UTHealth The University of Texas Health Science Center at Houston | McGovern Medical School

CLASSIFICATION, TREATMENT, AND MANAGEMENT OF EPILEPSY IN CHILDREN

CONVENTIONAL AND NON-CONVENTIONAL MEDICAL TREATMENTS

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DISCLOSURES

- None

LEARNING OBJECTIVES

Learn	Learn about the different types of Epilepsy
Recognize	Recognize epilepsy syndromes, atypical presentations of seizures, and genetic predispositions
Identify	Identify when treatment is necessary
Discover	Discover other options besides AEDs and their applications in epilepsy
Distinguish	Distinguish when patients need to be reevaluated and referred to advanced epilepsy centers

EPILEPSY BY THE NUMBERS

1 in 26

Americans will develop epilepsy in their lifetime

3 million

Americans currently live with epilepsy

65 million

Worldwide currently live with epilepsy

50K

Estimated amount of deaths occur annually in the US from seizure related disorders

$1.5 billion

Cost of epilepsy in the United States each year

2/3

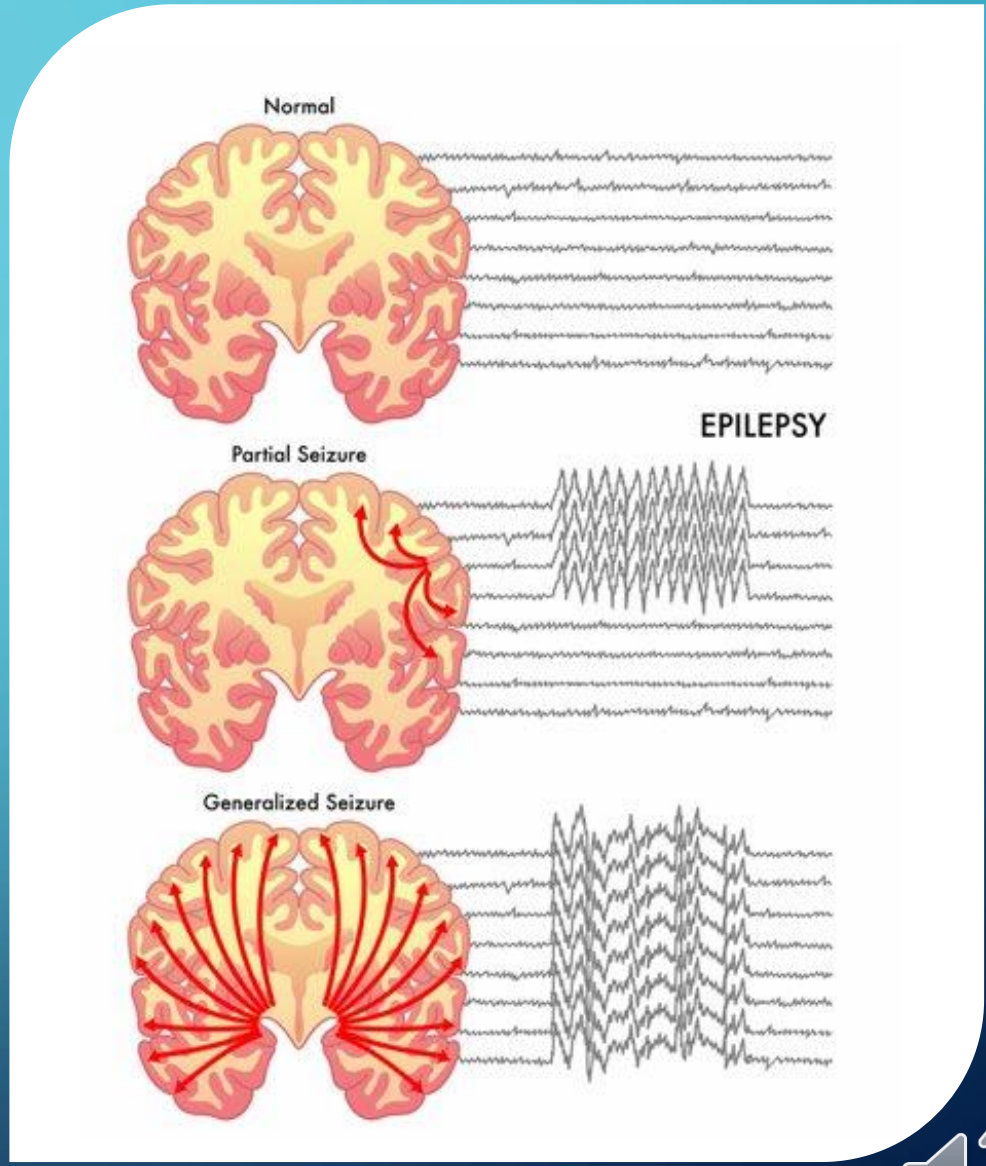
Patients diagnosed with epilepsy in which the cause is unknown

4th

Most common neurological disease after migraines, strokes, Alzheimer's

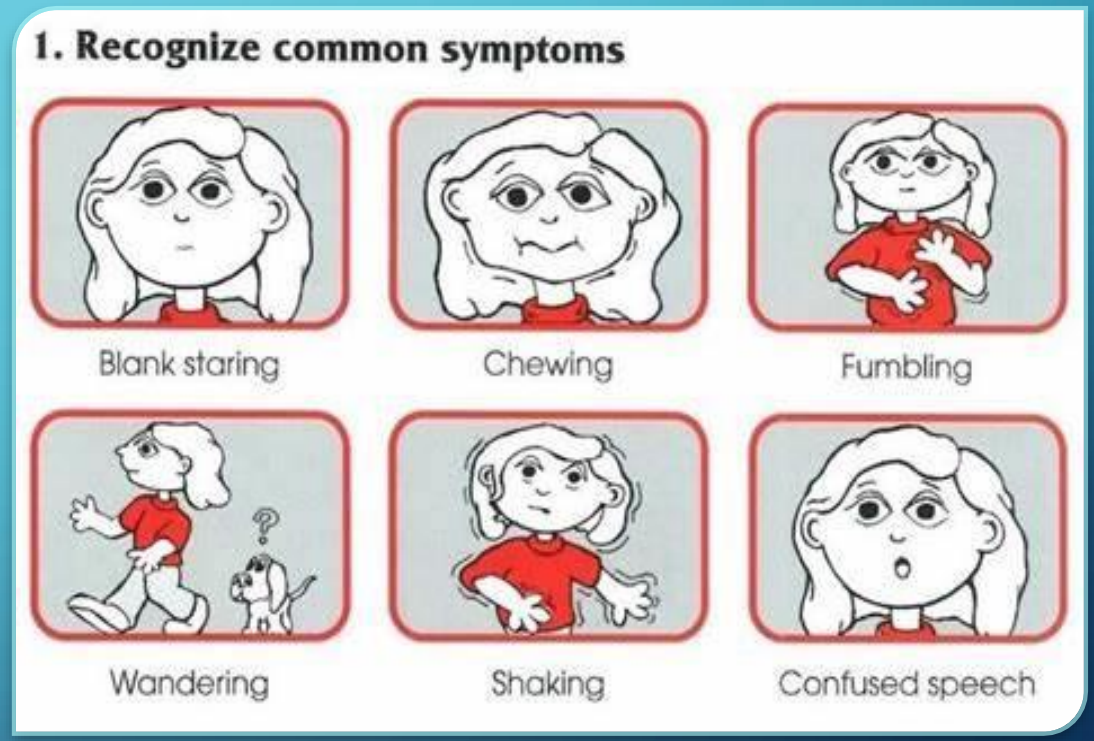
WHAT IS EPILEPSY?

- **Seizure** is an "electrical storm" in the brain causing altered movement, sensation, experience with or without loss of consciousness
- **Epilepsy** exists when someone had an epileptic seizure and their brain "*demonstrates a pathologic and enduring tendency to have recurrent seizures*".

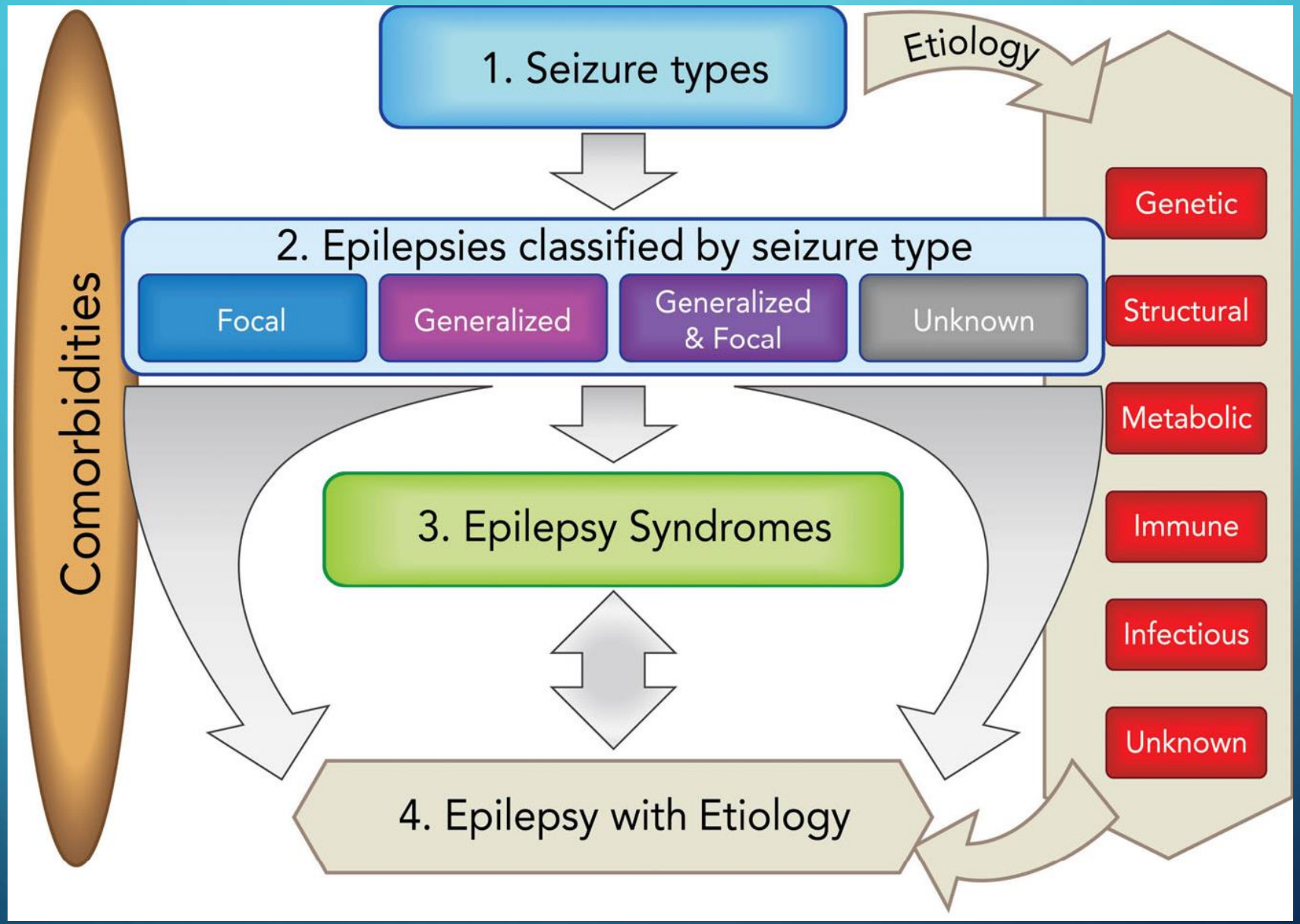


DIAGNOSIS OF EPILEPSY*

- 1) at least two unprovoked or reflex seizures > 24 h apart
- 2) one unprovoked or reflex seizure and a 60% probability of having another seizure over the next 10 years
- 3) an epilepsy syndrome



* by ILAE (International League Against Epilepsy)


1. Seizure types
Etiology
Genetic
Structural
Metabolic
Immune
Infectious
Unknown
2. Epilepsies classified by seizure type
Focal
Generalized
Generalized & Focal
Unknown
Comorbidities
3. Epilepsy Syndromes
4. Epilepsy with Etiology

CLASSIFICATION OF SEIZURES

Focal

- Limited to one cerebral hemisphere or one area
- Most common in 60% of all epileptic seizures

Generalized

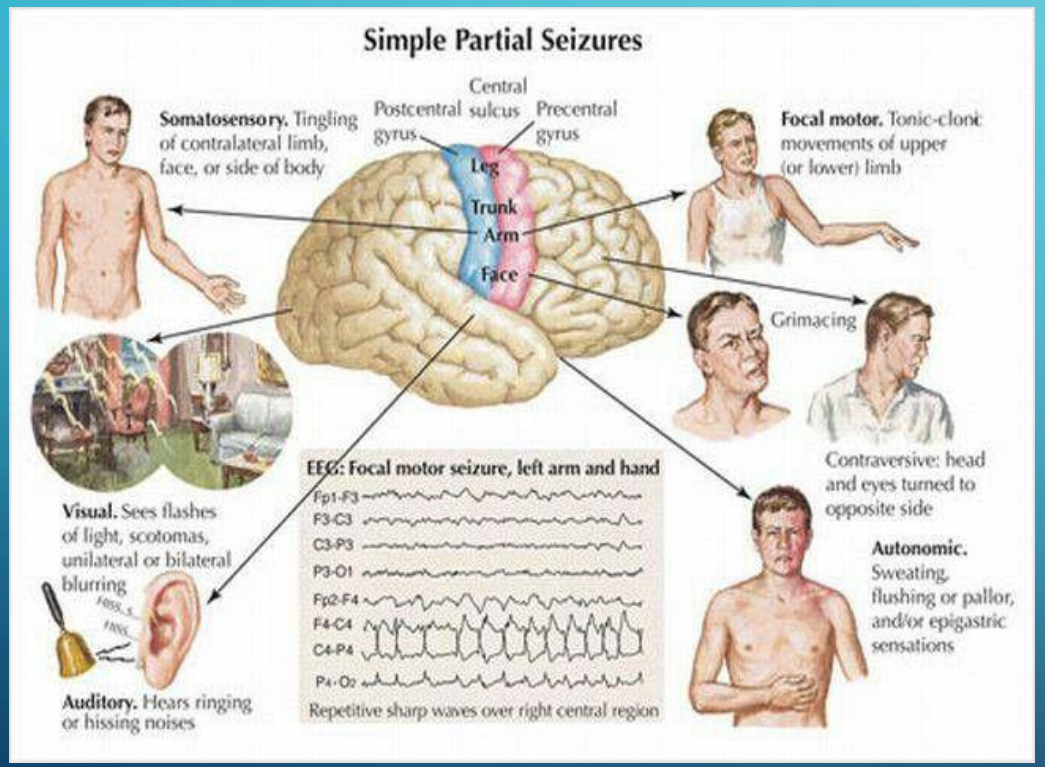
- Distributed in both hemispheres of the brain

Unknown

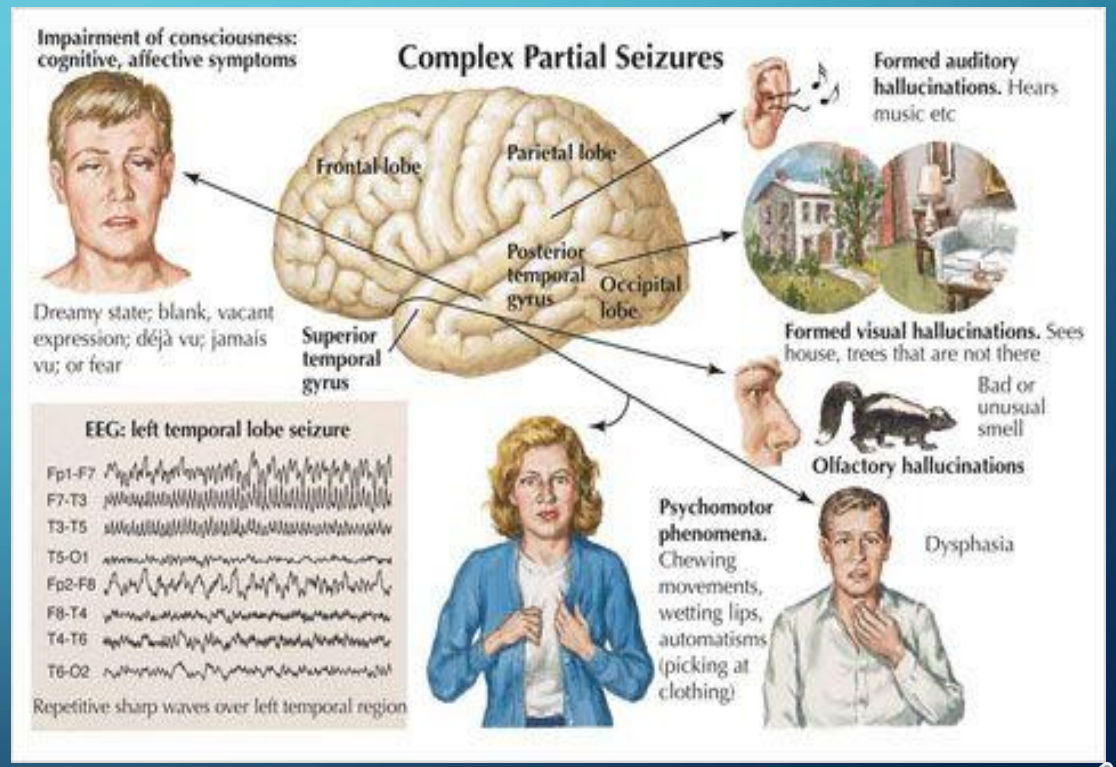
- Due to limited information or inability to place in other categories
- As more information is learned, it may later be diagnosed as a focal or generalized seizure.

FOCAL SEIZURES

Aware

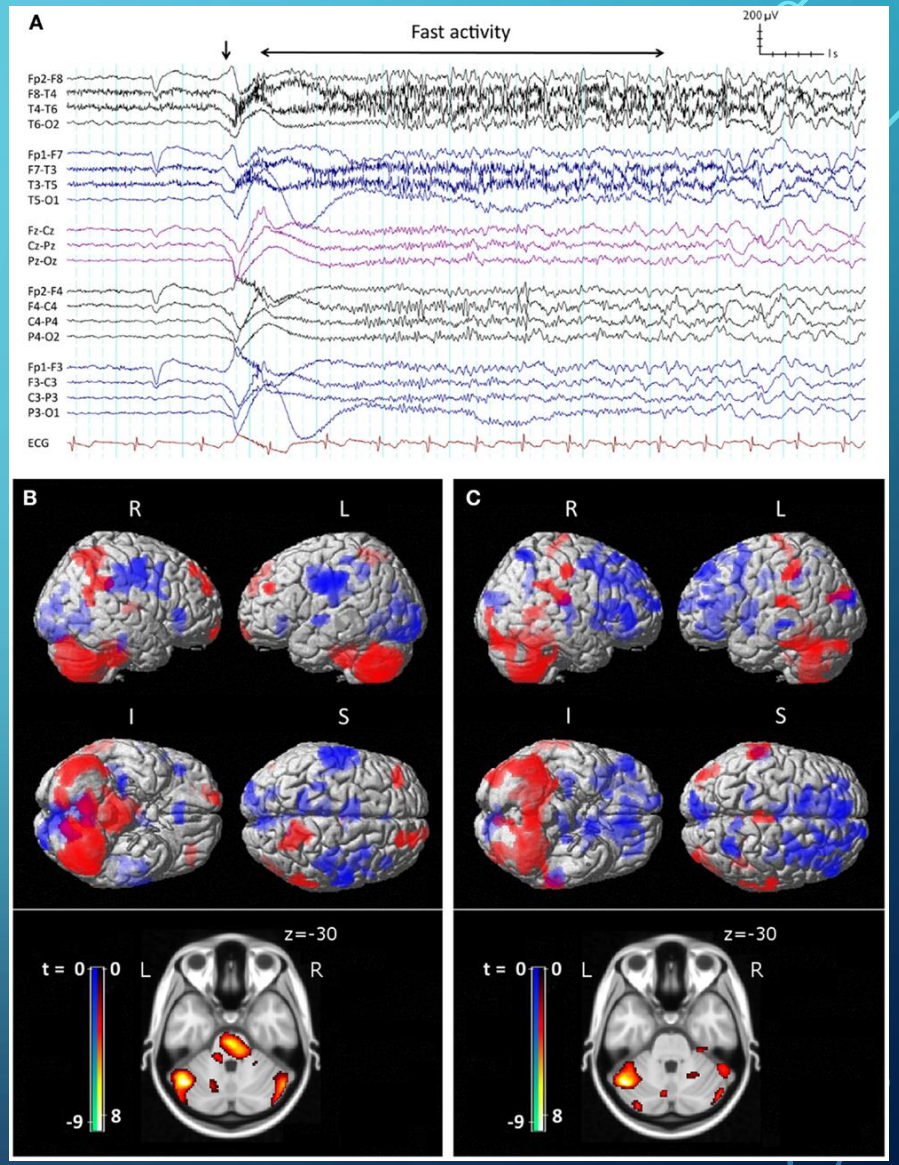


Impaired Awareness



GENERALIZED SEIZURES TYPES

- Diagnosis begins by taking a careful medical history and may include tests such as EEG, MRI, and blood tests.
- Loss of consciousness may be accompanied by spasms, stiffening, shaking, muscle contractions or loss of muscle tone.
- There are six different types of generalized seizures



GENERALIZED SEIZURES TYPES

Absence	These seizures involve a short period of time in which the patient loses a sense of awareness or "space out." This type is most common in children between the ages of 4 and 14 and usually lasts 20 to 30 seconds.
Tonic	These seizures cause the muscles to suddenly stiffen, which can prompt the patient to fall if they are standing up. Tonic seizures often happen during sleep and usually involve a loss of consciousness.
Atonic	The muscles lose tone and control, becoming limp, and the patient may collapse. These are often referred to as "drop seizures."
Myoclonic	These seizures involve sudden, quick jerks in arms or legs. The patient may have a number in a row or just one on occasion.
Clonic	Similar to myoclonic seizures, clonic seizures involve sudden, jerky muscle movement, only in this case, it's repetitive. Usually, clonic seizures are involved in a tonic-clonic seizure.
Tonic-clonic	These seizures are the type that most people associate with epilepsy. First, in the tonic stage, the muscles stiffen, then the patient loses consciousness and may fall to the ground. Next is the clonic stage, in which arms and sometimes legs begin jerking or twitching quickly and repeatedly.

GUESS A SEIZURE TYPE

Press Play to Watch the Video

Press Play to Listen to the Answer

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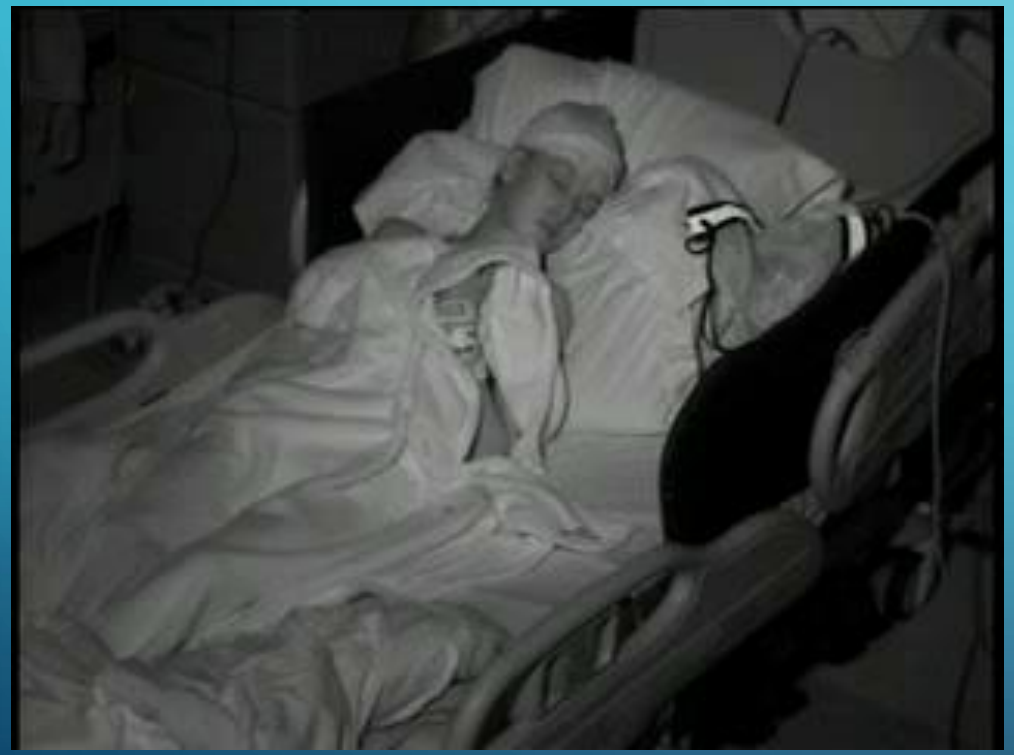

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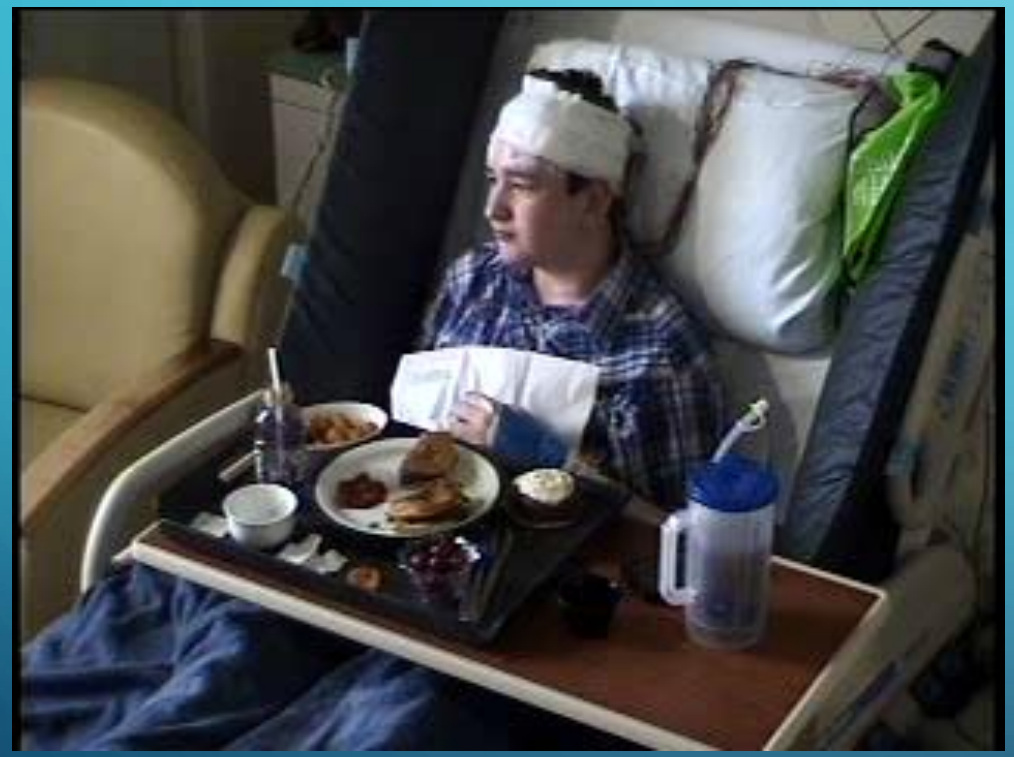


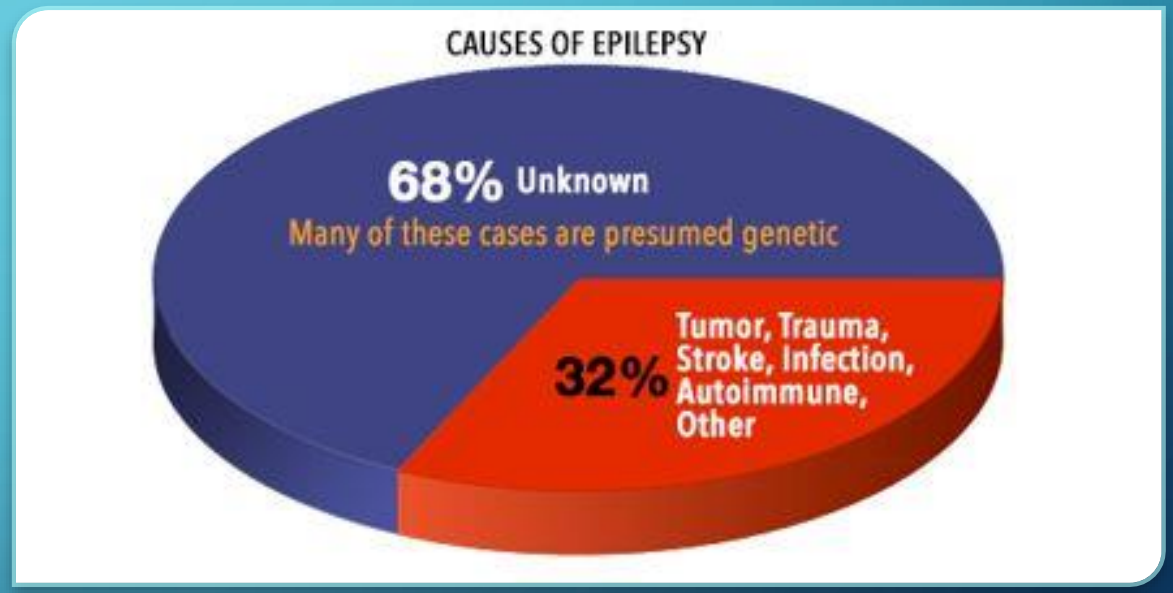
Press Play to Listen to the Answer

NON-EPILEPTIC SEIZURES

- Up to 20 % of people with epilepsy experience non-epileptic seizures
- Present like epileptic seizures, but aren't associated with the typical electrical discharge found in the brain.
- Deep source of seizures vs. Psychogenic seizures

GENETICS

- Inherited: autosomal dominant, autosomal recessive and Mendelian inheritance
- Acquired: de novo, sporadic, mosaicism, germline and acquired somatic
- Polygenic/complex genetic etiology: multiple gene abnormality with environmental factors that result in seizures



GENETICS CONSIDERATIONS

- Family history, refractory epilepsy, epilepsy syndromes
- Helps with identifying recurrence risk, prognosis, and treatment
- May be confirmatory in clinical diagnoses
- Most commonly identified genes: SCN1A,SCN2A,KCNQ2,CLN2, and more

EPILEPTIC SYNDROMES

- Defined by a cluster of signs and symptoms customarily occurring together
- Identification of an epileptic syndrome helps to determine:
  - Genetic Risk
  - Therapy
  - Prognosis

WEST SYNDROME

- 1-5 % of all childhood epilepsy
- Onset 3-12 months
- Tuberous Sclerosis is a common cause
- Triad of infantile spasms, an interictal EEG pattern termed hypsarrhythmia, and mental retardation
- Treatment: Vigabatrin, ACTH, steroids, valproate, zonisamide, ketogenic diet

DRAVET SYNDROME

- Prolonged Febrile seizure in 1st year
- Myoclonic seizures at 1-4 years
- Development normal early, then deteriorates including pyramidal signs and ataxia
- 70-80% with SCN1A mutations
- Treatment: Valproic Acid, Clobazam, Keto diet, CBD oil, Epidiolex
- Avoid treatment with Na channel medications

LENNOX-GASTAUT SYNDROME

- Seizure onset: 1-10 years
- Seizure types: tonic,atonic,atypical absence, focal, GTCs
- Infantile spasms precedes LGS in 10-25%
- 40 % with a history of developmental disabilities
- EEG with slow background, less than 2.5 Hz spike and wave complexes, paroxysmal fast in sleep
- Treatment: multiple AEDs, ketogenic diet,CBD oil, Epidiolex

BECTS (ROLANDIC EPILEPSY)

- Most common epilepsy in childhood
- Onset 2-14 years (Peak 7-10 yrs)
- Sensory and motor: Tongue, lips, gums, cheeks, drooling
- Usually during sleep but 10-20% have seizures only while awake
- EEG spikes bilateral or unilateral
- Typically outgrown by age 16
- Treatment: Valproate, Keppra, Oxcarbazepine, others

DOOSE SYNDROME

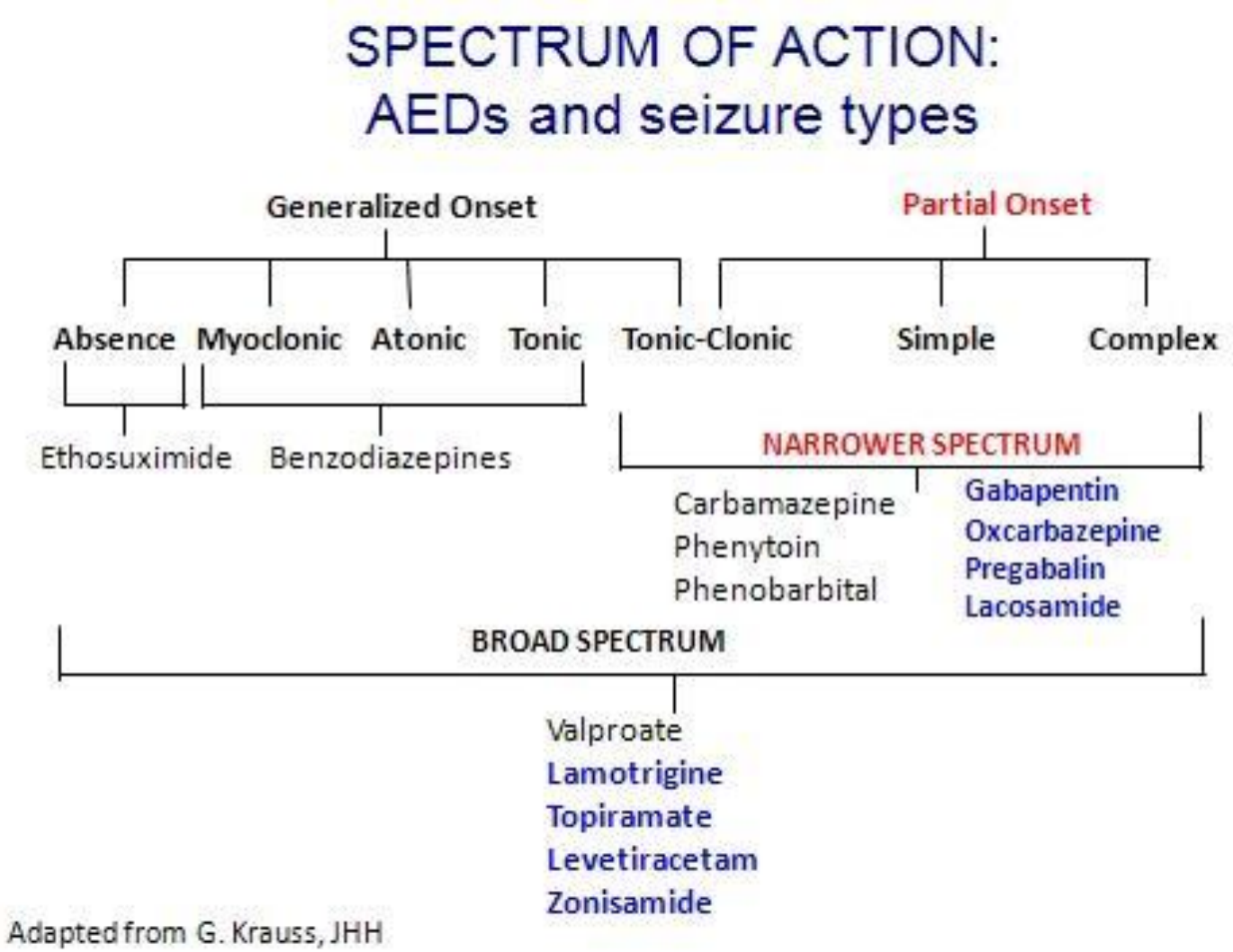
- Brief myoclonic jerks, then brief drop
- Two subgroups:
  - Normal development and 3 Hz spike-wave
  - Developmental disabilities and slow (less than 3 Hz) spike and wave
- Typically normal background(vs LGS)
- Genetics: GLUT1, SCN1A/B, GABRG, SLC6A1
- Treatment : multiple AEDs, ketogenic diet,steroids

PANAYITOPOULOS SYNDROME

- Peak onset: 3-6 years
- Starts with behavioral agitation, then headache, autonomic symptoms, motor seizures tend to be prolonged
- Autonomic: vomiting, pallor, cyanosis
- Interictal EEG: spikes can be anywhere, increased occipital spikes in sleep
- 85% have less than 5 seizures total, usually resolve by 11-13 years
- Treat according to clinical symptoms and EEG findings

TREATMENT OF EPILEPSY

- AED Selection depends on many factors including:
- Epilepsy type, mechanism of action, efficacy profile, side effect profile, compliance, pharmacokinetics, brand vs. generic, comorbidities, special population



AEDS MECHANISM OF ACTION

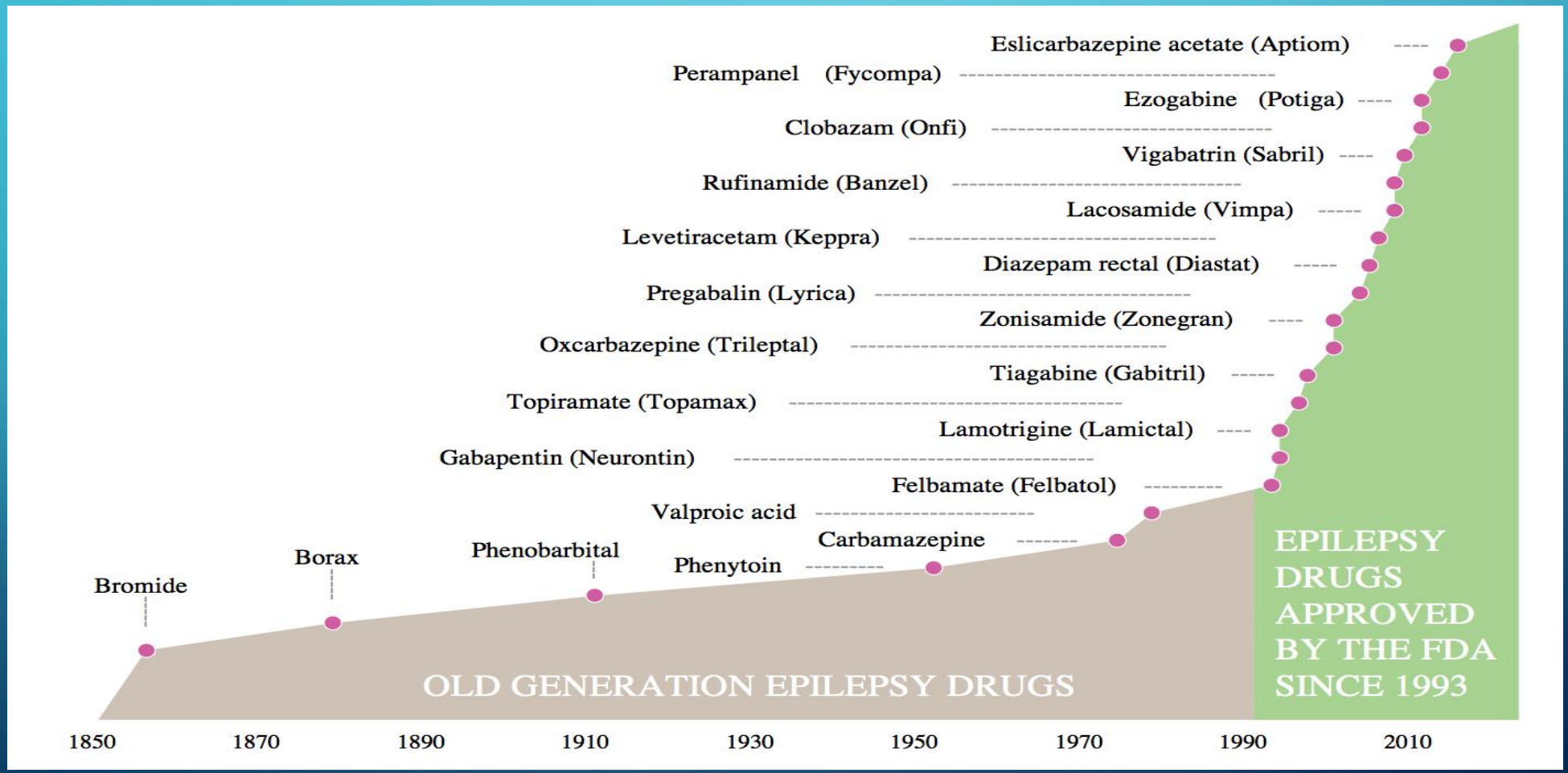
Mechanisms of Action of Key Antiepileptic Drugs

Sodium channel blockade	GABA analog	Synaptic vesicle protein 2A binding	Multiple mechanisms	AMPA antagonist
Carbamazepine	Clonazepam	Levetiracetam	Valproic acid	Perampanel
Phenytoin	Vigabatrin		Felbamate	
Lacosamide	Gabapentin		Topiramate	
Lamotrigine	Phenobarbital		Zonisamide	
Oxcarbazepine	Pregabalin			
	Tiagabine			

CBD OIL (CANNABIDIOL)

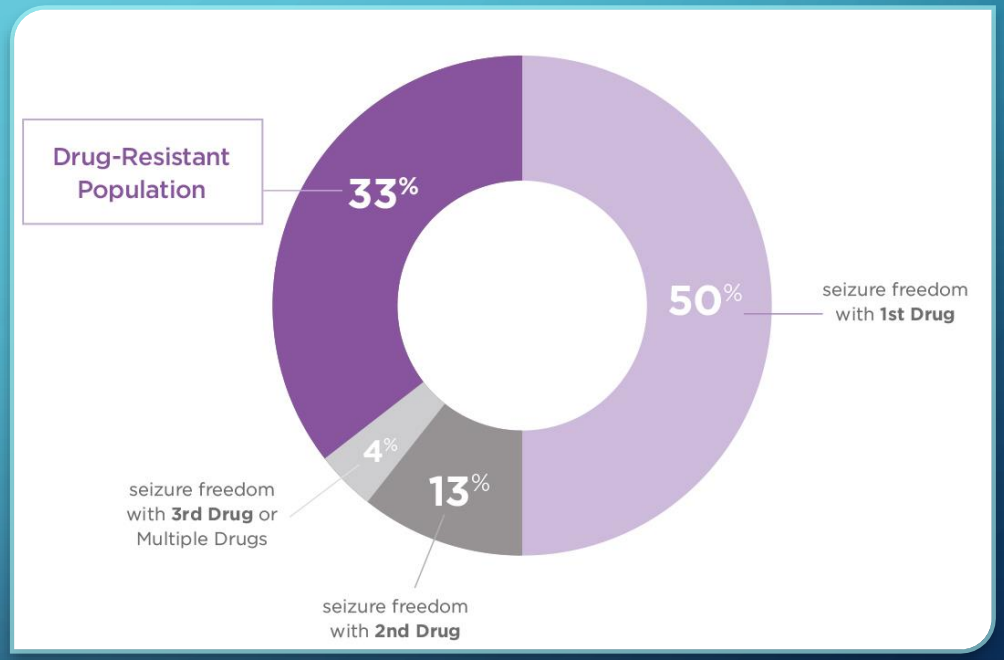
- Epidiolex is an FDA approved CBD oil for Dravet and Lennox-Gastaut syndrome
- CBD oil in selected three dispensaries is approved in TX by prescription only for epilepsy and other neurological conditions
- Offer Variety of ratio combinations CBD:THC (tetrahydrocannabinol)
- In our clinical setting, mostly used for intractable epilepsy, LGS and Dravet syndromes

AVAILABLE AEDS



DRUG RESISTANT EPILEPSY

- Epilepsy that is non-responsive to 2 or more AEDs on therapeutic doses
- 30% of population with epilepsy have drug resistant epilepsy
- Can be generalized, focal or both
- Consider other options besides AEDs



TREATMENT OF REFRACTORY EPILEPSY

- Epilepsy Surgery (>70% no seizures)
- VNS (>50% improvement)
- Ketogenic Diet (>50% improvement)
- Neuropace (RNS) (>50-60% improvement)

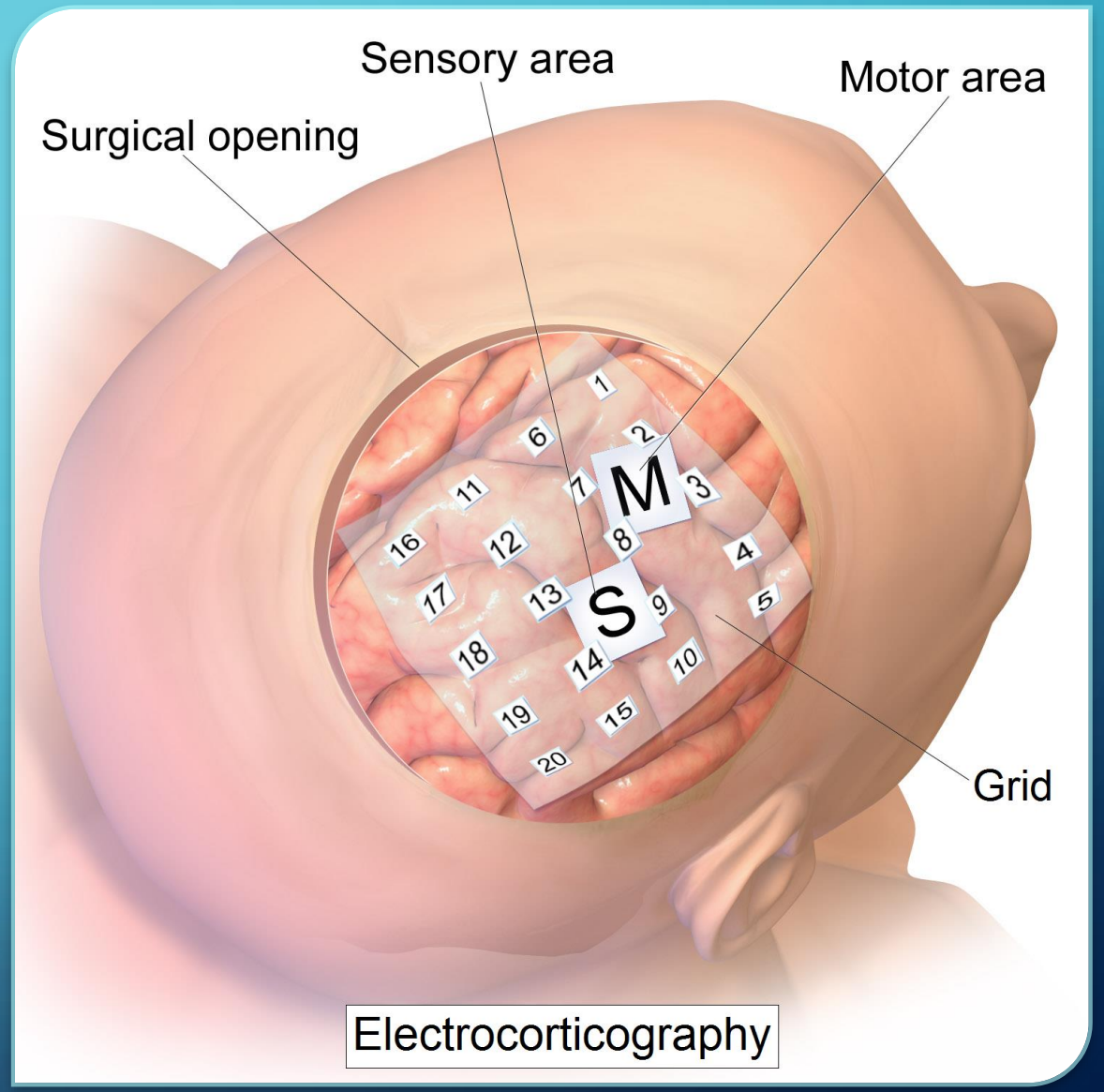
WORK-UP OF DRUG RESISTANT EPILEPSY

- The goal is to identify the best option besides medications

Non-invasive	Invasive
• Prolonged video EEG monitoring • 3T MRI • PET scan • MEG (magnetoencephalography) • SPECT • WADA • Neuropsychological testing	• Stereo-EEG, • Grid electrodes, • Stimulation Mapping

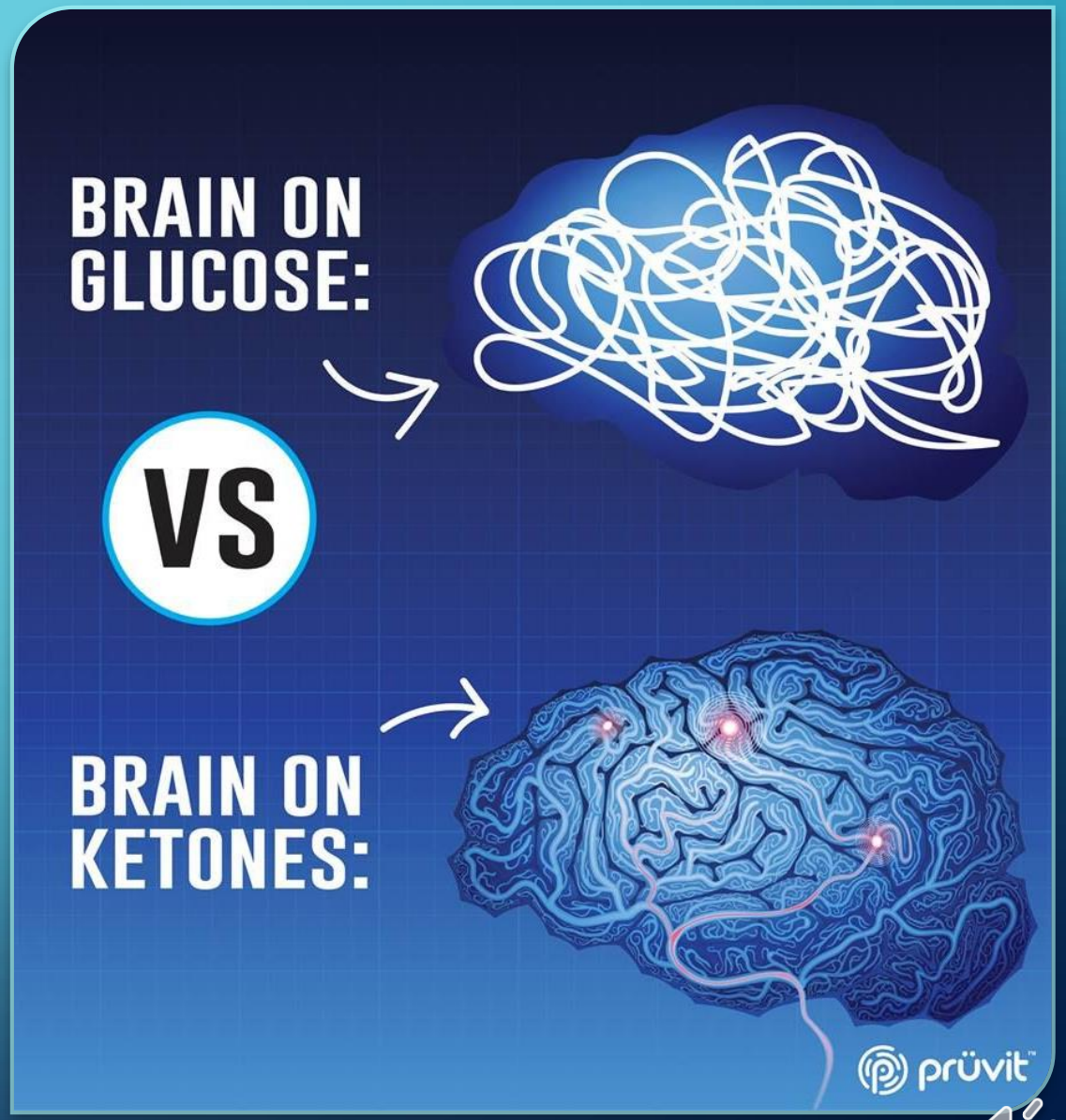
SURGERY

- Permanently removes seizure-producing brain tissue
- Resection
- Laser ablation
- Has limits due to functional areas of the brain that cannot be removed
- Corpus callosotomy for drop seizures



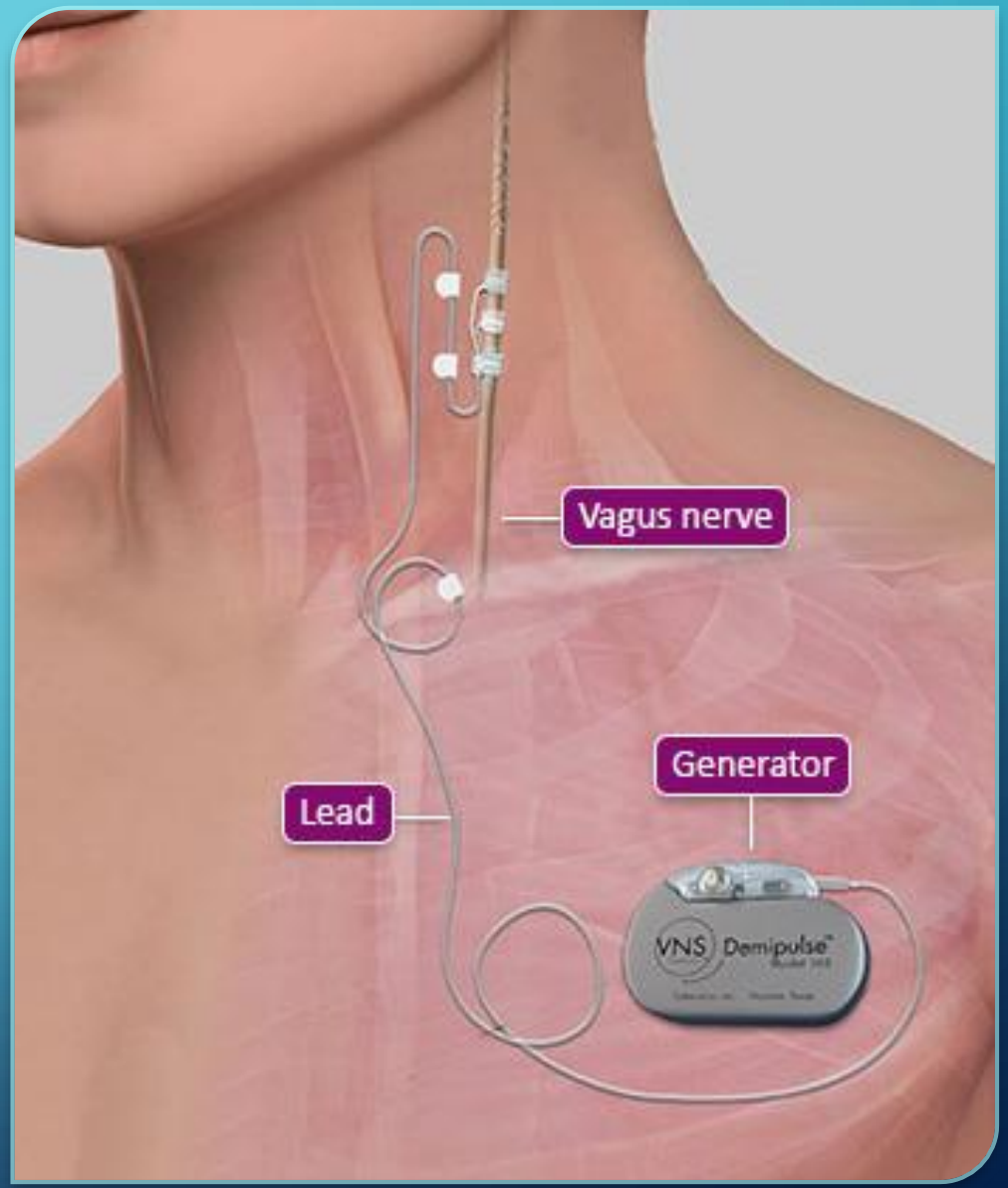
KETOGENIC DIET

- High fat,low carbohydrate,moderate protein diet that
- Forces body to use fat(ketones) as a main energy source instead of glucose
- Ratios: Grams of fats: grams of carbohydrate+protein 4:1, 3:1, 2:1
- Monitor ketones, labs, weight, ratios, calories
- Successful if at least 1/3 of seizures resolved
- Modified less strict diets are also available



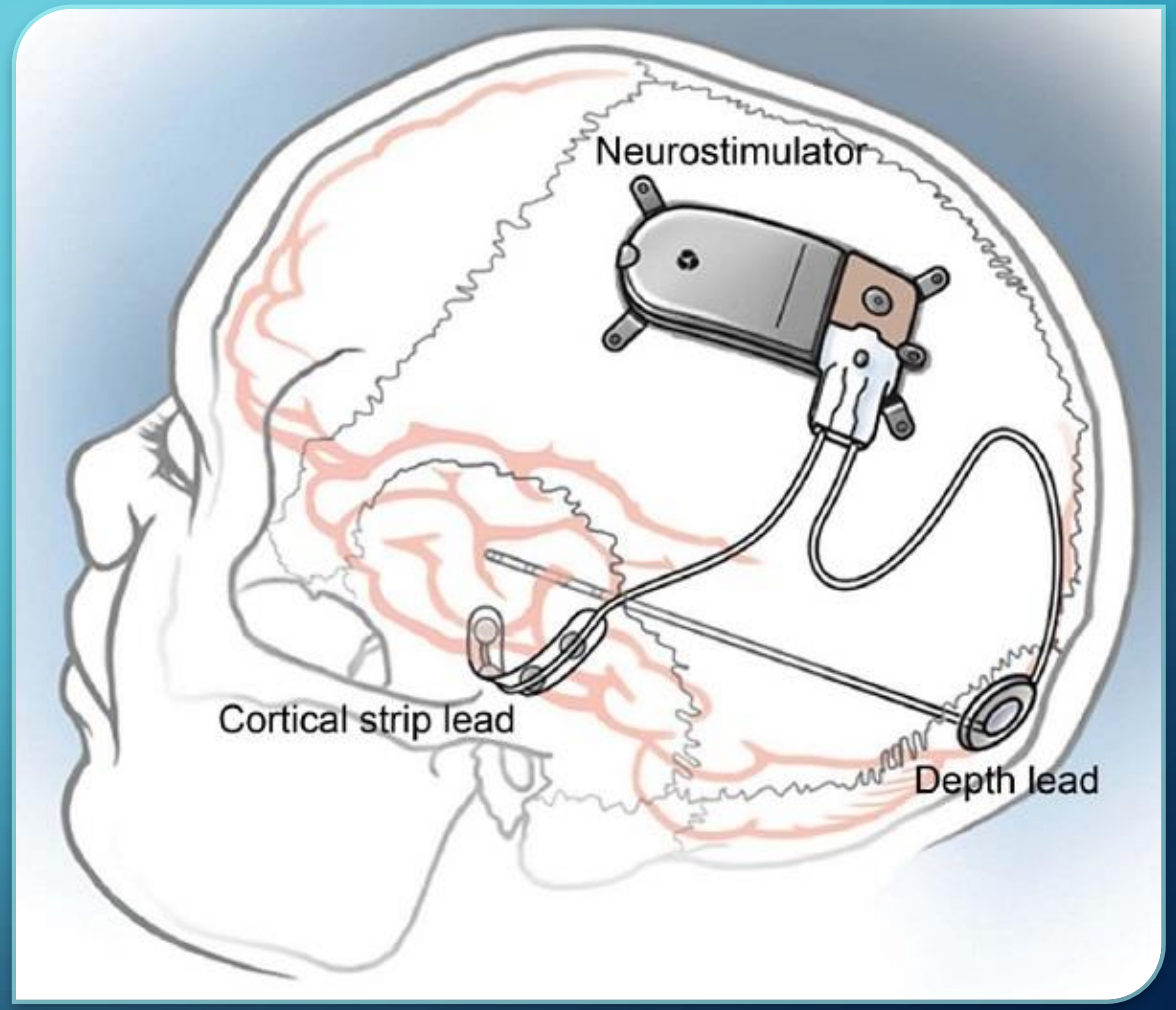
VAGAL NERVE STIMULATOR (VNS)

- Reserved for patients who are not candidates for surgery
- Outpatient procedure with 4 consecutive weekly visits to ramp the device up
- Exact mechanism is not known
- Pulse generator implanted under the left clavicle
- Connected to a lead wire with two stimulating electrodes around the left vagus nerve.



RESPONSIVE NEUROSTIMULATION SYSTEM (RNS)

- Implantation of a device with two leads connected to the seizure focus without removing it
- Electrical stimulation of a seizure focus in the brain
- Reduces intensity, severity, length and amount of seizures over time
- Provides EEG data to analyze the start of the seizures and adjust the settings accordingly



TREATMENT GAP IN EPILEPSY

- Less than 1% of patients with drug resistant epilepsy are referred to epilepsy centers
- 100,000- 200,000 patients in United States are eligible for surgery
- Only 2,000-3,000 procedures performed annually
- Many patients are not aware of other options beyond medications
- Treatment goals: seizure freedom or reducing the seizures with minimal side effects

QUESTIONS?

THANKS TO THE PEDIATRIC EPILEPSY TEAM

Epileptologists:	Gretchen Von Allmen, MD
	Michael Watkins, MD
	Geremy Lankford, MD
Dietitian:	Jennifer Newton
Manager:	Ardonia Toussant
Medical Assistant:	Inez Flores
Clinical Coordinator:	Lisa Caballero

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