Objectives

- Emphasize the importance and ubiquity of seizure disorders in adults.
- Provide an overview of the most common seizure disorders, their definitions and classifications.
- Discuss symptoms and signs that can help identify seizures.
- Discuss steps to manage some common seizures problems.
- Discuss the presentation and management of acute seizures and status epilepticus.
- Provide pictorial examples of the EEG waves, including examples of electrographic seizures.

Epidemiology

- Seizures occur in ~5% of the population, of which ~1% (2 million) have epilepsy
- Annual incidence: 44 per 100,000
- Prevalence: 6.42 per 1,000
- Cumulative incidence:
  - 1.2% by age 24
  - 3.1% by age 74
  - 4.4% by age 85

Definitions

- A seizure is a symptom, not a disease!!!! (You need to find the etiology, just like in fever.)
- Epileptic seizure:
  - Manifestation(s) (symptoms and signs) of excessive and hypersynchronous, usually self limited, activity of neurons in brain.
- Epilepsy:
  - A chronic disorder characterized by recurrent (more than 2), stereotypical, epileptic seizures (neuronal electric discharges).
The ILAE Classification of Seizures

1. Self-limited seizures types
   I. Generalized
   II. Partial (focal, localization related)

2. Continuous seizure types
   I. Generalized
   II. Focal

Self-limited seizures types

I. Generalized
   I. Clonic tonic
   II. Absence
   III. Myoclonic

II. Partial (focal, localization related)
   I. Focal sensory
   II. Focal motor
   III. Gelastic

Some Epileptic Syndromes

• Childhood absence
• Juvenile myoclonic epilepsy
• Generalized tonic-clonic epilepsy
• Lennox-Gastaut syndrome
• West syndrome
• Landau-Kleffner
• Reflex epilepsies (e.g. visual, reading, startle, etc)
• Febrile seizures
• Alcohol withdrawal seizures
• Epilepsy associated to other diseases (e.g. stroke, tumors, post-infectious, neurocutaneous syndromes, etc)

A Pathophysiological Explanation to a Common Epileptic Condition: Hippocampal Sclerosis

Seizure Precipitants

• Stress, emotion
• Sleep/sleep deprivation
• Hyperventilation
• Fever
• Medications, metabolic disturbance
• Reflex epilepsy
   – Photic stimuli: TV, flashing lights, visual patterns
   – Startle, music, reading, eating
Epilepsy Evaluation

- Detailed History
- EEG
  - should include sleep, photic, HV
- MRI
  - unless epilepsy is clearly genetic
- EEG-video monitoring
  - unusual attacks
  - refractory- needs seizure classification
  - refractory- needs localization for surgery
- PET, SPECT
  - Presurgical evaluation

Case

An 18yr female admitted in the Epilepsy Lab (EMU) for evaluation of recurrent spells. These atypical spells are associated with lightheadedness. Without warning she would become unresponsive and “go limp”. Myoclonic jerks were noted in the upper extremities. The patient has had vocalization, urinary or fecal incontinence and tongue biting.

Case

- Neurologic exam ---- normal
- EEG ---- normal
- MRI ---- normal
- EKG: episodes of asystole were recorded with patients typical spell
- Patient became asymptomatic after implantation of a cardiac pacemaker.

All that jerks is not a seizure!

- Syncope
- Hyperventilation/panic attacks
- Migraine and migraine equivalents
- Paroxysmal movement disorders
- Sleep disorders
- TIAs
- Transient global amnesia

Is That and Epileptic Spell?

<table>
<thead>
<tr>
<th>Non epileptic seizures</th>
<th>Epileptic seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precipitated by stress</td>
<td>Can be ppt by stress</td>
</tr>
<tr>
<td>Quivering, side-to-side movements of the head, pelvic thrusting, and uncontrolled flailing, thrashing, or asynch, rhythmic mov. of the limbs</td>
<td>Stereotypical</td>
</tr>
<tr>
<td>Variable features</td>
<td>Constant features</td>
</tr>
<tr>
<td>Eyes closed</td>
<td>Usually eyes open</td>
</tr>
<tr>
<td>No post-ictal change</td>
<td>Post ictal state</td>
</tr>
<tr>
<td>Refractory to adequate AED levels</td>
<td>Responsive to AEDs</td>
</tr>
<tr>
<td>Prolonged duration</td>
<td>Seconds to minutes</td>
</tr>
<tr>
<td>Normal plasma prolactin</td>
<td>Elevated prolactin</td>
</tr>
<tr>
<td>Rare but do occur</td>
<td>Self-injury and incontinence of urine or stool</td>
</tr>
</tbody>
</table>
CASE
An 10 year old boy is brought to you because his teacher at school complaints that the boy seems at times “spacey”, blinks a few times, smacks his lips for a few seconds, and then continues doing what he was doing. On your exam, everything seems normal, but you recall from the Epilepsy lecture that hyperventilation can unmask something. You ask the boy to breath deep and fast and you witness the spell that mom and teacher were talking about.
What is in your diagnostic list?
How do you further assess?
How do you treat?

Absence Epilepsy
• Age of onset is 3-20 years
• Short duration (~10 seconds)
• Rapid onset, without warning
• Very rapid recovery
• Automatism or mild clonic movements
• Precipitated by hyperventilation
• EEG: 3 Hz spike and wave

CASE
22 year old male developed seizure disorder at 15yrs of age. Prior neurologic exam was unremarkable. Over the years patient has experienced GTC shortly after awakening, often precipitated by sleep deprivation and excess alcohol use. In the early morning hours after waking body jerks would appear, interfering with eating and dressing.
• What epileptic syndrome may he have?
• What drugs are likely to control these seizures?

Juvenile Myoclonic Epilepsy (JME)
• An idiopathic generalized epileptic syndrome that occurs in 5% to 10% of patients with epilepsy
• Between ages 12-18 years, may persist throughout life (~80-90%) 
• Seizures predominantly shortly after awakening
• Diagnosis can be delayed many years
• Characterized by myoclonic seizures and GCTC seizures in about 90% of patients, and absence seizures (30%)
• Seizure precipitants: Emotional stress, alcohol, illegal drug use, late nights of studying or parties
• Therapy: valproic acid, clonazepam, topiramate
• EEG: 4-6 Hz SW discharges interictally and during myoclonic seizures
Treat or not to Treat

- The risk of recurrence of seizures is about 30-35% after the first unprovoked seizure
- The risk of recurrence is about 70% after second unprovoked seizure

EEG yield

- 1st EEG: 50%
- With repeated EEG and activation procedures the yield can go up to 90%
- No benefit after the fourth EEG, as it gives maximum yield

Drug Therapy Basic Principles

- Use a single drug whenever possible
- Start low and go slow
- Increase the dose of that drug to either seizure control or toxicity (decreasing the dose if toxicity occurs)
- If a drug does not control seizures without toxicity, switch to another appropriate drug used alone, and again increase the dose until seizure control occurs or toxicity intervenes

Drug Therapy Basic Principles

- "therapeutic range" is a guideline and not an absolute. Some patients achieve seizure control with blood concentrations below the range, and others tolerate concentrations above the range without toxicity.
- Consider using two drugs only when monotherapy is unsuccessful. Keep in mind that some patients may have more seizures when taking two drugs rather than one drug because of drug interactions
Drug Therapy

Basic Principles

- Be aware that the ability to metabolize anticonvulsant drugs is different in the young, the elderly, pregnant women, and people with certain chronic diseases, especially hepatic and renal disease, than in healthy, nonpregnant adults.

AEDs Toxicities

- Phenytoin: rash, lymphadenopathy, purple glove
- Carbamazepine: rash, hypersensitivity, low Na
- Valproic acid: liver failure, pancreatitis
- Phenobarbital: rash, connective tissue disorders
- Primidone: connective tissue disorders
- Ethosuximide: blood dyscrasias
- Felbamate: aplastic anemia, liver failure
- Lamotrigine: skin rash
- Topiramate: weight loss, psychosis, dysarthria

Case

A 27 yr woman with history of epilepsy has just received her positive pregnancy test. She is on carbamazepine. Her seizure frequency is 1-2 seizures in six months.

- She is concerned about teratogenic effects of the medication.
- Should we take her off the medication?
- What therapeutic and monitoring care do we need to think about?

Guidelines for the Management of Epilepsy During Pregnancy

- Baseline AED levels (total/free) and serum folate
- Folate supplementation level 1-4 mg/day
- Maternal alpha-fetoprotein level at week 15-16
- AED levels and fetal ultrasound at 18-19 weeks
- Repeat fetal ultrasound at 22-24 weeks
- AED levels at 34-36 weeks. Make adjustments to ensure therapeutic drug levels at term.
- Vitamin K 20 mg/day during eighth month or 10 mg IV 4 hours before birth and 1 mg IM to newborn at birth
- Monthly AED levels postpartum for 12 weeks

Drug therapy

1. Partial and Secondarily
2. Generalized Seizures

- Carbamazepine, phenytoin, and valproic acid are the first-line agents among most specialists for partial and secondarily generalized seizures.
- Gabapentin, lamotrigine, oxcarbazepine, tiagabine, topiramate, and vigabatrin are new anticonvulsants that are recommended for treatment of partial seizures.
Generalized Seizures

- **Primary Generalized Seizures**
- Ethosuximide and valproic acid are equally effective for treating absence seizures, but ethosuximide is not effective for treatment of primary generalized tonic-clonic seizures.
- Other AEDs: lamotrigine, topiramate, felbamate, tiagabine, zonisumide

Case

- 30 yr male with history of epilepsy has been seizure free on valproate for the last 2.5 years. He is not having any side effects. He is wondering if we can take him off medication.
- What should we do?

Discontinuing AEDs

- Seizure free 2-5 years on AEDs
- Single type of partial or generalized seizures
- Normal neurologic examination and normal IQ
- EEG normalized with treatment
- Relapse 31.2% children, 39.4% adults

What is status epilepticus?

- A seizure which shows no clinical signs of arresting after a duration encompassing the great majority of seizures of that type in most patients or recurrent seizures without resumption of baseline central nervous system function interictally.

SE Therapy

- ABCD+N
- Oxygen, vital signs, IV access and IV fluids, check glycemia (Rx with thiamine?)
- Protect patient and others from injury
- Position patient on one side (prevent aspiration)
- Treat seizures the earliest possible
- Drugs: IV lorazepam (or diazepam), IV phenytoin (fosphenytoin), IV barbiturates, anesthesia
- Get labs: SMA 6, SMA 12, CBC with diff and platelets, If on AED’s check AED levels, Hold urine and serum specimen, CXR, EKG, myoglobin
SE: Rx2
• Aspiration and seizure precautions
• For continued uncontrolled seizures:
  – Intubate and ventilate patient
  – Control seizures ASAP
  – Complete EEG
• For patient with decreasing seizures:
  – Additional dose of fosphenytoin
• Transfer to NeuroICU
• Consider head CT, EEG, LP

Case
• A 65yr. Old female is acting confused for the last 1 week. The confusion fluctuates and its nadir she is unable to recognize any of her family members.
• O/E she can not recall her address or DOB
• She is afebrile and neck is supple
• No history of epilepsy

Labs:
– CBC, SMA 7    normal
– Head CT     normal
– Spinal Tap  normal
– EEG  continues ictal discharge were seen
• Diagnosis: Non-convulsive status epilepticus

Do NOT miss non-convulsive SE
• Non convulsive status epilepticus is a term used loosely to describe absence status, complex partial status and end stage convulsive SE
• Do NOT give paralytics for patients in status epilepticus. This may abolish the outward expression of the seizures while the brain continues to have epileptic activity.

Other Therapeutic Approaches
• Epilepsy surgery – resection of seizure focus
• Ketogenic diet
### Generalized Absence (GA) vs Complex Partial (CP) Seizures

<table>
<thead>
<tr>
<th></th>
<th>Gen. Absences</th>
<th>CPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aura</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Onset</td>
<td>Abrupt</td>
<td>Gradual or abrupt</td>
</tr>
<tr>
<td>Duration</td>
<td>&lt;15 sec</td>
<td>&gt;30 sec</td>
</tr>
<tr>
<td>Termination</td>
<td>Abrupt</td>
<td>Usually Gradual</td>
</tr>
<tr>
<td>Postictal S &amp; S</td>
<td>-</td>
<td>Most often +</td>
</tr>
<tr>
<td>Frequency</td>
<td>Many daily</td>
<td>Weekly-monthly</td>
</tr>
<tr>
<td>PPT by HV</td>
<td>Usually</td>
<td>Unlikely</td>
</tr>
</tbody>
</table>

### Epilepsy surgery

**Surgical Procedures**

- **Focal Cortical Resection**
  - In general, an anterior temporal lobectomy is performed for mesial temporal lobe seizures, but variations include an anterior medial resection or, in some cases, an amygdalohippocampectomy. When a specific structural lesion is identified, such as a tumor or malformation, the goals of surgery are removal of the abnormality and resection of epileptogenic tissue with careful attention to sparing functional tissue.
  - Extratemporal cortical resections are less common because extratemporal epileptic foci are less common and more difficult to localize, and resection is more likely to cause a functional deficit.
Epilepsy surgery

- The seizure focus is defined in a part of the brain that can be resected with a low probability of causing a functional impairment that is worse than the intractable seizures.
- Presurgical evaluation may include:
  - EEG-CCTV
  - MRI
  - PET/ictal SPECT
  - Neuropsychological testing
  - Wada test

Ketogenic diet

- Ketosis improves seizure control
- The basic protocol calls for a diet with a fat-to-carbohydrate-plus-protein ratio of 4 to 1 on a caloric basis. A modification of the diet uses medium-chain triglyceride (MCT) oil and allows for a greater amount of carbohydrate.
- Beneficial in a subset of patients who have not responded to antiepileptic drugs. It is used predominantly in children.

Epilepsy surgery

- **Hemispherectomy**: Sturge-Weber syndrome, diffuse cortical dysplasias, hemimeganencephaly, unilateral congenital injuries, and Rasmussen’s encephalitis. Because the involved cortex is already dysfunctional, hemispherectomy usually does not significantly increase motor, sensory, or cognitive impairment.
- **Corpus Callosotomy**: Generalized seizures, especially atonic seizures, show the greatest benefit from callosal section.

Epilepsy surgery

- Approx. 20–30% of patients with epilepsy do not respond to anticonvulsant drugs
- Adequate time to establish that seizures are refractory to medical treatment. In adults, this is usually 6 months to 2 years, but in special circumstances, such as epilepsy partialis continua, less time is needed. In children, shorter waiting periods are indicated when seizures are causing developmental delay.
- A precise diagnosis of seizure type and exclusion of patients with nonepileptic events.

Epilepsy

Epilepsy is a treatable condition and epileptic patients can live a normal and healthy life.

Epilepsy should not be a social or medical taboo.