Refractory Epilepsy

FACES

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EPILEPSY

• from the Greek *epilepsia*: a taking hold of or seizing
• Epilepsy: Two or more unprovoked seizures.
• Seizure: The clinical manifestation of an abnormal and excessive excitation of a population of cortical neurons.
• 5% of people will have a seizure in their lifetime. .5% will be diagnosed with epilepsy.
Etiology of Seizures and Epilepsy, Rochester, MN 1935 – 1984*

*Data from a 50-year population-based study. Use of newer imaging and other diagnostic techniques might alter some percentages.


- Idiopathic/cryptogenic: 65.5%
- Vascular: 10.9%
- Congenital: 8.0%
- Trauma: 5.5%
- Neoplastic: 4.1%
- Degenerative: 3.5%
- Infection: 2.5%

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In the brain, information is highly spatially organized with different groups of neurons controlling specific body parts and responding to sensory stimulation.
**Event Type**

- **Nonepileptic**
  - Syncope
  - Migraine
  - Psychogenic
  - Toxic
  - Cerebrovascular
  - Metabolic
  - Parasomnia
  - Tremor
  - Movement disorder

- **Epileptic**
  - Generalized
    - Absence
    - Tonic-clonic
  - Partial
    - Simple
    - Complex
    - Secondarily Generalized

Guidelines for Epilepsy Pharmacotherapy

• Tailor therapy to seizure type
• Begin with low-dose monotherapy; titrate slowly to minimize side effects
• Keep dosing regimen as simple as possible
• Provide patient education regarding
  – Importance of compliance
  – Use of AEDs as preventive medicine
• Balance among efficacy, side effects, and quality of life
Response Rates for Newly Diagnosed Epilepsy Patients

1st AED
- 53% Sustain recurrences
- 47% Seizure-free (Cumulative Total)

2nd AED
- 40% Sustain recurrences
- 13% Respond to 2nd AED
- 60% Seizure-free (Cumulative Total)

3rd AED
- 39% Sustain recurrences
- 1% Respond to 3rd AED
- 61% Seizure-free (Cumulative Total)

4th AED
- 36% Sustain recurrences
- Refractory?
- 3% Respond to 4th AED
- 64% Seizure-free (Cumulative Total)

Refractory Epilepsy

- Three or more anticonvulsants have been tried and failed
- Failure is considered breakthrough seizures of any frequency
How can we treat refractory epilepsy?
Reasons for Failure of Epilepsy Drug Therapy

• Incorrect diagnosis
• Drug-resistant condition
• Underlying progressive neurologic disorder
• Inappropriate AED
• Suboptimal dosing
• Intolerable side effects
• Noncompliance
• Drug interactions
• Lifestyle
Drugs in development

- Brivaracetam - related to levetiracetam.
- Eslicarbazepine
- Lacosamide
- Ritigabine
- Carisbamate
- Rufinamide
Epilepsy Surgery

• Only indicated for partial epilepsy
• The focus of seizures is identified and removed.
• For mesial temporal sclerosis, epilepsy surgery can render 73% of patients seizure free.
Epilepsy surgery preoperative evaluation

EEG & video-EEG
MRI & CT
PET & SPECT
History
Exam
Neuropsychologic test
Neuropsychiatry
Wada (Intracarotid amobarbital test)
Social work evaluation

Invasive EEG
Pathophysiology/Syndromes
MEG - source localization
Ketogenic Diet

- Developed in the 1920’s
- Low carbohydrate and high fat intake
- 20% of children on the diet have a 90% reduction in seizure frequency.
- Very difficult to comply with.
Sample ketogenic Meal for a 7 year old

• Whip 35 gms cream with and artificial sweetener and vanilla extract
• Layer whipped cream with 21 gms of strawberries
• Mix remaining 35 gms cream with water for drink
• Mix hard boiled egg with bacon and mayonnaise
• Serve with lettuce leaf
• Modified Atkins or South Beach may have similar efficacy to the Ketogenic diet.
Brain and nerve stimulation for the treatment of epilepsy
Vagus Nerve Stimulator

• It is the only currently available FDA improved method for nerve stimulation.
• Mechanism of action poorly understood.
• Electrodes wrap around the left vagus nerve and connect to a generator placed under to skin.
• The stimulator delivers preprogrammed intermittent electrical impulses.
• In addition, it may be activated by the swipe of a magnet at the onset of seizure.
Vagus nerve stimulator - surgical placement
Neuropace

- Device implanted with strips or depth electrode placed over the area of seizure foci.
- Detects abnormal electrical activity and delivers stimulation to abort the activity.
- For multifocal partial epilepsy or for epilepsy that overlays “eloquent cortex”.
The beginning of a seizure is aborted with stimulation.
Deep Brain Stimulation in Movement Disorders
Anterior Thalamic Stimulation

Electrode depth is placed in the anterior thalamic nuclei and deliver stimulation. In trial for refractory partial or generalized epilepsy.
Future possibilities.

• Focal cooling of seizure foci with a subdural device.
• Medication delivery systems that bypass the blood brain barrier, minimizes systemic side effects.
• Stem cell transplant.
• “You are all healthy people, but you have no idea what joy that joy is which we epileptics experience the second before a seizure. [...] I do not know whether this joy lasts for seconds or hours or months, but believe me, I would not exchange it for all the delights of this world.”