



# Treatment Options in Intractable Epilepsy: One Woman's Story

## International Neuroscience Nurses Symposium



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# Objectives

- ❖ Define Intractable Epilepsy
- ❖ Summarize treatment options available in Intractable epilepsy
- ❖ State efficacy data of treatment options
- ❖ Comprehend psychosocial implications of living with uncontrolled seizures





# Introduction to Epilepsy

- ❖ Seizure – Paroxysmal, excessive, and disorderly electrical neuronal discharges in the brain “Electrical Storm in the Brain”
  - ✓ Focal - starts in one place
  - ✓ Generalized - starts over entire brain at same time
- ❖ Epilepsy – More than one unprovoked seizure
  - ✓ A tendency for recurrent seizures
  - ✓ Broad range of severity





# Incidence by Age

**1 in 26 will be diagnosed within the lifespan**





# Seizure Classification

International League Against Epilepsy (ILAE)

**Table 1. Classification of seizures<sup>a</sup>**

**Generalized seizures**

Tonic-clonic (in any combination)

Absence

Typical

Atypical

Absence with special features

Myoclonic absence

Eyelid myoclonia

Myoclonic

Myoclonic

Myoclonic atonic

Myoclonic tonic

Clonic

Tonic

Atonic

**Focal seizures**

Unknown

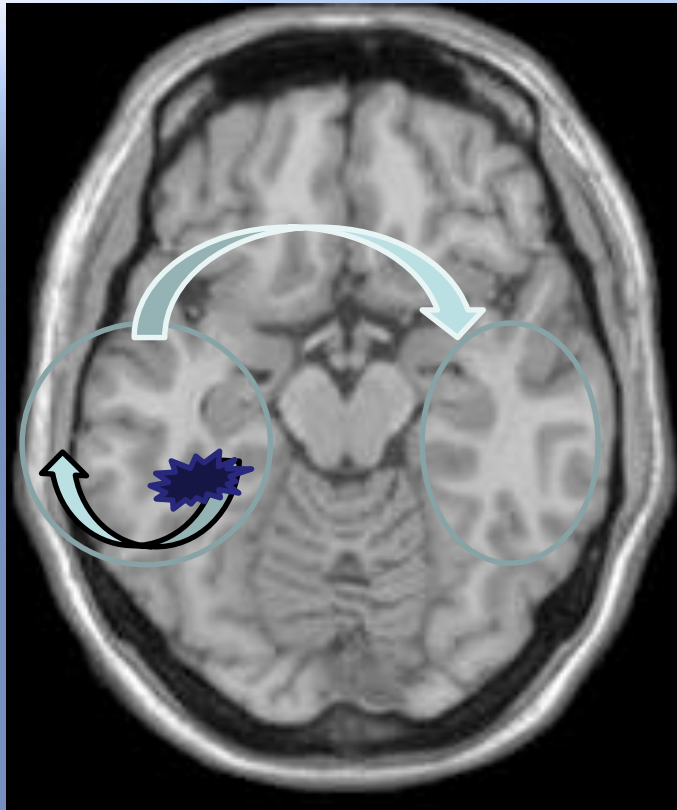
Epileptic spasms

<sup>a</sup>Seizure that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis. This is not considered a classification category, however.

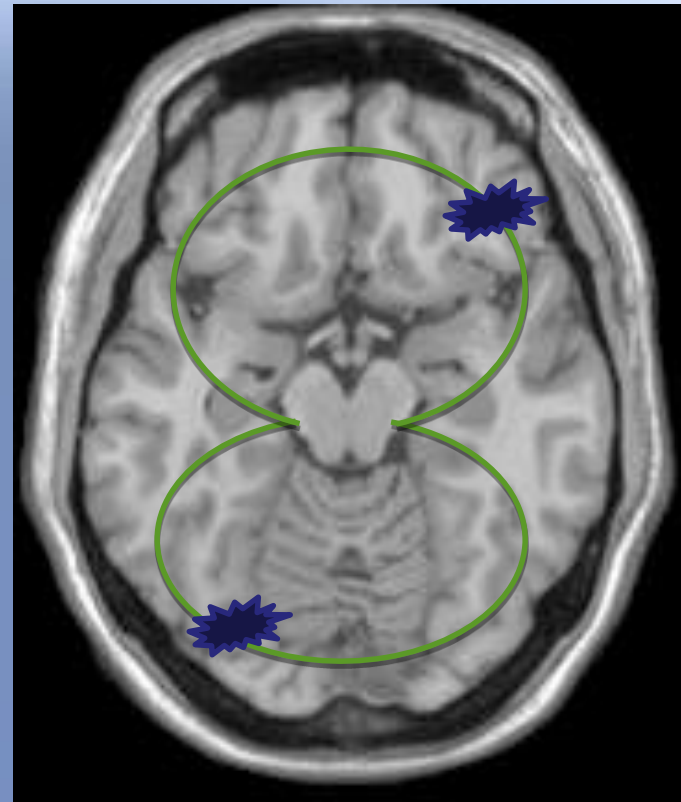




# Seizure Classification



Focal Seizure



Generalized Seizure



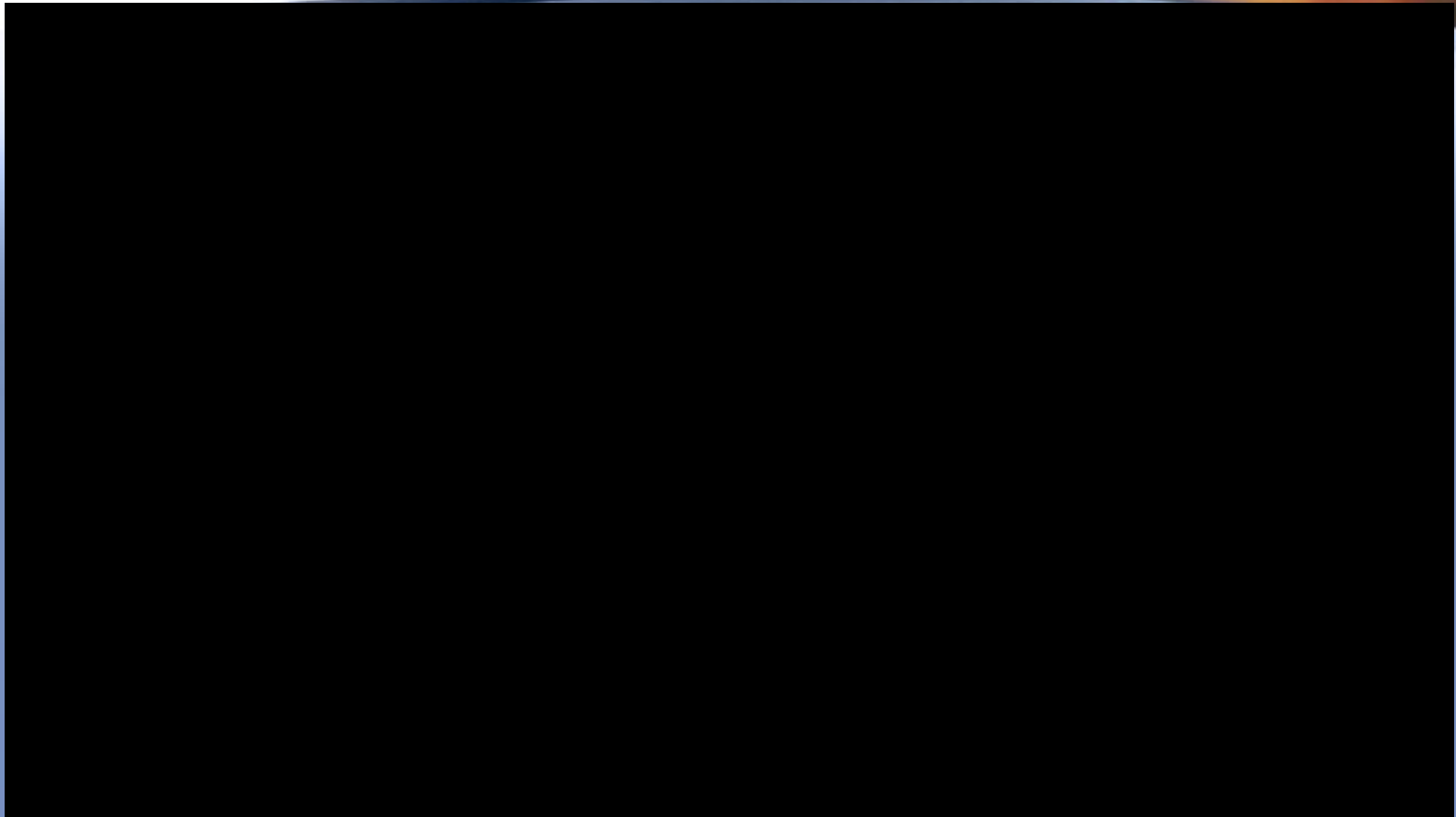
# Generalized Tonic Clonic Seizure





# Partial Complex Seizures







# Medically Refractory Epilepsy

- ❖ Failure to achieve sustained seizure freedom with adequate trials of at least two appropriately chosen and used AED regimens
- ❖ About 1/3 of people have very hard to control epilepsy
- ❖ Negative impact on quality of life, often significant





# Introduction to Cara

Largest stressor in my life is epilepsy. It affects nearly every aspect in my life. I cannot drive. I cannot work. I am under constant vigil by my family. My 8 year old daughter is protective over me, which is heartwarming on one hand, but sad on the other hand. She is 8, she worries that I might be having seizures when she is at work. She feels like she has to keep me safe, she tries to control what I do.





# Introduction to Cara

## Medical

- ❖ Seizure onset was age 5, seizures well controlled until age 22 (just prior to college graduation)
- ❖ Seizures are characterized by staring and unresponsiveness, sometimes laughing. Auras described as a loud bong tone have developed, causing great fear.
- ❖ Frequency is multiple seizures per week to daily, often clustering.
  
- ❖ AED tried and failed include dilantin, phenobarbital, lamotrigine, carbamazepine, vimpat, felbatol, keppra, gabitril, and topamax.
  - Currently prescribed Onfi and Trileptal
  - Frequent Lorazepam as rescue





# Introduction to Cara

- ❖ Admissions for status epilepticus, often following attempts to change medications.
- ❖ SIADH secondary to oxcarbazepine with frequent hyponatremia is challenging.
  - Dehydrates quickly, which impacts her ability to sustain coaching her daughter's soccer team.
- ❖ VNS was explanted secondary to poor efficacy and in preparation for surgical exploration
- ❖ Eventual Epilepsy Surgery evaluation with invasive video EEG using depth electrode and grid placement
  - ✓ Surgery evaluation was started in mid twenties. Not interested in surgery for many years. Interest grew once her daughter became older and sustaining employment was not possible. Seizures caused too much impact on daily function.





# Introduction to Cara

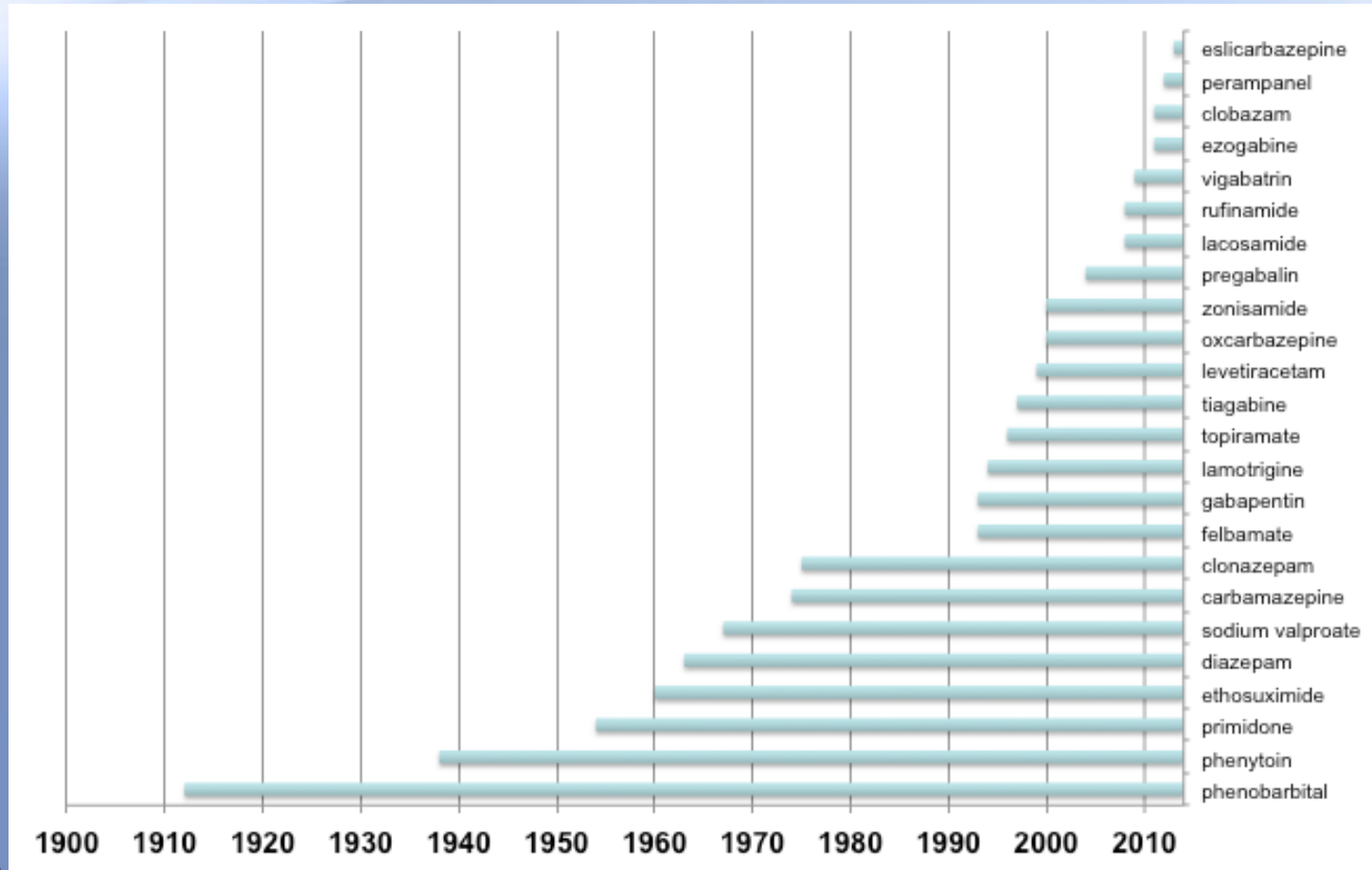
## Social

- ❖ Japanese and Caucasian ancestry, born on Midway Island. Lived in different areas of the world as a young girl and settled in Hawaii by young adulthood (father in the military).
- ❖ Graduated from a local HS, attended college in the states earning a degree in communications/advertising. Did well academically.
- ❖ Married, one 8 year old daughter. Lives in a shared home with her parents, in part for support.



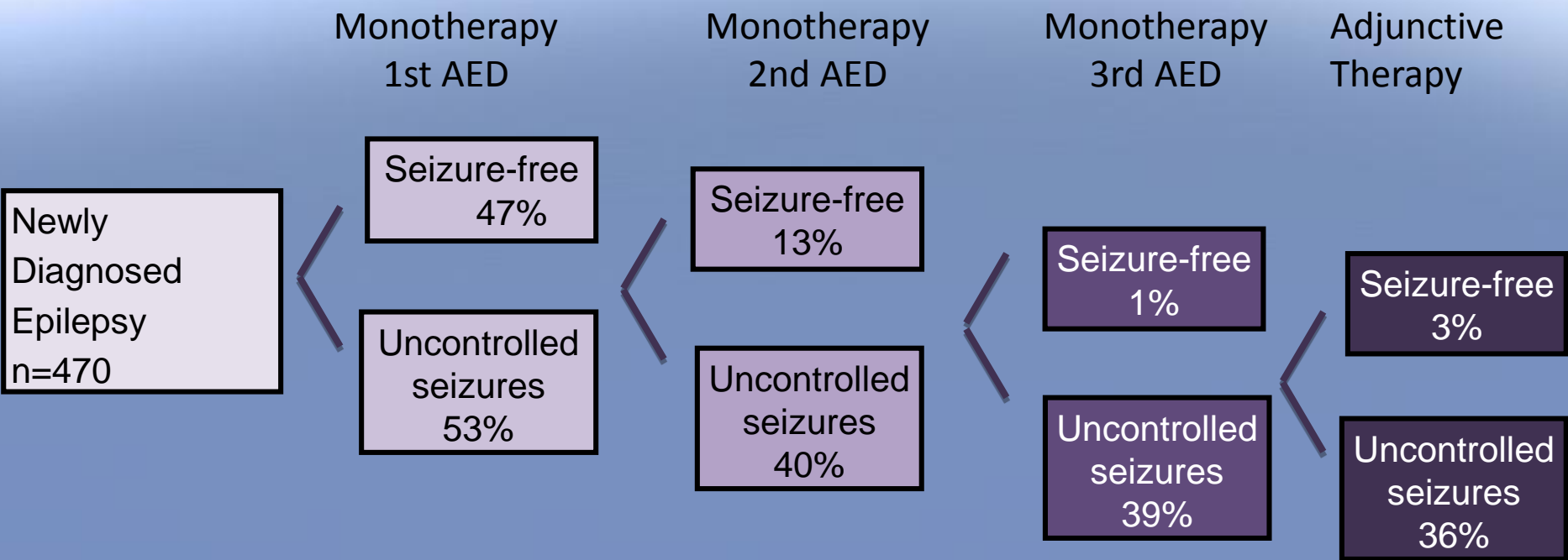


# Medications





# Medication Efficacy





# Consequences of seizures





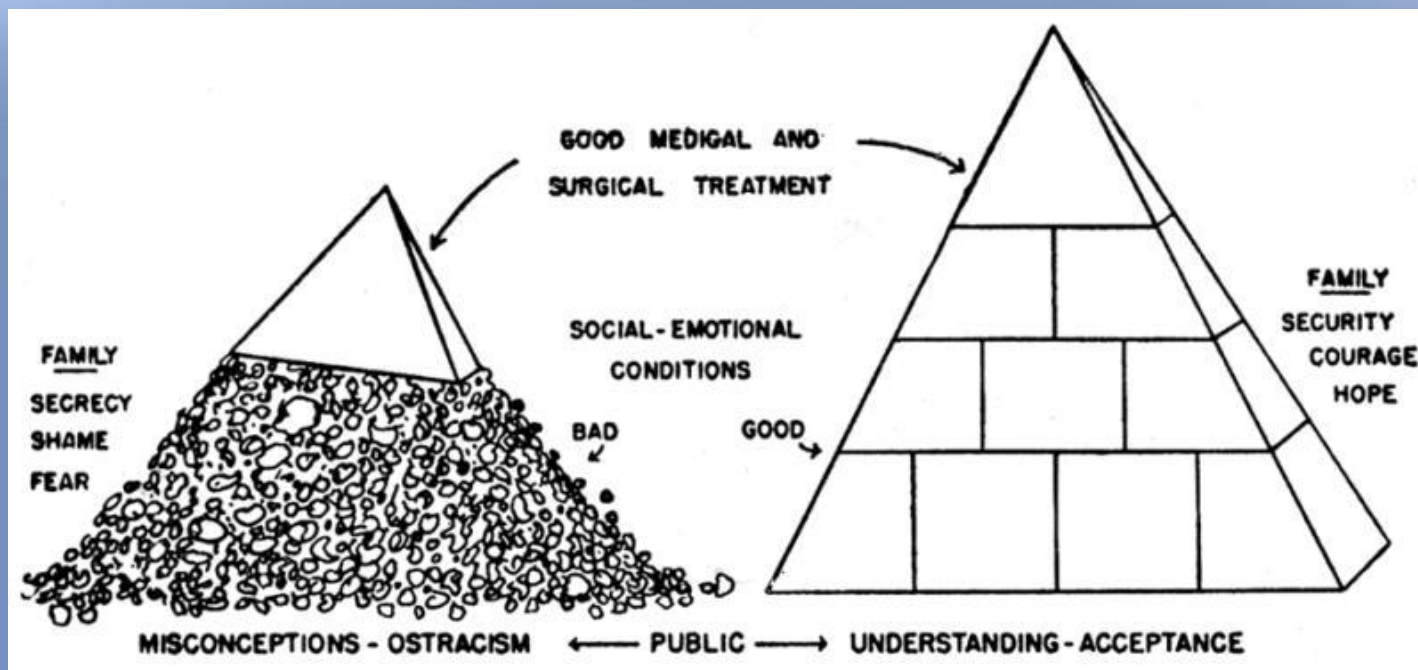
## Quality of Life

- ❖ People with intractable seizures endure the additional burdens of social discrimination, stigmatization, and social embarrassment when a seizure occurs in public.
- ❖ As with any chronic condition, epilepsy can be linked to demoralization and a negative perspective of life and to disturbances of affect and mood.





# Psycho Social Impacts



Lennox WG. Epilepsy and related disorders. Boston: Little, Brown and Co.; 1960





# Safety and Psychosocial

- ❖ Seizure precautions
  - ✓ Water safety, heights, heavy machinery
  - ✓ Childcare safety
- ❖ Driving
  - ✓ DMV
- ❖ Social issues
- ❖ Employability
- ❖ Self perception and identity - Dependent lifestyle





# Comorbidities in Epilepsy

- ❖ Psychiatric:
  - ❖ Lifetime rate of any psych disorder:
    - ✓ ~50 to 70%
  - ❖ Major depression:
    - ✓ ~20 to 40%
    - ✓ (Up to 57% in refractory epilepsy pts)
  - ❖ Anxiety disorders:
    - ✓ ~20 to 65%
  - ❖ Psychosis:
    - ✓ Inter-ictal: 9%
    - ✓ Post-ictal: 6%
  - ❖ Suicide rate: 5-fold risk up to 25-fold risk



Hermann, et al. The psychosocial impact of epilepsy in adults. Epilepsy Behav. 2009.





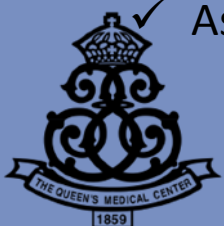
# Comorbidities in Epilepsy

## ❖ Sexuality and reproduction:

- ✓ Psychosocial issues with dating, intimacy
- ✓ 1/3 reduction in fertility rates
- ✓ Polycystic ovary syndrome
- ✓ Related to limbic system or indirectly through hypothalamic–pituitary axis

## ❖ Other

- ✓ Life threatening injuries, falls
- ✓ Premature Death
- ✓ Cognition
- ✓ SUDEP
- ✓ Aspiration





# Epilepsy in Women

## ❖ Women with epilepsy

- ✓ Folate, bone health, endogenous and exogenous hormone effects
- ✓ Pregnancy: 6 months advance notice!
- ✓ >90% have normal babies

## ❖ Stigma and Myths about Epilepsy

- ✓ Epileptics are not able to take care of children
- ✓ Epileptics should be sterilized to prevent passing it on
- ✓ Pregnancy is not safe in Epilepsy





# Treatments Options other than Medications

- ❖ Epilepsy Surgery
- ❖ Implanted devices –
  - ✓ Vagus Nerve Stimulator (VNS)
  - ✓ Responsive Neuro Stimulator (RNS) - Neuropace
- ❖ Diets in Epilepsy Treatment
  - ✓ Ketogenic Diet (Primarily children and tube fed individuals)
  - ✓ Modified Atkins Diet (Older children through adulthood)
  - ✓ Medium Chain Triglyceride Diet (MCT)
  - ✓ Low Glycemic Index Diet (LGIT)





# Epilepsy Surgery Evaluation

## ❖ Goals

- ✓ Identify an abnormal area of cortex (seizure focus)
- ✓ Remove this area without causing significant functional impairment

## ❖ Pre-surgical evaluation

- ✓ History and Physical
- ✓ Brain MRI (epilepsy protocols)
- ✓ Video-EEG (Epilepsy Monitoring Unit)
- ✓ Neuropsychological testing and assessment of psychosocial functioning

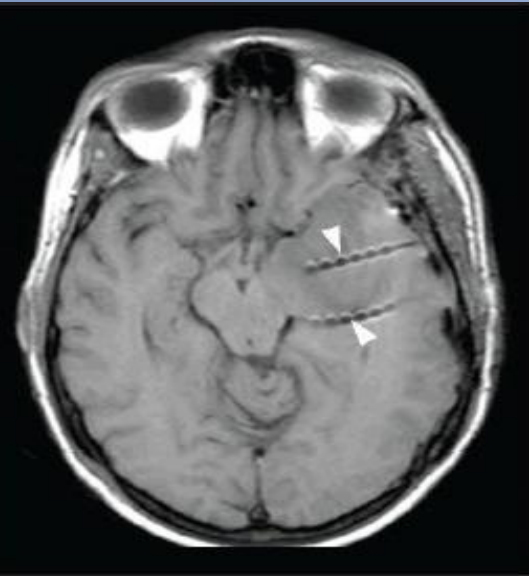
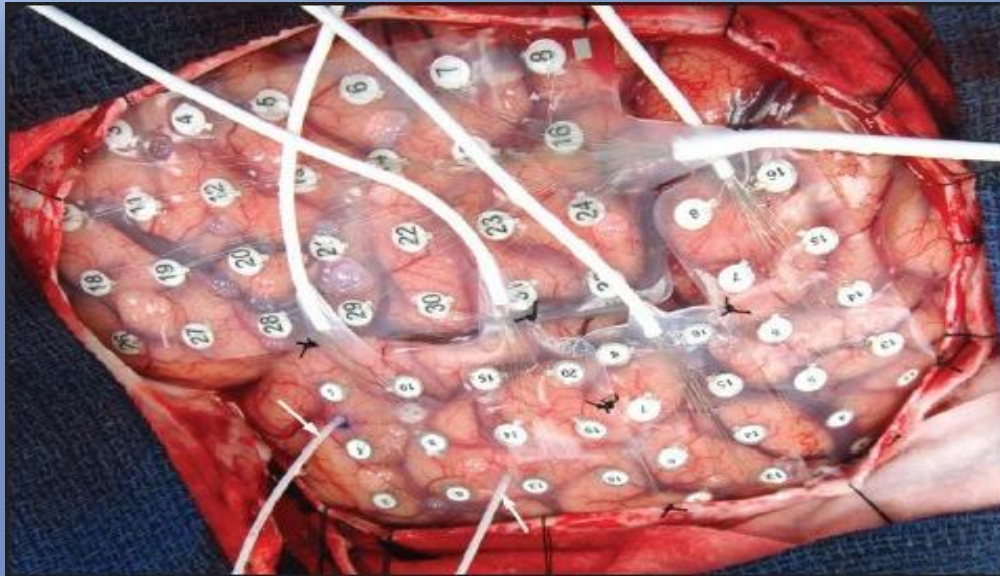
## ❖ Additional diagnostics

- ✓ Functional Imaging studies: PET and SPECT
- ✓ Functional MRI
- ✓ MEG





# Invasive Monitoring

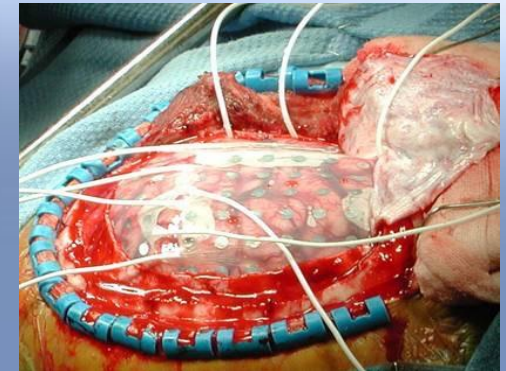




# Epilepsy Surgery type

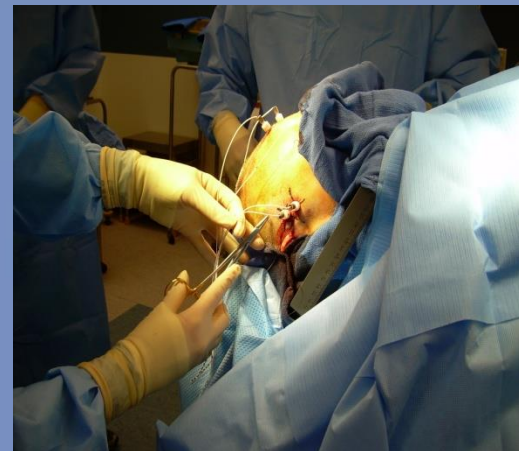
## ❖ Standard surgeries:

- ✓ Selective amygdalohippocampectomy
- ✓ Standard anterior temporal lobectomy



## ❖ Other surgeries:

- ✓ Lesionectomy
- ✓ Extra-temporal resections
- ✓ Hemispherectomy
- ✓ Corpus callosotomy
- ✓ Multiple subpial transections





# Surgical Outcomes

- ❖ Engel et al . 2003. A systematic review and meta-analysis of temporal lobe and localized neocortical resections for epilepsy that included 32 studies and 2,250 patients
  - ✓ 63% of patients remained seizure free after 2-5 years of follow-up
- ❖ Seizure freedom rates specific to type
  - ✓ 65% to 85% - temporal lobectomies (mesial temporal sclerosis)
  - ✓ 60-80% - extratemporal and well circumscribed lesion
  - ✓ 20-25% - non lesional extratemporal neocortical
    - ✓ Additional 25% having a worthwhile improvement
    - ✓ Rates doubled if functional imaging and EEG are concordant



Passaro, E. 2015. Outcome of Epilepsy Surgery.





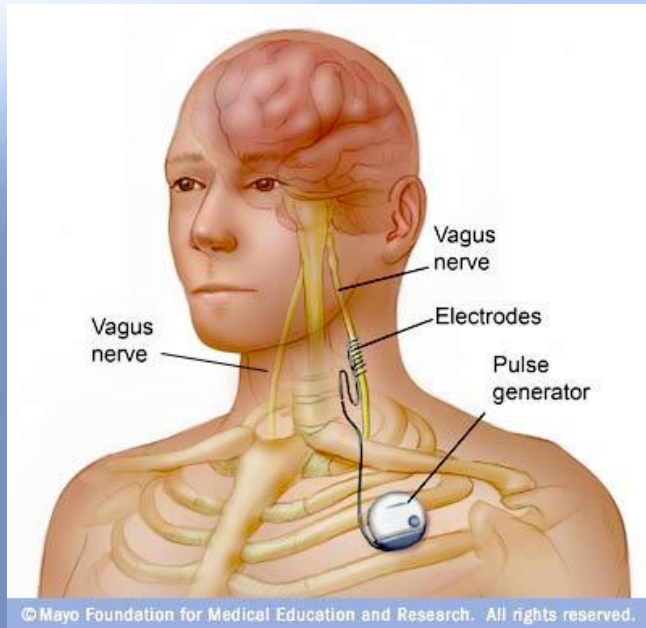
# Surgery - Outcomes

- ❖ Serious complications occur in only about 4 out of 100 temporal lobectomies
- ❖ Success rates can be predicted after test results are available
- ❖ Complication
  - ✓ Memory problems
  - ✓ Movement problems
  - ✓ Visual Problems
  - ✓ Sensory problems
  - ✓ Risk of infection after surgery





# Vagus Nerve Stimulator (VNS)



- ❖ Implantation of a pacemaker-like device into the chest
  - generates pulses of electricity to stimulate the vagus nerve.
- ✓ Settings entered to tell device how & when to stimulate
- ✓ Magnet used to deliver additional stimulation
- ❖ AspireSR- delivers responsive stimulation to heart-rate increases
- ❖ The VNS Therapy System is FDA-approved for adjunctive therapy for
  - ✓ Drug-resistant (medically refractory) epilepsy
  - ✓ No age or seizure type restriction
- ❖ Surgical work-up is recommended PRIOR to implantation of VNS





# Vagus Nerve Stimulator

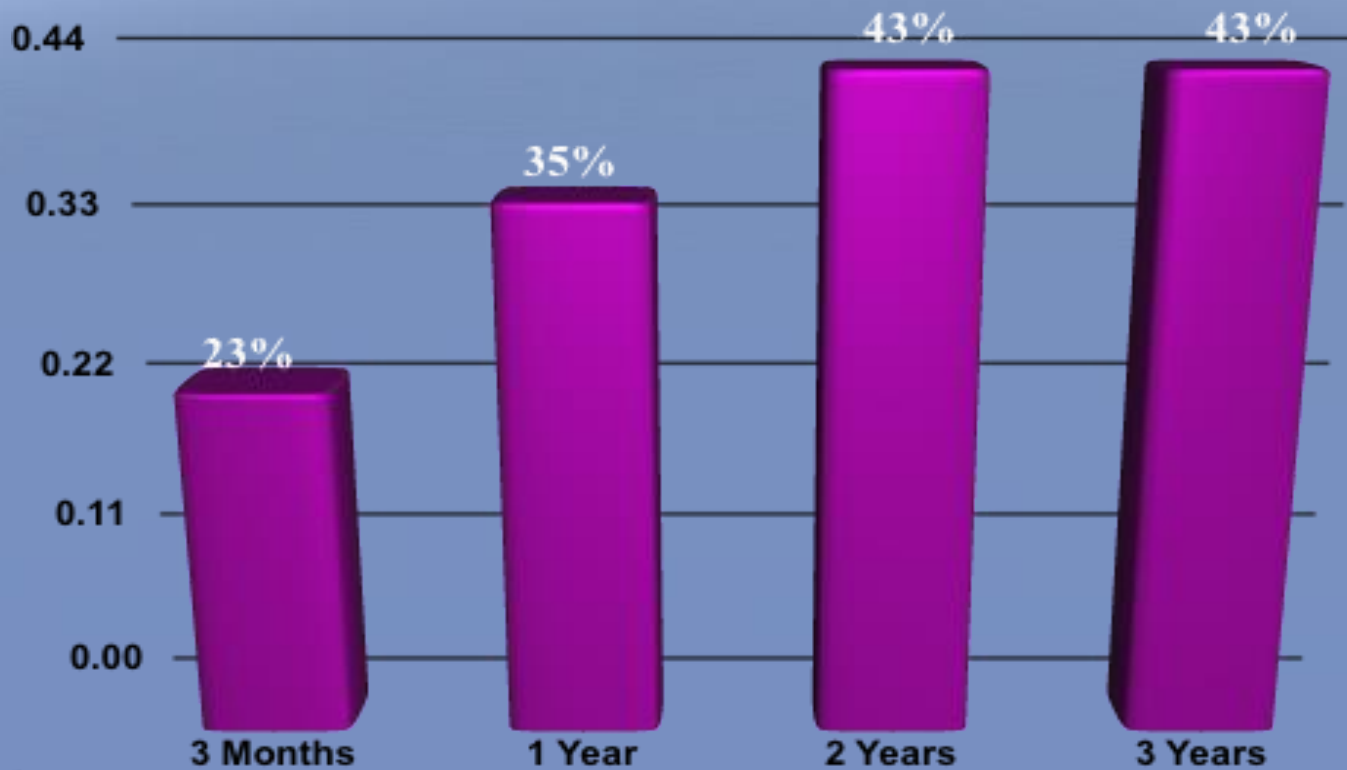
- ❖ Patient experience with VNS
  - ✓ Same day operation
  - ✓ Frequent visits for ramping up on settings (initial)
  
- ❖ Common Side effects during stimulation
  - ✓ Vocal Hoarseness
  - ✓ Cough
  - ✓ Shortness of Breath
  - ✓ Infection following implant surgery
  
- ❖ Goal of therapy
  - ✓ Reduction in seizures
  - ✓ Reduced severity, duration and/or post ictal recovery





# Outcomes - VNS

Patients With > 50% Seizure Frequency Reduction



Morris GL, et al. *Neurology*. 1999;53:1731-1735





## NeuroPace: Responsive Neurostimulation Device (RNS)

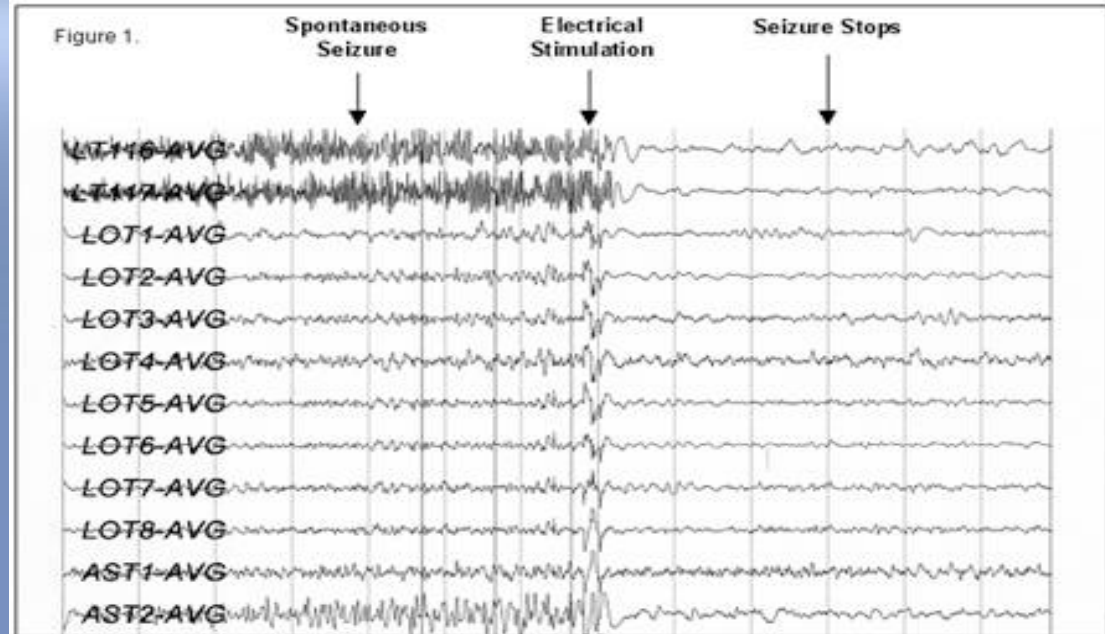


- ❖ Implantation of a small device on the skull with leads into the brain in or around foci.
- ❖ NeuroPace is FDA approved for adjunctive treatment in
  - ✓ Partial onset seizures
  - ✓ Failure of 2 antiepileptic drugs
  - ✓ Age 18
  - ✓ No more than 2 seizure foci



Image from: [http://www.nature.com/nrneurol/journal/v4/n4/fig\\_tab/ncpneuro0750\\_F3.html](http://www.nature.com/nrneurol/journal/v4/n4/fig_tab/ncpneuro0750_F3.html)





- ❖ Programmed to monitor brain wave activity (your seizure activity)
- ❖ Detects onset of seizure
- ❖ Delivers electrical stimulation to interrupt seizure



# Outcomes - RNS

- Patient experience
  - Requires identification of seizure focus, invasive VEEG may be required
  - Requires brain surgery and hospital admission
  - Education on use of equipment provided
  - Ongoing programming to target seizure onset
- 55% experienced a 50% or greater reduction in seizures two years post implant
- 66% median seizure reduction at 6 years
- 59% responder rate at 6 years
- Improvements in cognition and decreases in seizure worry.

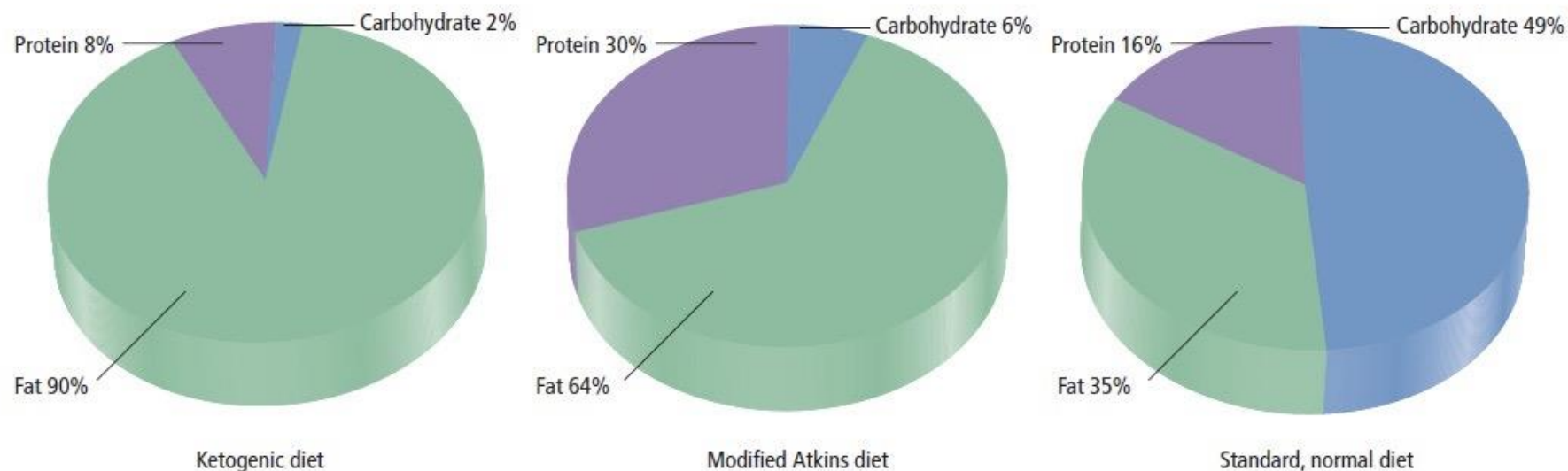




# Dietary Treatment in Epilepsy

- Ketogenic Diet
- Modified Atkins Diet
- Medium Chain Triglyceride Diet
- Low Glycemic Index Diet

Figure 1: Comparative Contents of the Ketogenic and Modified Atkins Diets





# Diet Treatment

- ❖ Think of a diet as similar to a medication
- ❖ Ketogenic Diets are medically supervised diets
  - ✓ Labs, complete history & physical, diet screening required prior to initiation
  - ✓ LOTS of education
- ❖ Ketogenic Diet may more likely be effective in certain syndromes
- ❖ Diets can be tried in
  - ✓ Children and Adults
  - ✓ Those with intractable epilepsy not surgical candidates
  - ✓ Both generalized and partial onset seizures
  - ✓ In combination with all epilepsy treatments
- Patients/Families willing to change diet preferences and maintain long term





# Potential Side Effects

- ❖ Side effects not common - Occur in less than 5% of cases
- ❖ Medical Management is aimed at reducing risk of the following
  - ✓ gastrointestinal upset
  - ✓ constipation
  - ✓ dyslipidemia
  - ✓ slowing of linear growth
  - ✓ kidney stones
  - ✓ acidosis
  - ✓ vitamin and mineral deficiencies (if not supplemented)
  - ✓ potential changes to menstruation
- ❖ Constipation and weight loss are the most common
- ❖ Other changes often seen as advantages include weight loss, improved migraine, improved concentration, improved memory



# Outcomes

## Ketogenic Diet

### ❖ Sirven, et al. 1999.

- ✓ prospective study, 11 adults
- ✓ 4:1 ketogenic diet
- ✓ 6 patients had > 50% reduction at 8 months
- ✓ 4 dropped out

### ❖ Barborka et al. 1930.

- ✓ 100 patient 18 + years
- ✓ 58% reduction at 3 months
- ✓ 14% became seizure free



## Modified Atkins

### ❖ Prospective studies in adults:

#### ❖ Kossoff et al. 2007.

- ✓ 30 patients, 18+ years of age
- ✓ Carbohydrates restricted to 15 g/day
- ✓ 47% had a >50% sz reduction at 3 mos
- ✓ 33% after 6 mos
- ✓ 14 (47%) completed the 6-month study

#### ❖ Smith et al. 2011.

- ✓ 18 patients, 18+ years of age
- ✓ Carbohydrates restricted to 20 g/day
- ✓ 12% had a >50% sz reduction at 3 mos
- ✓ 28% after 6 mos
- ✓ 21% after 12 months
- ✓ 78% remained at 12 months





# Epilepsy Diets

- ❖ Effective for all seizure types
- ❖ Efficacy similar between children and adults
  - ✓ More than half of patients experience  $\geq 50\%$  seizure reduction at 6 months
  - ✓ One out of ten have seizure freedom at 1 year
  - ✓ A 47% continuation rate at 1 year
  - ✓ Can accommodate all food preferences
  - ✓ Can be low cost





# Challenges

- Delay in referrals to an epilepsy Center is ~ 18 - 23 years.
  - Choi et al. 2009. Evaluation of duration of epilepsy prior to temporal lobe epilepsy surgery during the past two decades
- Vocational and social rehabilitation is more difficult after a patient has settled into a disabled lifestyle
- Referral sources for rehabilitation/return to work are absent
- Reimbursement for social work and case management is poor
- Irreversible adverse consequences of epilepsy, often with low Q o L
- Quality of Life indicators correlates directly with seizure freedom





## In Closing

- ❖ This case represents a challenging epilepsy to treat.
- ❖ ~36% of patients with epilepsy have intractable epilepsy
- ❖ Surgical resection of the seizure focus provides the best chance at seizure freedom
- ❖ Meaningful seizure control or seizure freedom can be achieved through Epilepsy Surgery, VNS, NeuroPace and/or Diet treatment or (less likely) trial of additional anticonvulsants.
- ❖ If seizure freedom or meaningful seizure control is not achieved, significant social, medical and economic burdens occur





Questions?

# ALOHA

