Medical Management of Epilepsy

Anna Larson, MD
Child Neurology Resident
MassGeneral Hospital for Children
Clinical overview

Definitions
Clinical evaluation
Seizure etiologies
Seizure types

Treatment of epilepsy

Medications
Dietary therapy
Vagus nerve stimulator
Epilepsy surgery
Epilepsy affects 1-2% of individuals worldwide. It is the most common neurologic problem in childhood.
Seizure

Manifestation of abnormal and excessive **synchronized discharge** of a set of cerebral neurons. Clinical manifestations are sudden and **transient**. Symptoms depend on part of brain involved in discharge

Epilepsy

Two or more seizure episodes
Status epilepticus

Condition in which seizure activity continues or is repeated without regaining consciousness for a period of 15 minutes or more

Medical emergency
Epileptic encephalopathy

Cognitive and behavioral impairments in individuals with epilepsy that result from epileptiform activity

Add to baseline impairments

May worsen over time

? May improve with treatment
Clinical evaluation

History, general and neurological examination

Physiology
   EEG, ictal video
   MEG, PET, SPECT

Anatomy
   MRI

Genetics
   Dravet’s, GLUT1, ARX, CDKL5, TSC
Clinical evaluation

History of the seizure from the patient situation in which arose, trigger factors, pattern, prodromal symptoms, onset of seizure including aura or focal motor features

Seizure itself
Duration of loss of consciousness
Postictal symptoms
History of seizure from witness
Differential diagnosis for seizure

Syncope
  Vasovagal
  Cardiac
  Postural
  Breath-holding spells

Daydreaming

Migraine

Transient ischemic events

Parasomnias

Normal physiological movements in sleep
Differential diagnosis for seizure
Acute rise in intracerebral pressure
Gastro-esophageal reflux
Vestibular disorders
Hyperekplexia
Involuntary movement disorders
Psychotic hallucinations and delusions
Panic attacks
Psychogenic non-epileptic seizures
Etiology of epilepsy

Inherited genetic

Congenital (inherited or acquired)
  Cortical dysplasia/dysgenesis
  Tumor
  Vascular malformation
  Prenatal injury
Etiology of epilepsy

Trauma
Neurosurgery
Infection
Vascular disease
Hippocampal sclerosis
Neurodegenerative disorders
Metabolic disorders
Toxic exposure
Clinical seizure types

Focal
  Starts in a specific part of the brain

Generalized
  Starts in a large area of the brain in both hemispheres
Focal seizure types

Focal seizure with preserved awareness
   *simple partial*

Focal seizure with impaired awareness
   *complex partial seizure*

Focal seizure with secondary generalization
Focal seizure with impaired awareness

Aura
Altered consciousness
Automatisms
  Oro-alimentary — chewing, lip smacking, swallowing, drooling
  Mimicry — laughter, fear, anger or excitement
  Gestural — fiddling movements of hands, tapping, patting or rubbing, ordering and tidying movements
Ambulatory — walking, circling or running
Focal seizure with impaired awareness

Aura
Altered consciousness
Automatisms
   Verbal — meaningless sounds, humming, whistling, grunting, repeating words
   Responsive — quasi-purposeful behavior, seemingly responsive to environmental stimuli
Violent behavior
Generalized seizure

Consciousness impaired from onset due to extensive cortical and subcortical involvement

Motor changes bilateral, symmetric

EEG patterns bilateral, grossly synchronous and symmetrical
Generalized seizure

Typical absence (petit mal)
Atypical absence
Myoclonic
Clonic
Tonic
Tonic-clonic
Atonic
Typical absence seizures

Abrupt onset with loss of consciousness
Abrupt end with resumption of activity
No postictal period, child often unaware of seizure
Automatics can occur

EEG
  ictal: 3 Hz spike and wave
  interictal: normal

Induced by hyperventilation, occasionally photic stimulation
Tonic clonic seizure

Prodromal period

*Aura: focal seizure with secondary generalization*

Loss of consciousness, occasional vocalization

- Tonic phase, cyanosis common (10-30 sec)
- Clonic phase (30-60 sec)

Postictal phase (2-30 min)
Epilepsy treatment

Goal is for seizure control without significant side effects

Appropriate therapy requires accurate diagnosis
Seizure classification
Epilepsy classification
<table>
<thead>
<tr>
<th>Year</th>
<th>Medicine or Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1857</td>
<td>Bromides</td>
</tr>
<tr>
<td>1912</td>
<td>Phenobarbital</td>
</tr>
<tr>
<td>1920’s</td>
<td>(Ketogenic Diet)</td>
</tr>
<tr>
<td>1938</td>
<td>Phenytoin</td>
</tr>
<tr>
<td>1950’s</td>
<td>ACTH</td>
</tr>
<tr>
<td>1970’s</td>
<td>Valproate, carbamazepine</td>
</tr>
<tr>
<td>1993</td>
<td>Felbamate, Gabapentin</td>
</tr>
<tr>
<td>1994</td>
<td>Lamotrigine</td>
</tr>
<tr>
<td>1997</td>
<td>(Vagal Nerve Stimulator), Topiramate</td>
</tr>
<tr>
<td>1998</td>
<td>Tiagabine</td>
</tr>
<tr>
<td>2000</td>
<td>Levetiracetam, Oxcarbazepine, Zonisamide</td>
</tr>
<tr>
<td>2005</td>
<td>Pregabalin</td>
</tr>
<tr>
<td>2009</td>
<td>Rufinamide, lacosamide, vigabatrin</td>
</tr>
<tr>
<td>2010</td>
<td>ACTH</td>
</tr>
<tr>
<td>2011</td>
<td>Clobazam</td>
</tr>
<tr>
<td>2017</td>
<td>Breviteracetam</td>
</tr>
<tr>
<td>Primary generalized</td>
<td>Focal onset</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Absence</td>
<td>Focal w/ preserved awareness</td>
</tr>
<tr>
<td>Myoclonic</td>
<td>Focal w/ impaired awareness</td>
</tr>
<tr>
<td>Atonic Tonic</td>
<td>Secondary Generalized Tonic-Clonic</td>
</tr>
<tr>
<td>Tonic-Clonic</td>
<td>Ethosuximide</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine, Phenytoin, Phenobarbital, Primidone, Gabapentin, Tiagabine, Pregabalin, Oxcarbazepine, Vigabatrin, Lacosamide</td>
</tr>
<tr>
<td></td>
<td>Valproate, Felbamate, Lamotrigine, Topiramate, Levetiracetam, Zonisamide, Rufinamide, Lacosamide, Clobazam</td>
</tr>
</tbody>
</table>
Intractable seizures

Seizures that are **not controlled by medications**, or are controlled only by medications that have significant side effects.

1/3 of children with epilepsy will develop intractable epilepsy
Dietary therapy of epilepsy

Ketogenic Diet
Low Glycemic Index Treatment
Modified Atkin’s diet
Distribution of nutrients as a proportion of the daily caloric intake
Ketogenic Diet

High fat diet designed to mimic the biological effects of starvation

Developed in the 1920’s

Probably the best single anticonvulsant treatment

But not easy for the child or family
Vagus Nerve Stimulator

Pacemaker generator
Nerve stimulation electrode
Intermittent stimulation
Magnet on demand therapy
Epilepsy surgery

Should be considered after failure of $\geq 2$ appropriately chosen medications

“Ideal” surgical candidates
- Single seizure phenotype
- Focal seizures
- Focal EEG
- MRI shows a single well differentiated lesion
Pediatric epilepsy
Age-related seizures
Etiology of seizures
Benign syndromes
Developmental delay
CNS plasticity
Thank you

Elizabeth Thiele
Ron Thibert
Patricia Bruno
Leigh Horne-Mebel
Amy Morgan
Grace Shanks
Robyn Bluestein
T’Asia Zayas

Patients and families