New Onset Seizures

Understanding Epilepsy diagnosis, management and care

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Disclosures

- No financial disclosures
- I will be discussing some products which are off label for its FDA approval

Objectives

- Understand criteria for epilepsy diagnosis
- Understand current terminology for seizures and epilepsy types
- Review common epilepsy syndromes in childhood
- Review current treatment options for those with intractable epilepsy

What is a seizure?

A transient occurrence of signs and/or symptoms of abnormal excessive, synchronous neuronal activity in the brain

What is epilepsy?

- What is epilepsy?
- A disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neuro-biologic, cognitive, psychological, and social consequences of this condition.
- To have epilepsy, you must have had at least one unprovoked seizure.
- Classically, epilepsy is 2 or more unprovoked seizures, however, it can also be defined by 1 seizure with increased risk of further seizures (either determined by imaging, EEG, or other risk factors)

Fisher, et al 2005

Epidemiology – Pediatric Epilepsy

- 50 million people worldwide with epilepsy
- 456,000 children in the U.S. have active epilepsy
- 1 in 26 people will develop epilepsy at some point in their lives

Nomenclature

Old terms:

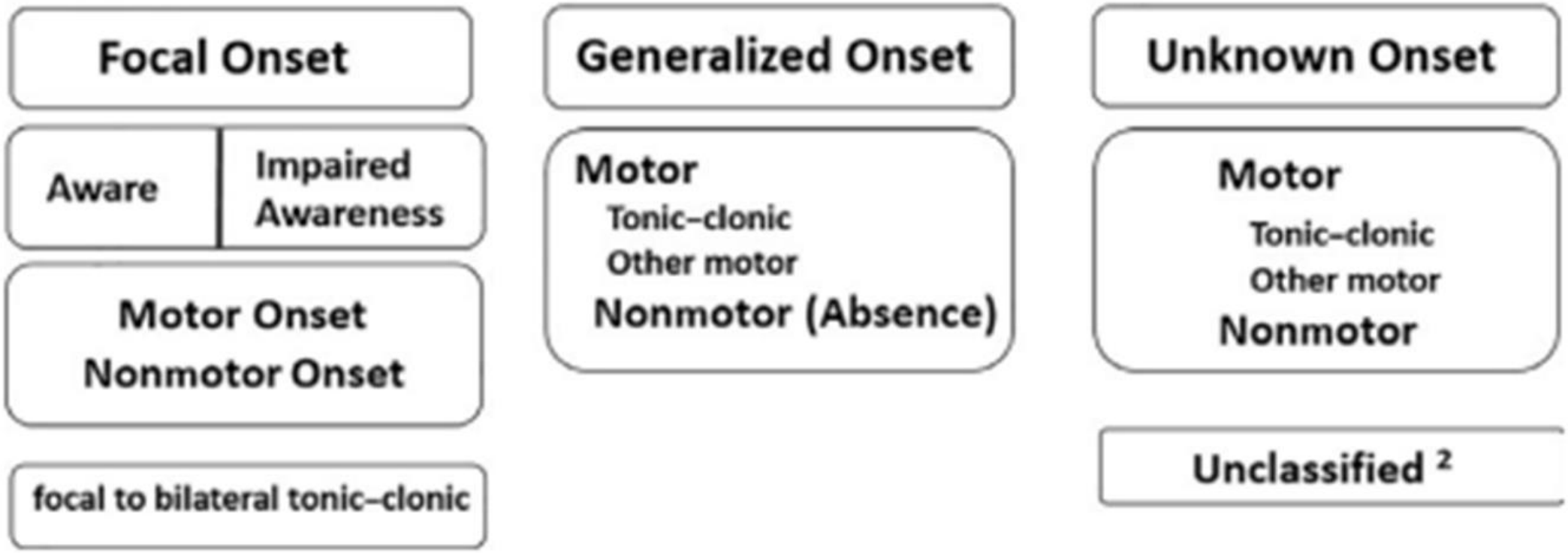
- Grand Mal seizure
- Petit Mal seizure
- Secondary generalized seizure
- Complex partial seizure
- Simple partial seizure

The OLD → NEW

Why does terminology matter?

- Allows better and consistent communication between patient, neurologist and rest of healthcare team.
- Treatment may change based on type and etiology of seizure.
- May help direct level of urgency.
- Can help predict risk of other seizure types.

ILAE 2017 Classification of Seizure Types Basic Version [1]



Fisher, et al. ILAE – Operational classification of seizures types -Epilepsia; 2017

ILAE 2017 Classification of Seizure Types Expanded Version [1]

Focal Onset

Aware | Impaired Awareness

Motor Onset
- automatisms
- atonic [2]
- clonic
- epileptic spasms [2]
- hyperkinetic
- myoclonic
- tonic

Nonmotor Onset
- autonomic
- behavior arrest
- cognitive
- emotional
- sensory

focal to bilateral tonic–clonic

Generalized Onset

Motor
- tonic–clonic
- clonic
- tonic
- myoclonic
- myoclonic–tonic–clonic
- myoclonic–atonic
- atonic
- epileptic spasms

Nonmotor (absence)
- typical
- atypical
- myoclonic
- eyelid myoclonia

Unknown Onset

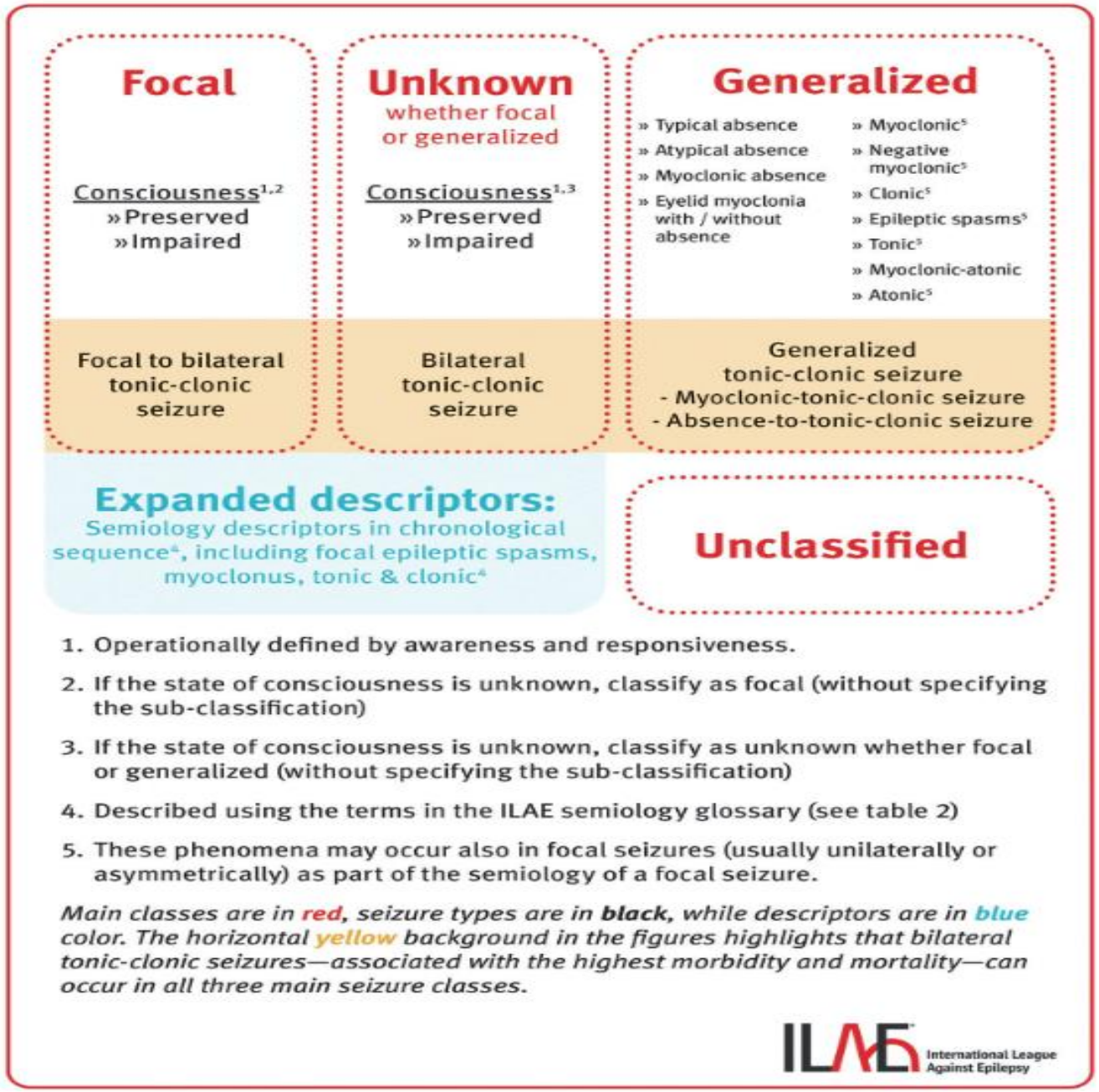
Motor
- tonic–clonic
- epileptic spasms

Nonmotor
- behavior arrest

Unclassified [3]

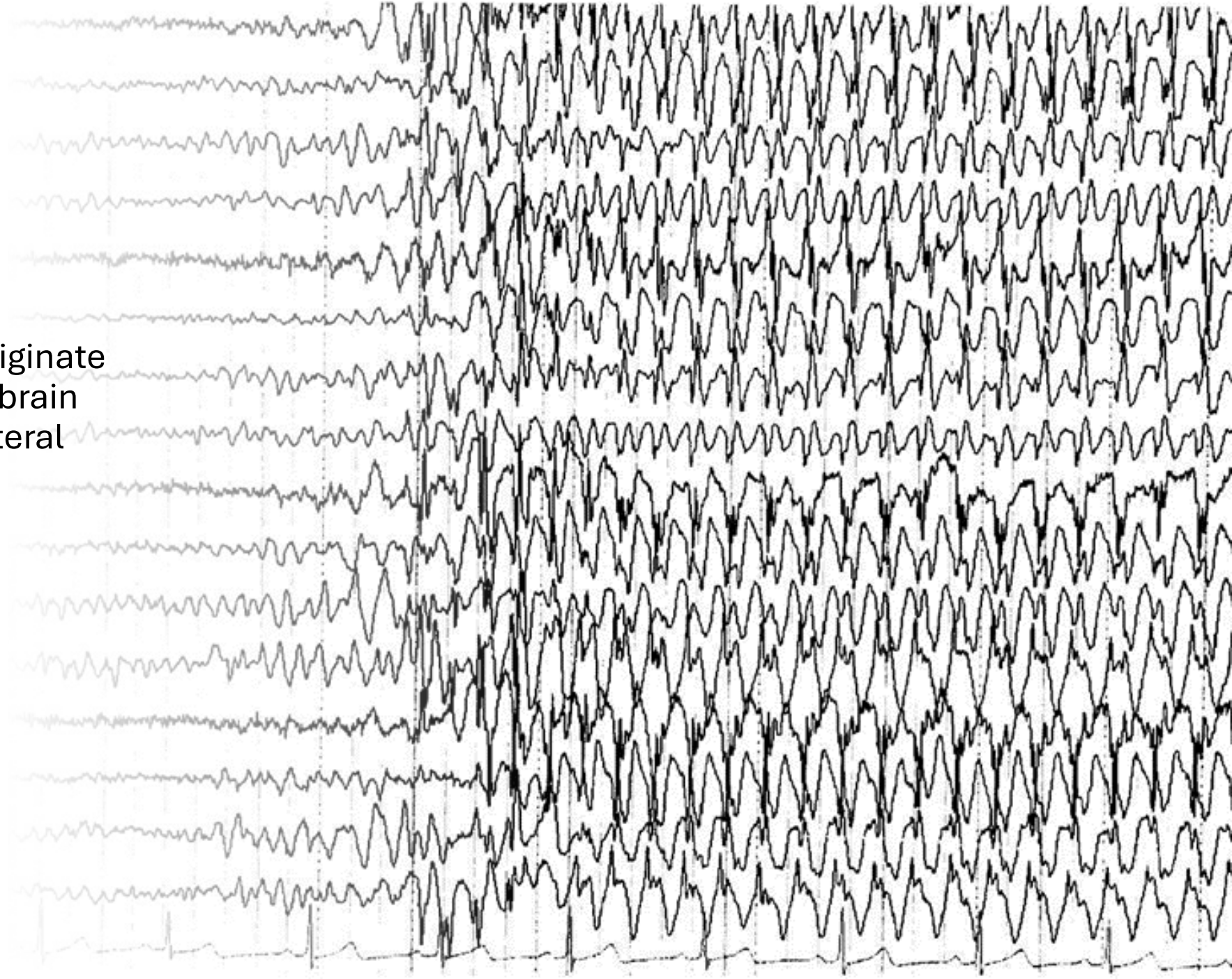
Fisher, et al. ILAE – Operational classification of seizures types -Epilepsia; 2017

2025 Update Classification



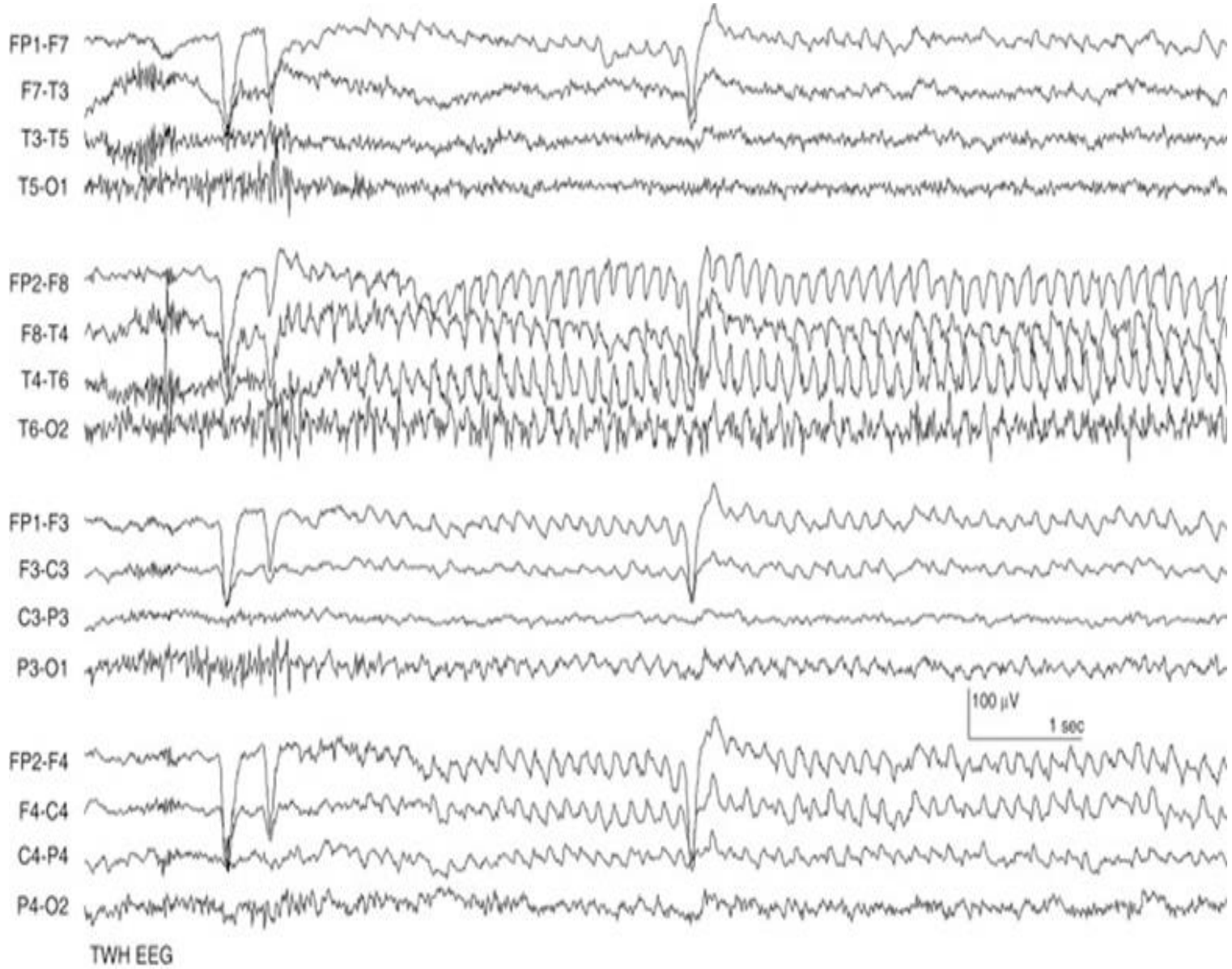
Generalized Seizures

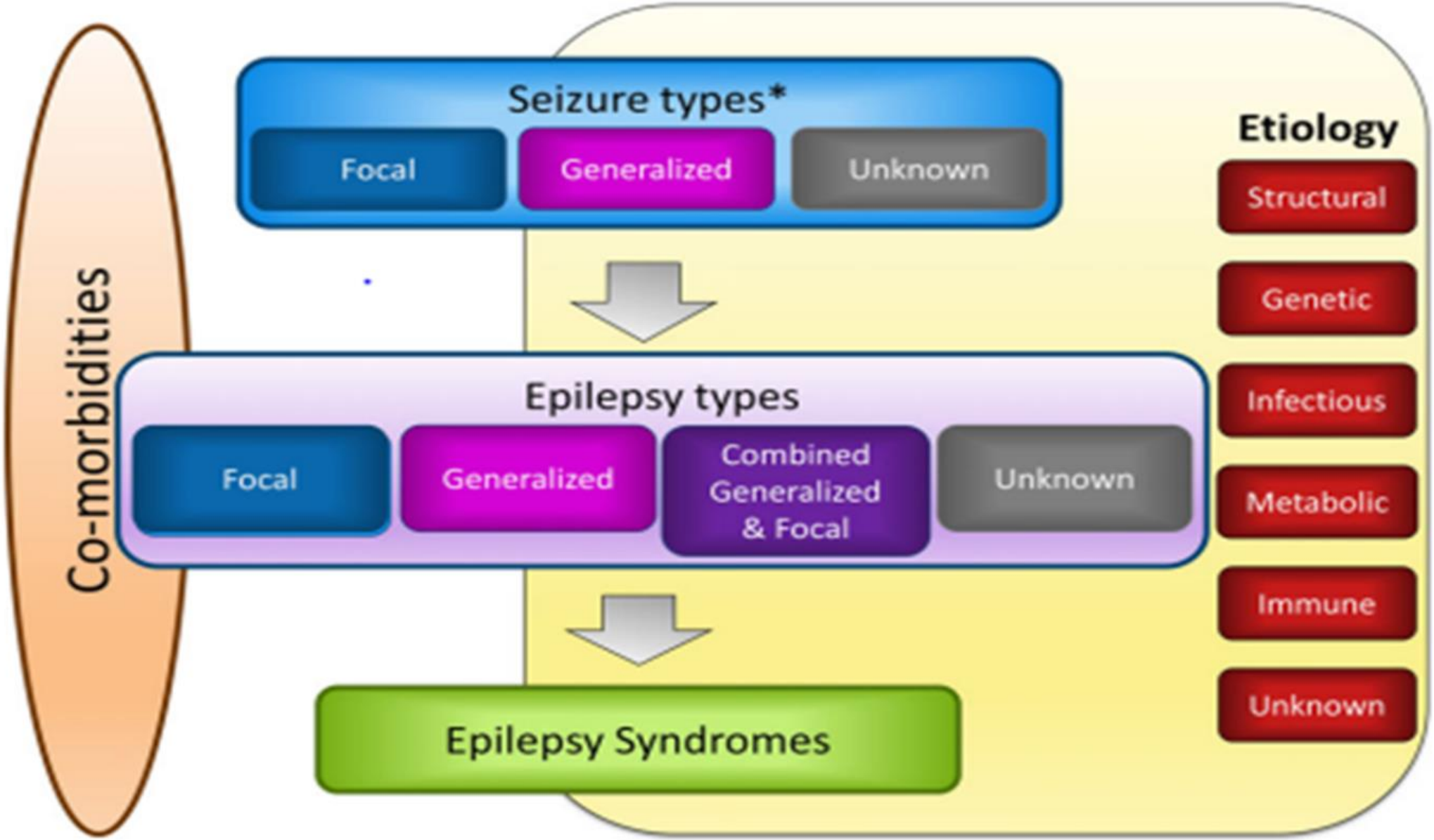
- Generalized seizures originate at some location in the brain and rapidly engage bilateral distributed networks.



Focal Seizures

- Focal seizures originate in a neuronal network limited to one hemisphere
- May be discretely localized or more widely distributed




Co-morbidities
Seizure types*
Focal
Generalized
Unknown
Epilepsy types
Focal
Generalized
Combined Generalized & Focal
Unknown
Epilepsy Syndromes
Etiology
Structural
Genetic
Infectious
Metabolic
Immune
Unknown

Common Seizure Triggers

- Sleep deprivation
- Missed medications
- Dehydration
- Alcohol/Drug use
- Hormonal changes
- Illness/fever
- Photosensitivity (Only present in 3% of epilepsies)
- Hyperventilation

Sudden Unexplained Death in Epilepsy Patients (SUDEP)

- 1 in 4,000 in pediatric epilepsy will die each year from SUDEP. Increases to 1 in 150 in those with intractable epilepsy
- Etiology unclear –apnea? Arrhythmia? Or other/mixed
    - Often patients found in prone position with evidence of a seizure occurring temporally to being found.

SUDEP

- Risk factors
  - Intractable epilepsy
  - Tonic-clonic seizures particularly with nocturnal onsets
  - Non-compliance with anti-seizure medications
  - Living alone
- Studies have shown that monitoring devices and neuromodulation (VNS/RNS/DBS) can be helpful in reducing incidence of SUDEP
- Improving awareness is a huge step in prevention
  - www.epilepsy.com, www.dannydid.org, www.knowsudepnow.org

Seizure detection devices

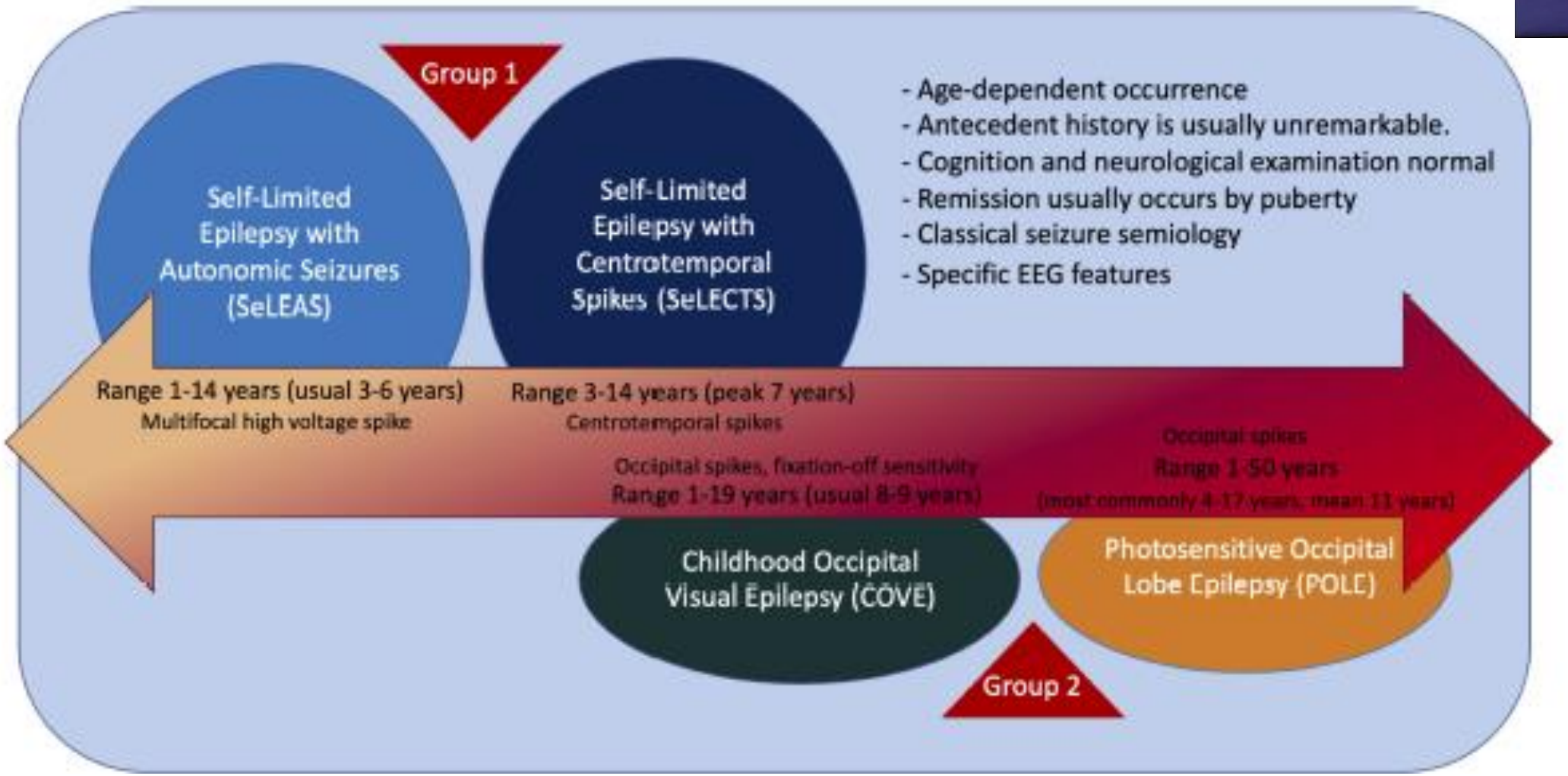
- Epimonitor
  - Watch device
  - FDA approved of tonic clonic events
  - Detection tools
    - Acclerometer
    - Electrodermal activity sensor
    - Heart rate detection
- Video monitors
  - No FDA approval
  - Monitor used for detecting sleep movements (inclusive of seizures)
- Various other beds/mattresses that claim to detect seizures, but no FDA approved

Women with Epilepsy

- Anti-seizure medications have an increased risk of teratogenesis in women who are pregnant.
  - General population is 2.5% compared to 6% in those with epilepsy
- It is important to discuss the current anti- seizure medication for women who are of child baring potential
- Supplementation of folic acid should be included with a daily multivitamin in all women having periods
- Anti-seizure medications can decrease effectiveness of certain oral contraceptive pills
- Up to 30-50% of patients can have increased seizures corresponding with their menstrual cycle

Epilepsy Syndromes in Childhood

Self-Limited Childhood Epilepsies



Self-limited Epilepsy with Autonomic Seizures (SeLEAS)

- Previously called Panayiotopolous Syndrome or early onset benign occipital epilepsy
- It accounts for 13% of epilepsies between 3-6 years old
- SeLEAS is the most common cause of afebrile non-convulsive status epilepticus in childhood

- Presents 3-6 years (70% of time)
- Normal developmental history
- Low seizure frequency – 25% of patients can have only 1 seizure
- Focal seizures with autonomic features
  - Retching, pallor, flushing, nausea, malaise, vomiting
  - Seizures evolve to head/eye deviation and at times focal hemiclonic twitching.
  - Usually. awareness is preserved at onset and then may fluctuate.
  - 70% of the time seizures are from sleep
  - Often prolonged – up to 30 minutes

Self-limited epilepsy with centrotemporal spikes (SeLECTS)

- Previously known as Benign Rolandic Epilepsy and Benign Epilepsy with Centrotemporal spikes (BECTS).
- Most frequent self-limited focal epilepsy - 6-7% of all childhood epilepsies
- Family members may show EEG features and never have seizures.
- Age of onset between 4-10 (peak 7 years)
- Often involve focal clonic or tonic activity often involving the throat or tongue initially.
  - Usually less than 10 lifetime seizures and very pharmacoresponsive.
  - Seizure occur in sleep in 80-90% of patients
- Normal developmental history
- EEG shows specific high amplitude centro-temporal spikes which are greater in sleep and have very specific morphology and pattern.
- Seizures resolve by puberty.
- Frequently see behavioral, learning disability, executive functioning deficits in these patients

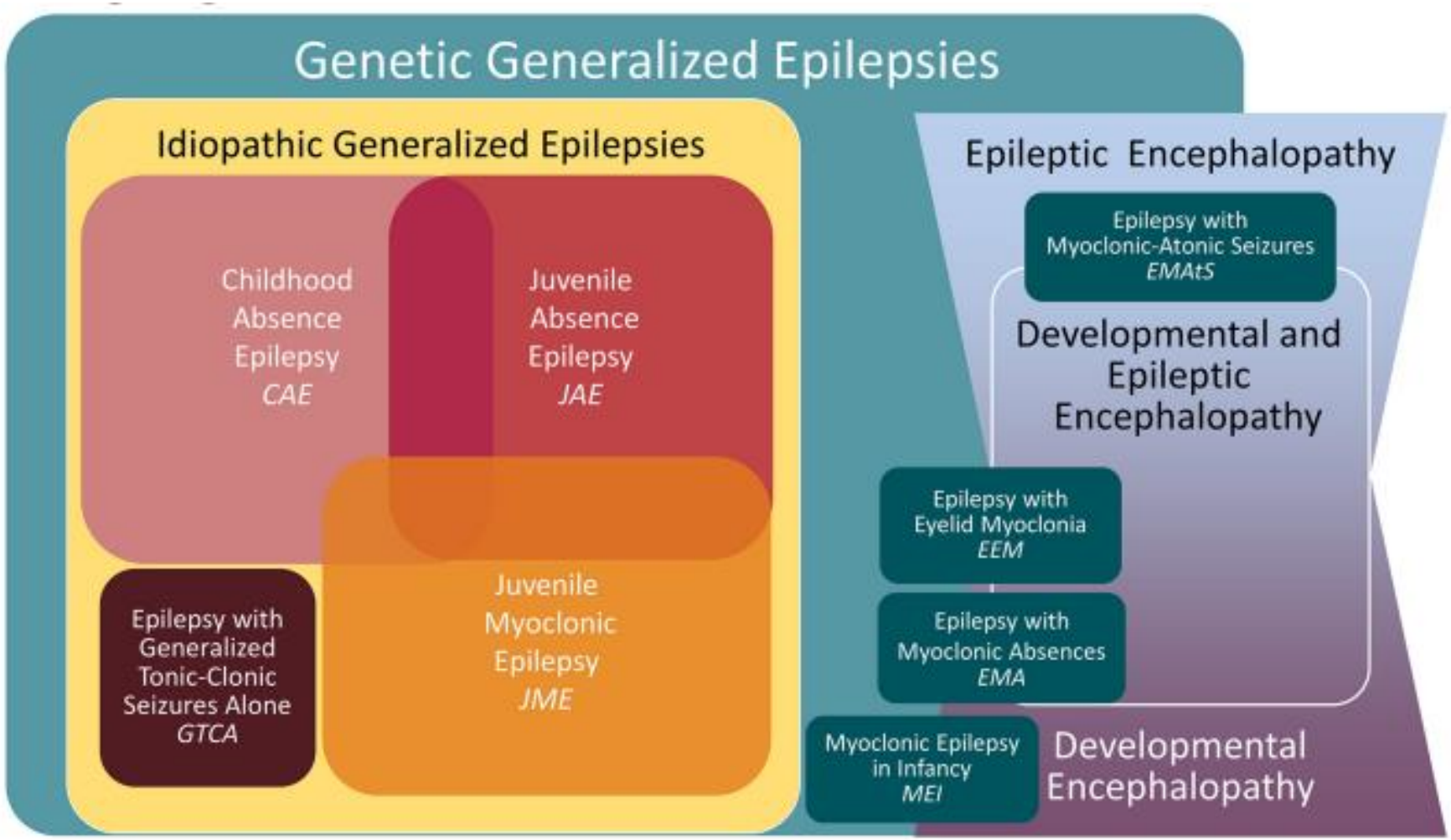
Childhood Occipital Visual Epilepsy (COVE)

- Previously known as late onset benign occipital epilepsy- Gastaut type.
- Prevalence of 0.3% of children with newly diagnose seizures

- Age of onset usually 8-9 years
- Normal developmental history
- Frequent brief seizures with visual phenomena with preserved awareness.
  - Primary visual phenomena.
  - This can often be followed by deviation of the eyes or turning of the head to the ipsilateral side of seizure onset.
- Often this can be followed by headaches (50% of patients)
- EEG often shows occipital epileptiform discharges
- Remission often achieved within 2-7 years of seizure onset, usually by puberty.
- History of bilateral tonic clonic seizures are associated with lower rate of remission

*Differentiate from migraines by the character of the visual phenomena (primary vs. spectral), more gradual development and longer duration of aura in migraine.

Generalized Genetic Epilepsy Syndromes



Childhood Absence Epilepsy (CAE)

- Accounts for 18% of epilepsy in school-aged children
- Patients can have dozens and up to hundreds of seizures per day
- Up to 10% may have generalized convulsions

- Age of onset around 4-10 years old
- Normal developmental history
- Absence seizures provoked by hyperventilation.
  - Oral and manual automatisms present in 86% of patients
  - Eye blinking, eye opening or subtle myoclonus seen in 76.5% of patients
  - Duration 3-20 seconds and immediate return to baseline
- Usually, pharmacoresponsive with remittance by early adolescence in 60% of patients
- Those where is persists may evolve into other generalized epilepsy syndromes
- EEG shows classic 3Hz spike and wave discharges. OIRDA is a rhythmic pattern often seen. Seizures are often provoked by hyperventilatlon
- If absence seizure onset <4 years old consider genetic testing

Juvenile Absence Epilepsy (JAE)

- 2.4-3.1% of new onset epilepsy in children and adolescents
- Generalized tonic-clonic convulsions are seen in 90% of patients

- Onset around 9-13 years old
- Absence seizures (much less common than in CAE) – occurring less than daily
  - Brief staring lasting 5-30 seconds
  - Sometimes there is incomplete loss of awareness and patient can follow some commands, but cannot perform complex tasks.
  - 20% of patients can develop absence status epilepticus
  - Seizures can be provoked by hyperventilation
- 25% of patients can have photoparoxysmal respnose
- Normal developmental history
- Typically drug responsive, but often lifelong therapies required
- Broad spectrum medication needed
- Higher rates of ADHD and learning problems even if seizures are well controlled

Juvenile Myoclonic Epilepsy (JME)

- Accounts for 9.3% of all epilepsies
- 5-15% of CAE cases evolve to JME

- Age of onset is 10-24 years old
- Three major seizure types
  - Myoclonic –usually right after waking – mandatory for diagnosis
  - Absence (occur 1/3 of the time)
  - Generalized tonic clonic – often preceded by myoclonic seizures
- Seizures are usually drug responsive
- EEG with rapid spike and polyspike and wave. Often photoparoxysmal response.
- Major trigger is sleep deprivation
- Sodium channel blockers can aggravate myoclonic seizures

Intractable Epilepsy

Intractable Epilepsy

- Despite an ongoing drug development for epilepsy the likelihood of responding to first anti-seizure medication still remains at 45%
- After moving to the 2nd anti-seizure medication the chance of responding is 15-20%
- Once on a 3rd (or more) anti-seizure medication and chance of responding is 2-5%
- 1/3 of all epilepsy remain intractable which means ongoing seizures despite treatment with 2 appropriately chosen anti-seizure medications
    - These patients should automatically be referred to an epilepsy center.

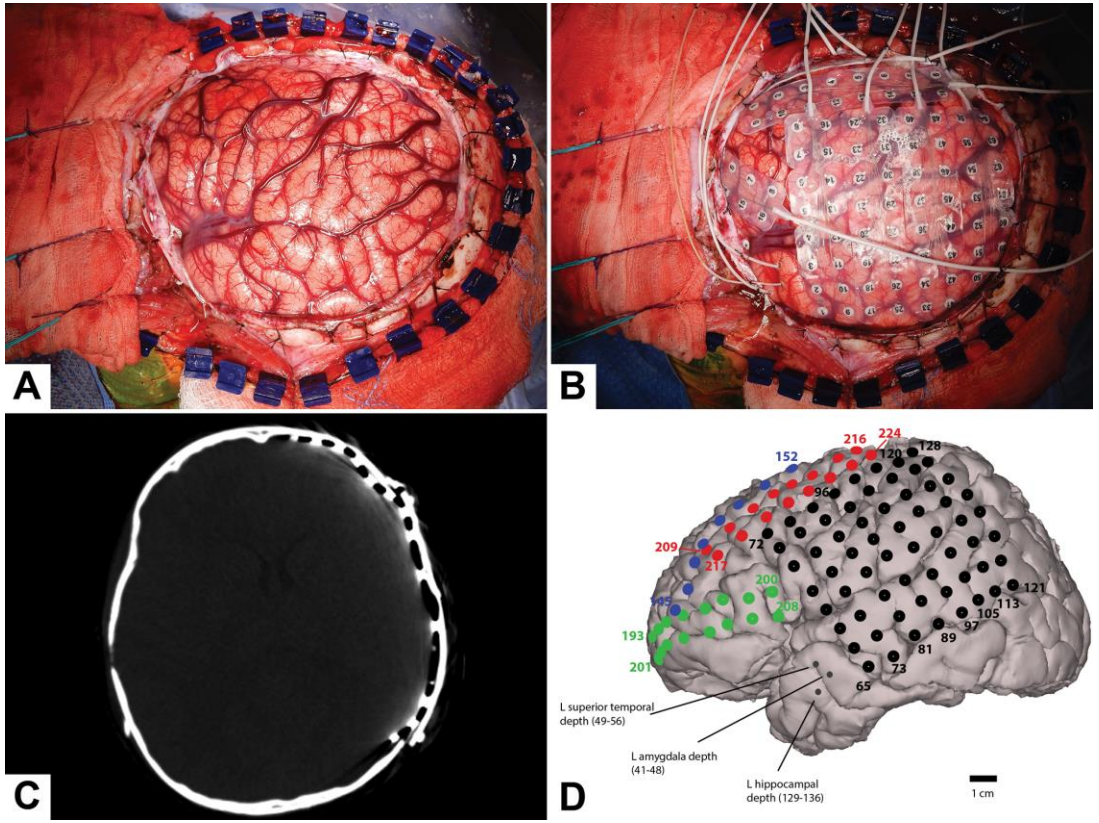
Referral Delays

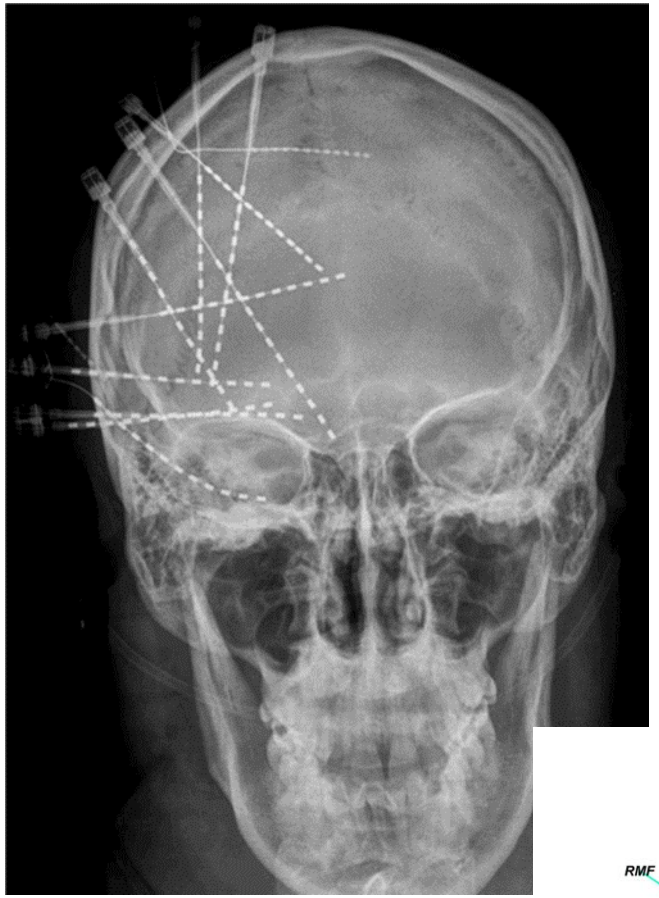
- The American Academy of Neurology treatment guidelines recommend those with intractable epilepsy be referred to a level 4 epilepsy center
- Average mean duration of epilepsy prior to surgical intervention is 18.8 years
    - The longer the duration of refractory epilepsy and greater the deterioration in cognition, overall functional ability especially in the pediatric population

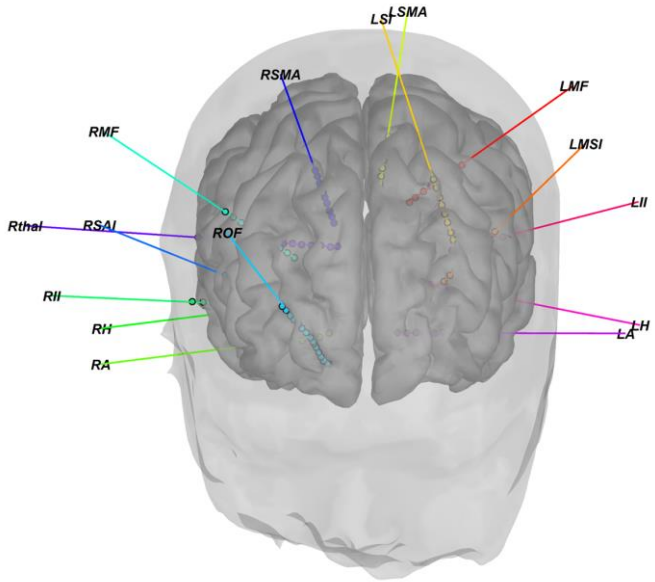
Phase I Pre-surgical evaluation

- Pre-surgical work up is completed at an Epilepsy Center. This includes:
  - 3T Brain MRI
  - Multiple day stay in the Epilepsy Monitoring Unit to capture, characterize and potentially localize seizure onsets
  - PET Scan Head
  - Neuropsychological Evaluation
  - +/- MEG scan, SISCOM/SPECT Scan, fMRI

Phase II – Subdural Grids and Stereo EEG







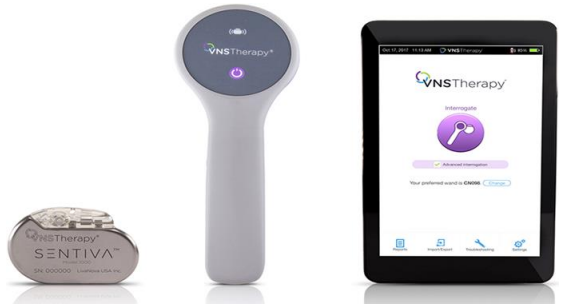
Resection

- Based on results of Phase I and if necessary, Phase II a decision may be made for anatomical resection of seizure onset zone as captured during Phase II evaluation
    - May be a lobectomy (partial vs. complete), hemispherotomy, limited resection of known anatomical abnormality (i.e. focal cortical dysplasia), topectomy
- Goal is to remove regions of the brain sufficient for initiation of seizures and whose removal is necessary for complete resolution of seizures – also referred to the epileptogenic zone -with avoidance of functional deficits (i.e. motor, speech, memory)

LITT – Laser Interstitial Thermal Therapy

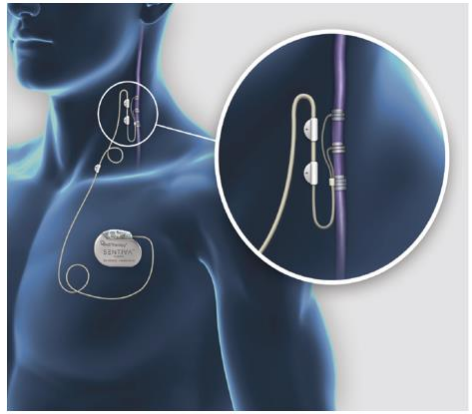
- Minimally invasive approach with the same criteria as resection
- MRI guided to approach target region of interest and laser energy changes to thermal energy effectively burning and destroying the tissue at the target
- Has become a mainstay in treatment of mesial temporal sclerosis, hypothalamic hamartomas and small lesions such as focal cortical dysplasias

Vagus Nerve Stimulator (VNS)



- Sends signals to the brain via the vagus nerve at set intervals throughout the day
- Monitors heart rate and can send signals when there are abrupt changes in heart rate
- Magnet available to swipe the device by patients or caregivers during a seizure and this will send a strong pulse.

Approximately 50% of patients will have a 50% or greater reduction in seizures

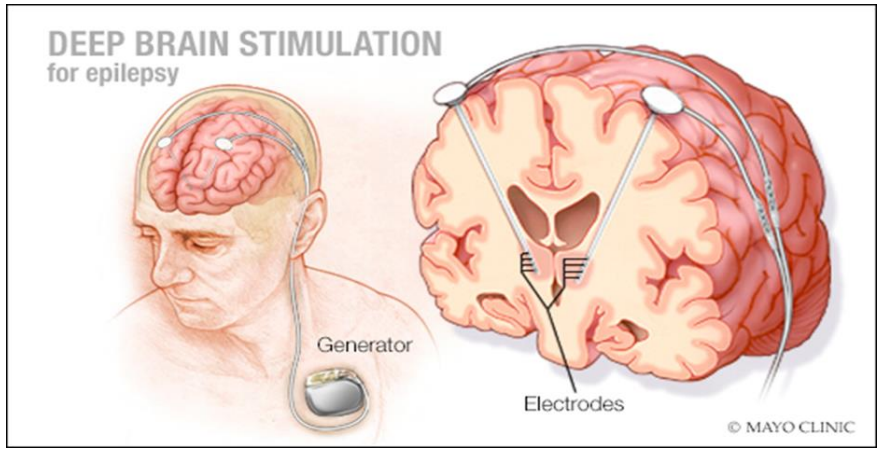


Responsive Neurostimulation (RNS)

- Approved for patients 18 years and older with intractable epilepsy
- Electrodes placed directly on the brain of the patient and are continuously monitoring for seizure activity
- Two electrode strips can be placed in 2 distinct locations, either on the cortex or as a depth electrode
- Patterns are reviewed by treating epileptologist who can then program the device to send signals to abort the seizure.
- Device has shown improved efficacy over time

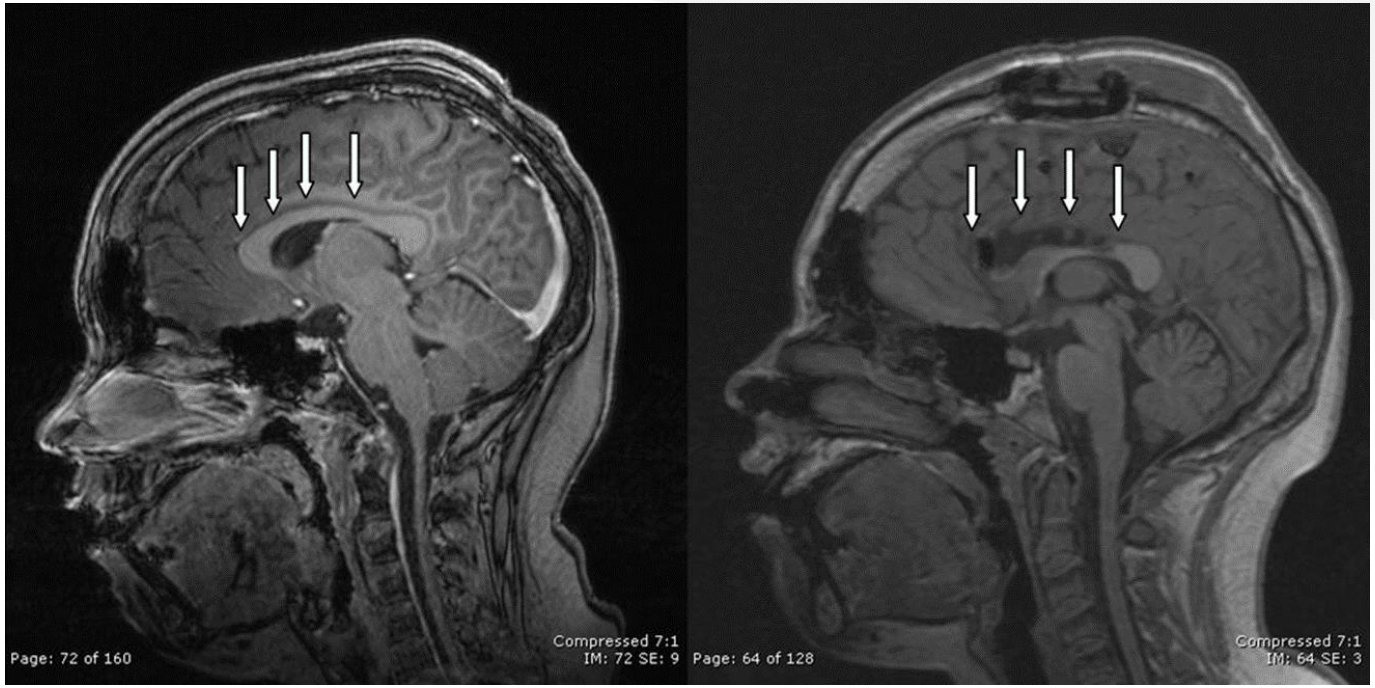
Deep Brain Stimulation (DBS)

- Has been utilized previously for the treatment of Parkinson's Disease and essential tremor
- Now approved in intractable epilepsy in patients over 18 years old
- Target locations are distinct from movement disorders
  - Anterior Nucleus of the thalamus - >50% reduction in seizures in 43% at 1 year and 68% at 5 years – Salanova, et al, 2015.
  - Other thalamic nuclei being evaluated including Centromedian, Pulvinar based on network projections



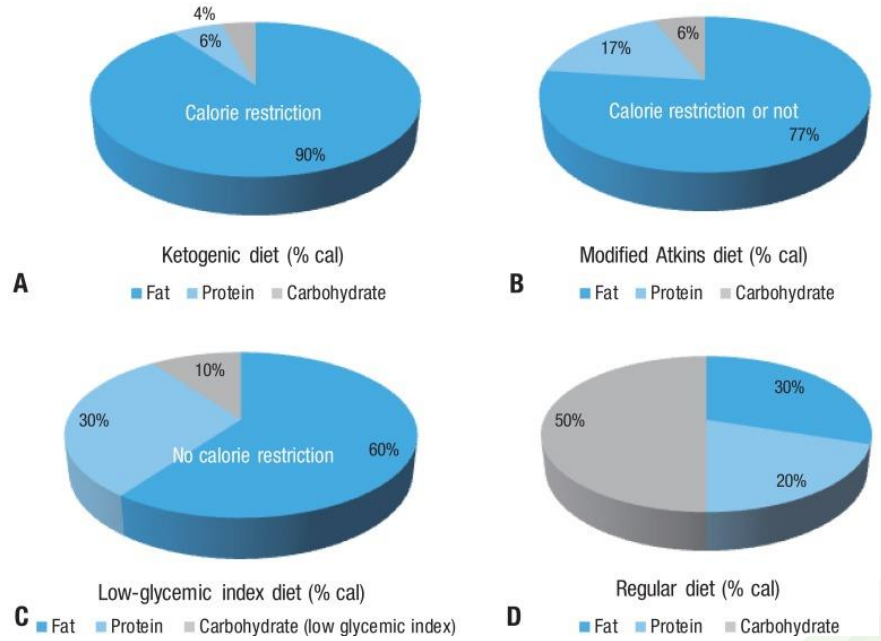
Corpus Callosotomy

- Often utilized in seizures with rapid secondary generalization.
- Most effective in the treatment of atonic events which can be very disabling for patients and family – up to 80% effective



Ketogenic Metabolic Therapy

- Has been utilized as a medical therapy in the treatment of epilepsy since the 1920s, but variations of the theme date back to B.C. where documentation of children with seizures were starved for some days to control seizures (forcing the body into a state of ketosis).
- High fat, adequate protein, low carbohydrate diet



Ketogenic Metabolic Therapy

- Greater than 50% reduction in 30-70% of patients depending on seizure type
- Requires significant “buy-in” from the patient and family
- Complications:
  - Metabolic acidosis and associated lethargy, vomiting
  - Electrolyte disturbance
  - Hyperlipidemia and hypertriglyceridemia
  - Vitamin deficiencies
  - Nephrolithiasis
  - Prolonged QT
  - Effects on growth and weight

Conclusions

- Epilepsy is a common neurologic condition in children
- Terminologies are changing, but it is important to stay current so that we are all speaking the same language
- Specific epilepsy syndromes in childhood have predictable patterns and prognosis
- Treatments continue to grow however a portion of our patients remain intractable and evaluation at a level 4 epilepsy center is crucial
- Surgical and other treatment modalities are available for those who have failed medication options

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