Appropriate Epilepsy Care: Diagnosis to Treatment

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Outline

- Epilepsy definition
- Diagnostic tools
- When to see an epileptologist
- Other providers
- Medication
- Alternative treatment options
- Barriers to care
Seizures and Epilepsy

- Epilepsy
  - 2 or more unprovoked seizures
  - One unprovoked seizure + risk of ongoing seizures
  - Diagnosis of an epilepsy syndrome

- 1 in 26 (4%) people will develop epilepsy at some point in life

- About 300,000 American children under 14 years of age have epilepsy
Epilepsy

- NOT JUST SEIZURES
- Comorbid conditions
  - Mood problems
  - School problems
    - ADHD
    - Learning difficulties
    - Behavior difficulties
    - Social problems
  - Developmental delays
First visits

Questions to answer:
- What?
- Why?
- Will it happen again?
- How should we treat your child?
History

- Child’s history
  - Birth history, early development
  - Medical problems, surgeries
    - Brain injury/Meningitis/Encephalitis
  - Medications/Allergies
  - Family history
  - School and social factors

- What happened
  - Witness, video
  - Preceding events: triggers? aura?
  - Event details: duration, features, ER details
  - Post–event details
Neurological exam

- Development
- Learning and speech skills
- Coordination and motor function
- Skin findings
Tests

- Goal: Determine seizure type and etiology
- Most common
  - EEG
  - MRI
EEG

- Small electrodes are attached to the scalp
- Records the electrical activity from the brain
- May show a risk for seizures or difference in function in one part of the brain
- Recording test, no electricity sent to the brain
EEG

- Looks at:
  - Electrical activity in the brain

- What it tells us:
  - Risk for focal vs generalized seizures
  - Characterize events
  - Snapshot in time
    - Can be normal

- Duration?
Brain MRI

- Cross-sectional pictures of the brain
- Pictures are created using a magnet—no radiation
- Loud noises
- 1–2 hours
Head CT

- Quick
- Emergencies
- Less detailed than MRI
- Radiation exposure
First few visits, other things

- Preparation for the next seizure
  - First aid tips
  - Emergency plan/abortive medicines

- Education
  - What do different seizure types look like
  - What to do during the next event
  - Who to call
    - Establish a good way to communicate
Seizure First Aid

As Seizure Ends, Offer Help
Stay Calm, Don't Hold Down
Cushion Head, Remove Glasses
Observe and Record What Happens
Don’t Put Anything in the Person's Mouth, Turn on Their Side
Loosen Tight Clothing

LEARN MORE AND GET A DOWNLOADABLE VERSION OF THIS ACTION PLAN AT:

Image adapted with permission from the Epilepsy Foundation of America

Child Neurology Foundation
Danny Did Foundation
Epilepsy Foundation
SUDEP Institute
Seizure Action Plan

- Description of seizure type
- Daily medication(s) and dose(s)
- Triggers
- First Aid
- Emergency Action Plan
Rescue Medication

- Diazepam/Diastat—rectal
- Midazolam/Nayzilam—intranasal
- Clonazepam/Klonopin—oral dissolving
Common Seizure Types

- Generalized tonic–clonic (grand mal)
  - Full body convulsion, rigid muscles, jerking
  - Typically 1–3 minutes
- Generalized absence (petit mal)
  - Blank staring, may having blinking or mouth movements
  - Typically a few seconds
- Focal onset–impaired awareness (complex partial)
  - Staring, confusion, abnormal speech or movements
  - Typically 1–2 minutes
- Focal aware (simple partial)
  - Motor or sensory symptoms in one or more parts of the body
Common Seizure Types

- Atonic (drop attacks)
  - Sudden collapse, recovery within a minute
- Tonic
  - Full body stiffening
- Myoclonic
  - Sudden, brief jerks of all or part of the body
Preventative Treatment Options
Medications: Timeline of FDA Approval
Medications

Finding the right medication

- Goals
  - No seizures
  - No side effects
  - Minimal number of medications
  - Lowest effective dose
Medications

- Finding the right medication
  - Seizure type
    - Broad spectrum vs focal medications
    - Specialized:
      - Infantile spasms
        - ACTH, vigabatrin, prednisolone
      - Absence
        - ethosuximide, valproic acid, lamotrigine
Medications

- Finding the right medication
  - Side effect profile
    - Medication interactions
    - Other organ system considerations
    - Childbearing age
  - Other health conditions
    - Migraine
      - topiramate, valproic acid
    - Depression/bipolar disorder
      - lamictal, valproic acid, oxcarbazepine
    - Tics
      - topiramate, valproic acid, keppra
Medications

Finding the right medication
  ◦ Convenience
    • Frequency of dosing
      • Long half–life or extended release formulation
    • Available forms
      • Liquid, pill, oral film, IV
    • Need for lab monitoring
How is the medication adjusted

Every medication has a recommended dose range based on your child’s weight

- Mg/kg/day
- Ex: levetiracetam
  - Your child weighs 36 pounds, (~16.4 kg)
  - ~160 mg twice daily to 500mg twice daily

- Start low and go slow
- Increase if your child has a breakthrough seizure
Changing Medications

- Intolerable side effect
- Medication is not effective
- Medication cannot be given as instructed
- Please tell us!
Follow-up Visits

Topics of discussion at next visit(s)

- Seizure frequency
- Seizure type(s) and duration
- Triggers
  - Sleep deprivation, infections, compliance, alcohol
- Medication compliance
- Medication side effects

- Logs and videos can help
Subsequent visits

- Discuss test results
  - You can ask to see pictures of EEG findings and MRI findings
  - Keep a folder with results, medications
- Review your emergency plan
- Update your seizure action plan if needed
- Ask questions about safety if needed
  - Driving, working, water safety, helmets
Epilepsy Visits

- Before school age
  - Behavior
  - Developmental milestones
  - Therapies
  - Early Childhood programs
    - Early On (<3)
    - Early Childhood Special Education (3–5)
**Epilepsy Visits**

- **School age**
  - **Behavior/Mood**
    - Treatment of ADHD, learning disorders, mood problems
  - **School performance**
    - Individualized Education Plans (IEP)
    - 504 Plan
    - Seizure Action Plan
    - School safety
  - **Therapies**
Epilepsy Visits

- School age/ Teens
  - Increasing independence
  - Hormonal influence
  - Pregnancy planning, Folic Acid
  - Effects of drugs and alcohol on seizure control
  - Behavior/Mood
Epilepsy Visits

- School age/ Teens
  - Driving
    - https://www.epilepsy.com/driving-laws
  - Long-term planning
    - Transition topics
    - Guardianship
    - Continued school options
  - Therapies
Other possible providers

- Neuropsychologists
- Psychologists
- Psychiatrists
- Social workers
- Therapists
  - OT/PT/Speech/ABA
- Nurse practitioners
- Neurosurgeons
- Dietitians
Tips to prepare for visits

- Keep a log of events
- Monitor compliance
- Bring details about family history
- Bring a list of questions and concerns
- Bring your medication bottles
- Look at your abortive to see the dose and expiration date
- Maintain a folder with results and prior records
  - bring this if you are seeing a new provider (or send a copy in advance)
When Medications Do Not Work

- Drug Resistant Epilepsy
  - Continued seizures despite 2 or more well-chosen medications at good doses

- Likelihood of response
  - ~2/3 will have their seizures controlled with one or more medications
  - ~1/3 will continue to have seizures despite medications
Kwan and Brodie 2001: Effectiveness of first Antiepileptic Drug
- Scotland
- Looked at 470 newly diagnosed, untreated patients with epilepsy
- The majority of patients were adults, ~10% were between 9–15 years of age
- About 47% seizure–freedom with first medication
- About 64% had 1 yr seizure freedom total with subsequent drugs
- Rate dropped with each subsequent medication
Kwan and Brodie 2018: Treatment outcomes in Patients With Newly Diagnosed Epilepsy Treated with Established and New Antiepileptic Drugs: A 30-Year Longitudinal Cohort Study

- Scotland, mostly adults
- Included 1795 newly diagnosed, untreated patients with epilepsy
- About 64% had 1 yr seizure freedom
- ~50% seizure-free with first medication
- Rate dropped with each subsequent medication
  - Likelihood of seizure freedom 11.6% with second, 4.4% with third
  - 2.12% attained seizure control with subsequent medications
Evaluation of drug resistant epilepsy

- Is the diagnosis correct??
  - Imitators
    - Fainting spells
    - Mini–strokes
    - Low blood sugar
    - Migraine symptoms
    - Sleep disorders
    - Movement disorders
      - Tics, tremors, dystonia
    - Panic attacks
    - Nonepileptic spells
Is the diagnosis correct?

- Compliance
  - Drug levels, pill counts, history
- Capture and characterize spells
  - Overnight EEG
- Re-evaluate medication choices
- May seek other opinion(s)
  - Epileptologists provide expert care for patients with epilepsy
  - A Comprehensive Epilepsy Center specializes in care for patients with epilepsy
    - Has experts who can provide extra care for patients with epilepsy
Evaluation of drug resistant epilepsy

- Consider need for further testing
  - Repeat MRI?
  - Genetic testing
  - PET scan
  - SPECT scan
  - MEG
Genetic Testing

Basics

- Genes carry information that determine traits
  - Ex: eye color
  - Genes are passed to you from your parents
  - Each cell in the body contains ~25,000–35,000 genes
  - Genes are grouped together on structures called chromosomes
Basics

- Humans have 23 matching pairs of chromosomes
  - one of each set from each parent
- Hundreds to thousands of genes are on each chromosome
Each gene has a special job
They spell out instructions, make unique proteins
When genes have problems (mutations, duplications or deletions), the instructions may be wrong and cause something in the body to function incorrectly
Problems with the genes may cause a risk for seizures
Genetic Testing

- Types of gene problems
  - Single gene
  - Multifactorial
    - Multiple genes and environmental factors
  - Mitochondrial disorders
  - Chromosomal disorders
    - Chromosome is changed
  - Epigenetic disorders
    - Change the way genes are expressed
How can it help?

- Can confirm a specific diagnosis
- Provide information about other associated neurologic or medical conditions
- May help with medication or treatment selection
- May help to limit unnecessary or invasive testing
- May assist with understanding the prognosis
- Provides a basis for further genetic counseling
Example

- Glut 1: Glucose transporter type 1 deficiency
  - Glucose from the blood cannot be transported into brain cells
  - The brain receives inadequate energy
  - Children may have multiple seizure types, developmental delays, movement disorders
  - SLC2A1 mutation, Chromosome 1
  - Uniquely responsive to ketogenic diet
GLUT 1 deficiency

- Typically seizures begin within the first few months of life
  - May be focal initially, then multiple different types
  - Early and refractory absence have been reported
- Other symptoms may include abnormal body or eye movements, microcephaly, developmental delays
Genetic Testing

- How is it done
  - Blood or saliva test

- Possible outcomes
  - Pathogenic mutation
  - VUS
  - Negative
PET Scan

- Positron Emission Tomography
- Shows the brain’s use of sugar (glucose) or oxygen
- A low dose radioactive substance is injected into the patient’s arm and then the scan is performed
- May be done with an EEG at the same time
- Shows areas of the brain with abnormal metabolism
**PET Scan**

- Used often in epilepsy surgery evaluation
- Helps us find the area where seizures may start
- Ex below: left temporal hypometabolism, normal brain MRI, child with focal epilepsy
SPECT SCAN

- Single-photon emission computed tomography (SPECT)
  - Nuclear radiology study that measures blood flow in the brain both at seizure onset and in between seizures
  - The study is performed during an admission to an Epilepsy Monitoring Unit
SPECT SCAN

- Single-photon emission computed tomography (SPECT)
  - Injection of small dose of radioactive tracer is given within seconds of seizure onset and then the scan is performed
  - A second injection is given in between seizures to look at blood flow between seizures
  - The images are then combined and placed on an MRI
A fifteen-year-old female with intractable seizure

Injection at 5 s and total duration of seizure of 8 s

A. hyperperfusion in left frontal lobe, compared with right side

B. Interictal SPECT focal hypoperfusion involving the posterior left frontal lobe

MEG

- Magnetoencephalography
  - Often combined with structural imaging and is then called magnetic source imaging
- Measures small electrical currents arising inside the neurons in the brain
- Can be used to see location of brain function
- Can be used to see areas of the brain that may generate seizures
- Can be helpful when the MRI and EEG give different information
10 yr old medically refractory epilepsy

Video EEG suggested that her seizures arose from the right side of the brain.

MRI showed multiple left-side lesions and none on the right.

FDG PET showed bilateral hypometabolism.

MEG showed interictal epileptiform discharges from a restricted location in the deep gray matter of the right middle frontal gyrus.

Repeat MRI in the region identified by MEG revealed a subtle hyperintensity extending centrally to the ventricle.

Intracranial electrodes guided by the MEG findings → limited resection of the epileptic focus, sparing motor function and eliminating the patient’s seizures.
Treatment of Refractory Epilepsy

- Epilepsy Surgery
- Vagus Nerve Stimulator
- Responsive Neurostimulation
- Ketogenic or Modified Adkins Diet
Treatment of Refractory Epilepsy

- Epilepsy Surgery
  - Potentially curative vs palliative
    - Focal resection
    - Lesionectomy
    - Multiple subpial transections
    - Laser interstitial thermal therapy
    - Hemispherectomy and hemispherotomy
    - Stereotactic radiosurgery
    - Corpus callosotomy
    - Neurostimulation device implantations (VNS/RNS)
Epilepsy Surgery

- Potentially Curative
  - Removal of one specific lesion or region of the brain that is causing the seizures
  - Best outcomes in people who have abnormalities on MRI and EEG
  - Avoid areas that are critical for speech, movement, vision
  - Minimally invasive options may be available
    - Laser interstitial thermal therapy, ex MTS
    - Stereotactic radiosurgery (radiation to very precise brain location)
Ex: Temporal lobectomy
  ◦ One of most common
  ◦ ~60–70% of people become free of seizures that impair consciousness or cause abnormal movements
  ◦ In general >85% have a significant reduction in seizure frequency (10–15% have no reduction)
  ◦ May need to remain on medications, may be able to lower medications
  ◦ Depending on lesion, region etc, rates vary
Corpus callosotomy

- More of a palliative procedure
- Reserved for people with severe, refractory generalized seizures, or bilateral involvement with frequent atonic or GTC seizures
- Cuts the connection between the 2 hemispheres of the brain
- May result in more than 50% seizure reduction in at least 2/3 of people
Corpus Callosotomy

85% of patients had at least a 50% seizure reduction

Outcome data from 20 patients from Children’s Hospital of Michigan, published in 2017, Dr. Luat et al. Journal of Child Neurology
Vagus Nerve Stimulator

- Prevents seizures by sending regular, mild pulses of electrical energy to the brain via the vagus nerve
- Stimulator device is implanted under the skin in the chest
- A wire from the device is wound around the vagus nerve in the neck
- A person with a VNS device is usually not aware it's operating
Vagus Nerve Stimulator

- Approved as add on for adults and kids 4 years and older
- A review of 65 people who had VNS for 10 years or more, showed improvements in seizure control over time
- Seizures decreased by:
  - 36% after 6 months,
  - 58% after 4 years,
  - 75% by 10 years after the VNS was placed
FDA approved 2013 for focal seizures in people 18 and older
- Monitors brain waves at the seizure focus, all the time – even during sleep
- Detects unusual electrical activity that can lead to a seizure
- Responds quickly (within milliseconds) to seizure activity by giving small bursts or pulses of stimulation
- Goal is to help brainwaves return to normal, even before it could turn into a seizure
Responsive Neurostimulation

- Settings can be adjusted over time
- Seizure frequency can be tracked
- 230 patients with the RNS® System were followed over time in a controlled trial
  - The average decrease in seizures was
    - 44% after 1 year
    - 53% at 2 years
    - up to 66% after 3 to 6 years
    - ~2/3 people with RNS have their seizures at least cut in half after 7 years of using it
**Ketogenic Diet**

- Low carbohydrate and protein
- High fat
- Body uses fat instead of glucose for energy
- 4:1, 3:1
  - 3–4 grams of fat for every 1 gram of carbohydrate and protein
  - No breads, pasta, sugary things
  - Lots of butter, oils, mayo
Ketogenic Diet

- Requires close oversight by trained dietitian
- Side effects
  - Constipation
  - Kidney stones
  - High cholesterol
  - Risk for fractures
  - Slow growth
- Typically reduces seizures by at least 50% in >50% of kids
Summary

- What to expect
  - Diagnosis
  - Follow-up Visits
  - Treatment Options
  - Refractory epilepsy
Barriers

- Why great care may be disrupted
  - Communication
  - Geographic barriers
  - Insurance challenges
  - Physician–patient relationship
Barriers

- Communication
  - Translator, ask at scheduling
  - Set expectations early
    - When should call?
    - What number (s) should call?
      - Emergency plan
      - Office number
      - Patient portal
      - On call
  - Think about what will work best for you
    - Work 9–5?
    - Phone often changing numbers?
    - Other family members very involved in care?
  - Get to know the nurse working with the practice
Barriers

- Geographic
  - Remind your doctor if you live far away
    - Telemedicine
    - Ask why the follow-up interval is set as it is, maybe you can extend
    - Know the visit grace period time
    - Call ahead if you are stuck in traffic
    - Ask about accommodations for families who live far away
      - Ronald McDonald House Charities
  - Call your insurance company to understand benefits
Insurance challenges
- Testing costs—call ahead for co-pay information
  - Neuropsych
  - Genetic
  - Imaging
- Prescription costs
  - Prescription copay cards?
  - Drug assistance programs?
- Provider limitations
  - Choose your plan around the preferred network
- Secondary insurance options
Barriers

- Children’s Special Healthcare Services
  - Michigan Health and Human Services

- Goal:
  - Assist individuals with special health care needs to receive appropriate medical care, health education and supports
  - Care coordination
  - Educational resources
  - Coverage and referrals

- Eligibility:
  - NOT income based.
  - Fee is waved in children with Medicaid, MIChild, a court-appointed guardian or lives in a foster home.

- For more information:
  - Contact your local county health department CSHCS office
  - Contact our CSHCS Family Phone Line at 1–800–359–3722 or cshcsfc@michigan.gov
Barriers

- Physician–Patient Relationship
  - You will work closely with this person for several years
    - Be open and honest so we can figure out together WHY something is not working
    - Talk early and often about goals and expectations
      - Ex: infantile spasms and child with global delays involved with palliative care
    - Advocate for your child and family
      - Do not be afraid to speak up and ask questions
    - Bring a list of questions
Barriers

- Epilepsy Foundation of Michigan
  - Access line: Here For You Help Line
  - Education
  - Support groups
  - Public Policy and Advocacy
  - Monthly Learn & Share Conference Calls
  - Epilepsy Awareness & First Aid Trainings
  - Camp Discovery
  - Self-Management Programs
  - Social & Networking Opportunities

- http://www.epilepsymichigan.org