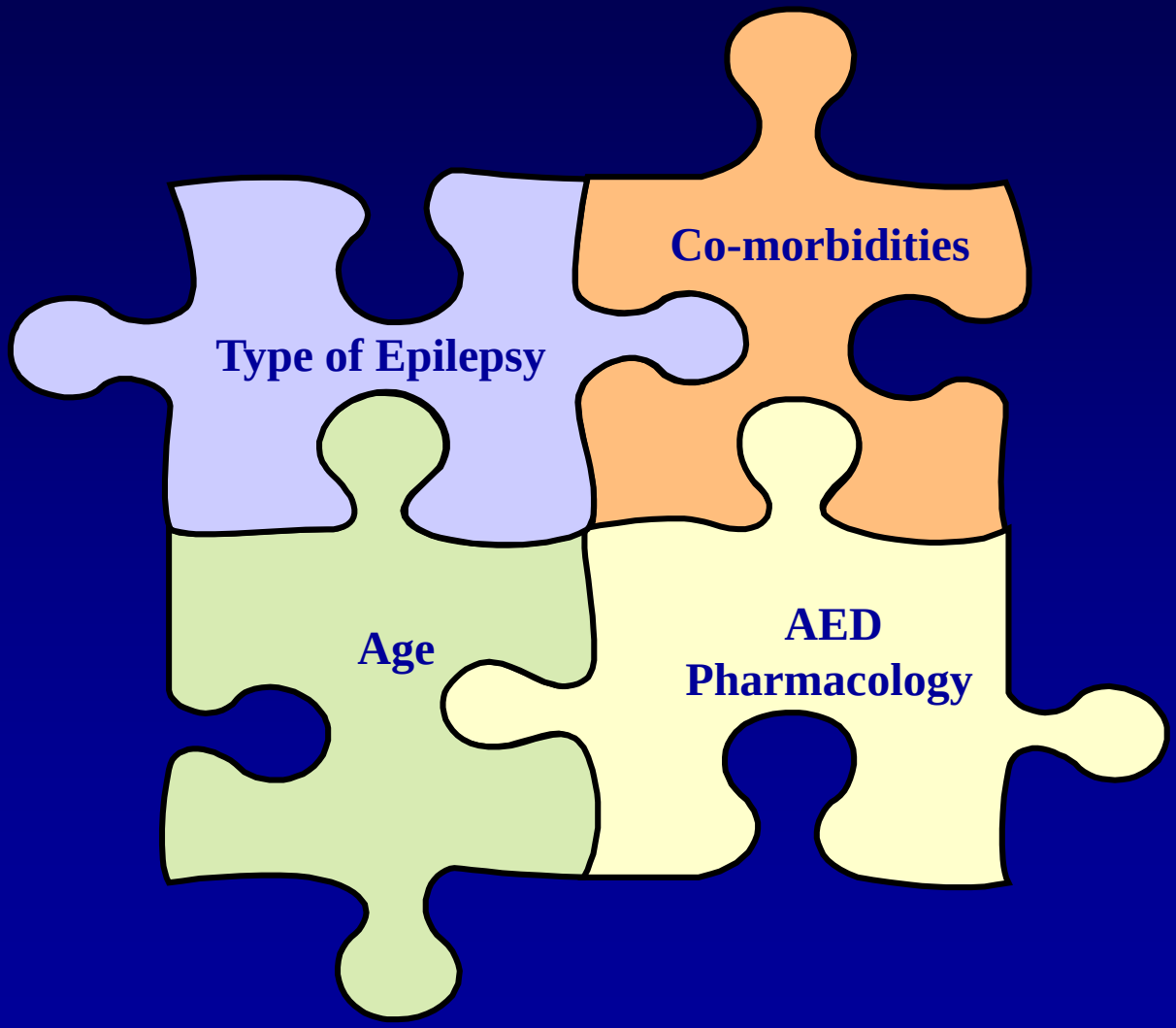
Making the pieces fit



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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 interactions
- Drugs with different mechanisms of action:? "rational" polytherapy/synergism

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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

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Choice of AEDs

- AED pharmacology
  - Rapidity of titration
  - Side effect profile

- Most important parameters:
  - Efficacy
  - Safety

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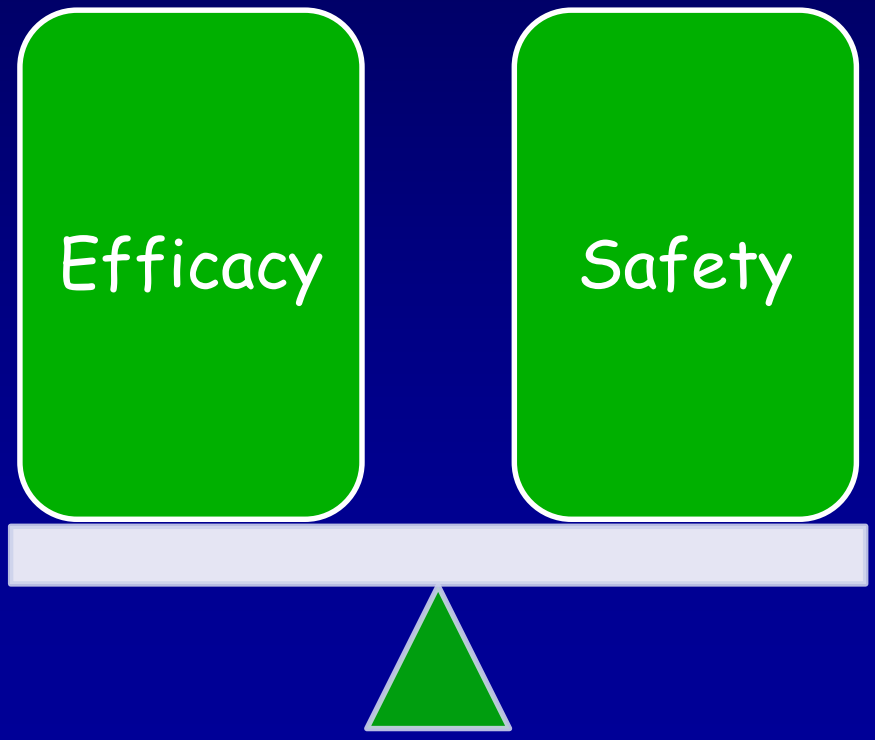
Choice of AEDs



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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

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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

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Management of Epilepsy

Treatment of seizures

(just the tip of the iceberg)

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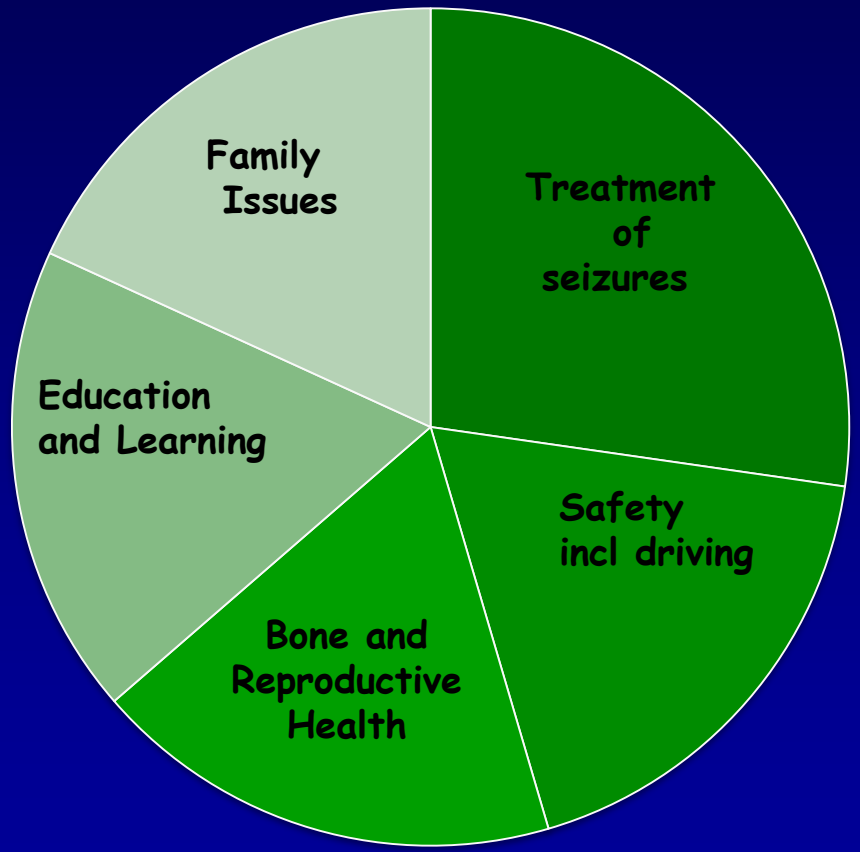
Management of Epilepsy: the bigger picture



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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

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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.

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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.

Dunn, et al. Dev Med Child Neurol. 2003;45:50-54.
Gucuyener, et al. J Child Neurol. 2003;18:109-112.
Koneski, et al. Epilepsy Behav. 2011;3:228-232.

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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

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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

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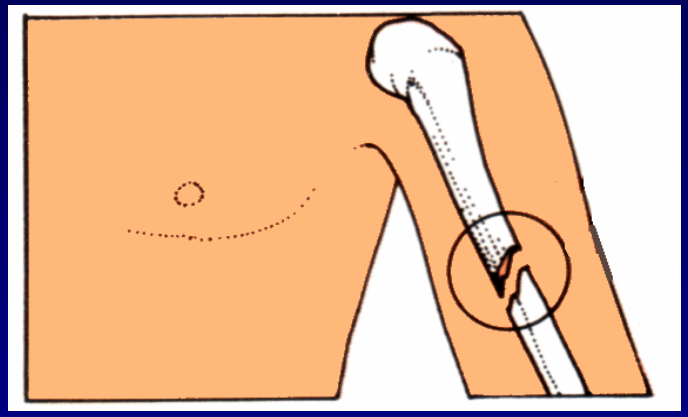
Bone Health



- Epilepsy = risk for poor bone mineralization.
- Seizures = risk for falls & fractures.

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Bone Health & Epilepsy

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

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Vitamin D

- Vitamin D insufficiency is common.
  - 25-hydroxyvitamin D <32ng/mL
  - ~60% of all US children[1]
  - ~75% of Michigan children with epilepsy[2]
- Risk factors: female sex, obesity
- All anticonvulsants implicated.
- All epilepsy syndromes implicated.

1. Kumar, et al. Pediatrics 2009;124:e362-70.
2. Shellhaas & Joshi. Pediatr Neurol 2010; 42:422-428.

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Typical scenario

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

25-OHD (ng/mL)	Supplement	Recheck	Additional studies
≥30	400 IU daily	Yearly	
15-29	1000 IU BID	Every 4 weeks until normal	Ca, Mg, PO_4
<15	2000-4000 IU per day in divided doses	Every 3-4 weeks until normal	PTH, Ca, Mg, PO_4, and consider Dexa

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Shellhaas & Joshi. Pediatr Neurol. 2010;42: 385-393.

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Reproductive Health

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

Camfield. Neurology. 2009; 73:1041-5.

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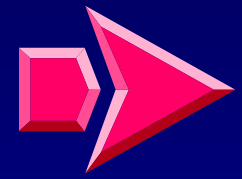
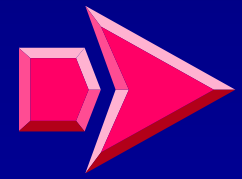
Reproductive Health

Neural Tube Defects

- Valproic Acid  1-2%

- Carbamazepine  0.5%

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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)

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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
  - 1st AED 47%
  - 2nd AED 13%
  - 3rd or subsequent AED 4%

Kwan and Brodie NEJM 2000

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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

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Who follows these kids?

Neurologist?

Epilpetologist?

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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

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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

NATIONAL ASSOCIATION OF EPILEPSY CENTERS
NAEC

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Level 3 Epilepsy center

Table 2. Third level epilepsy centers (adapted from *Epilepsia*, 42(6):804-814, 2001)

SERVICES PROVIDED	PERSONNEL
Electrodiagnostic EEG services including long term monitoring	Neurologists (Adult and/or Pediatric) with special expertise in epilepsy EEG technologists and related personnel
Epilepsy Surgery including VNS (routine lesional surgeries and those not requiring invasive monitoring)	Neurosurgeon(s) with special expertise in epilepsy
Neuroimaging	Neuroradiologist
Neuropsychological and psychological services	Neuropsychologist/neuropsychometrist Psychosocial personnel including clinical psychologist, social worker, school services for children
Pharmacological expertise	Access to consultation with Clinical Pharmacist
Nursing support (specific to epilepsy)	Nurse specialist
Rehabilitation (in patient and outpatient) including physical, occupational and speech therapy	Rehabilitation service personnel
Consultative expertise in multiple fields: neurosurgery, psychiatry, internal medicine, pediatrics, general surgery, obstetrics/ gynecology	Interdisciplinary clinical services available
Other	Biomedical engineer and IT support

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Level 4 Epilepsy Center

Table 3. Features distinguishing Level 4 centers

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

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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

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- 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

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- 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

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- 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.

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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

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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

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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.

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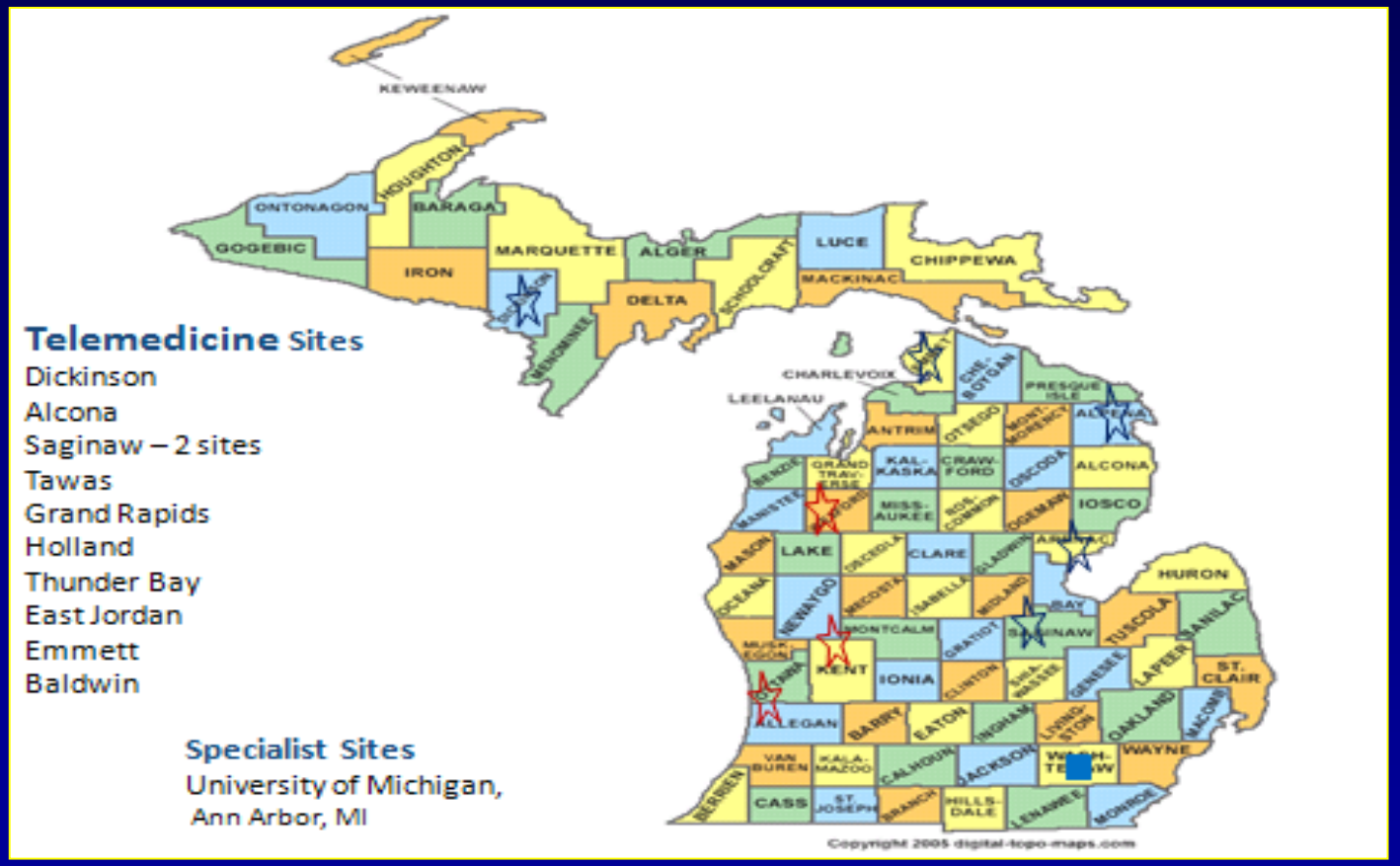
Telemedicine in MI (2013)



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