

# What to do when medications fail: Non pharmacologic treatments for pediatric epilepsy.

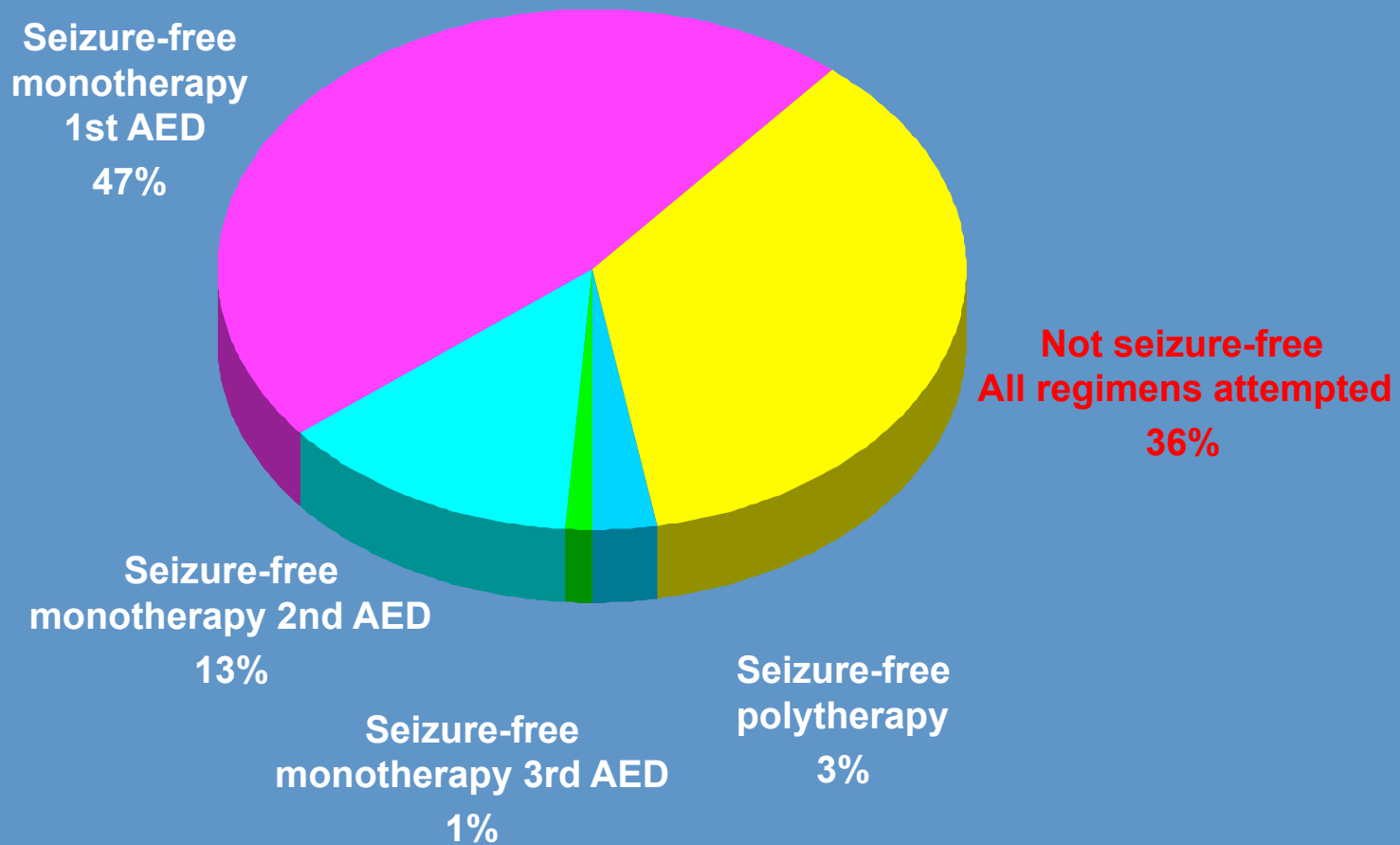
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# Outline

- Scope of the problem
- Epilepsy surgery
- Ketogenic diet
  - clinical aspects
- Vagus nerve stimulator
- Responsive neurostimulation
- Deep brain stimulation

# Seizure-Free Rates With Different Strategies

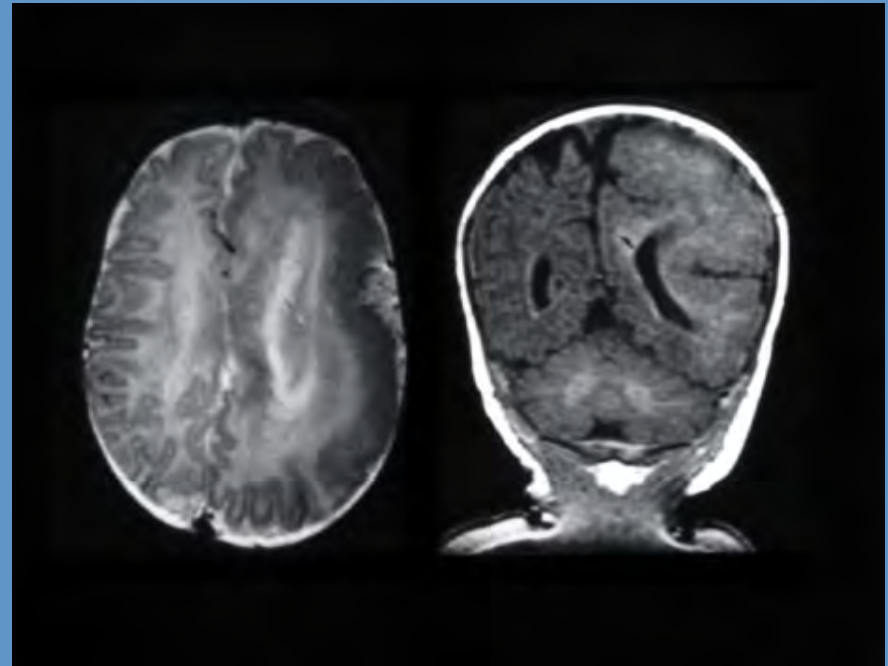


# Surgery for Seizures

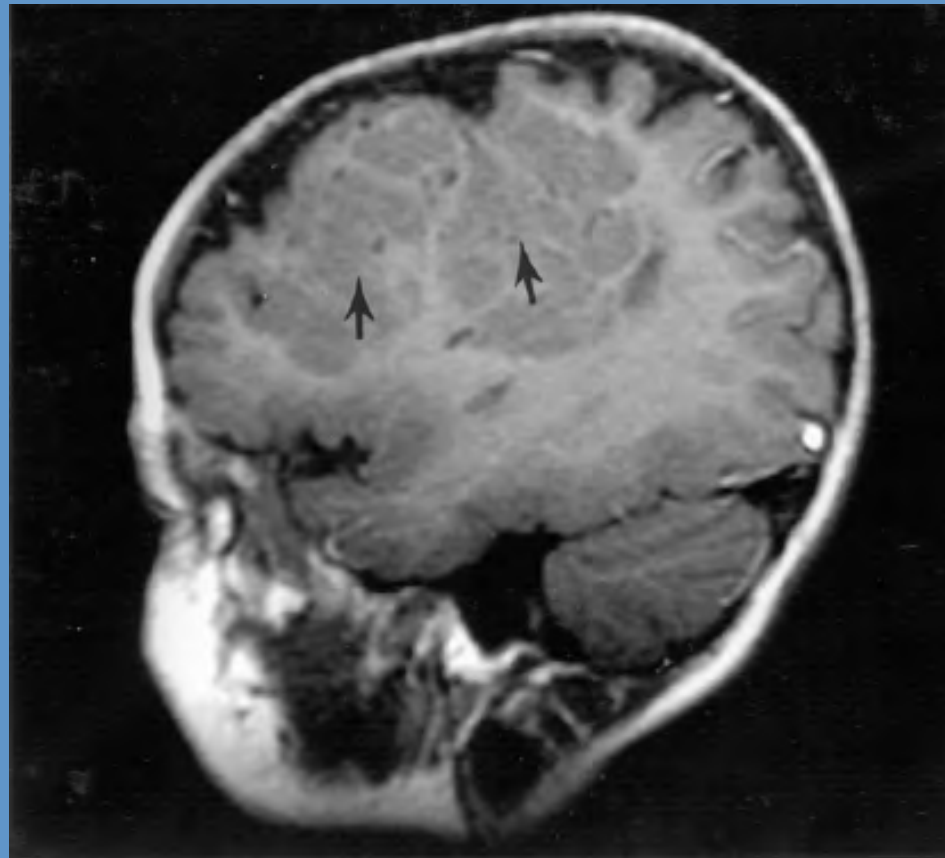
- Considered after failing AED therapy
- Surgical evaluation includes inpatient video/EEG monitoring
- Other tests may include: MRI, SPECT scan, PET scan, and neuropsychological testing
- Procedures include focal resection, temporal lobectomy, lesionectomy, hemispherectomy and corpus callosotomy
- Post-surgical seizure-free rates vary
- Patients usually go home after a short stay at the hospital and will likely miss several weeks or months of school

# Surgery

- Early surgery can be life-altering
- Unique conditions such as Rasmussen's, hemimegalencephaly, Sturge Weber can be remedied in children surgically
- Outcomes beneficial



# Cerebral Dysgenesis- Heterotopia



# MRI - Schizencephaly



# Epilepsy Surgery Outcomes

	Temporal	Extra Temporal	Lesional	Hemispheric	Callosotomy
Seizure Free	68%	45%	66%	45%	8%
Improved	23%	35%	22%	35%	61%
Not improved	9%	20%	12%	20%	31%
Total	100%	100%	100%	100%	100%

Reference: Engel, J. NEJM, Vol 334 1996, 647-653



# Therapeutic Diets

- Ketogenic Diet
- Low Glycemic Index Diet
- Atkins Diet

# What is the ketogenic diet?

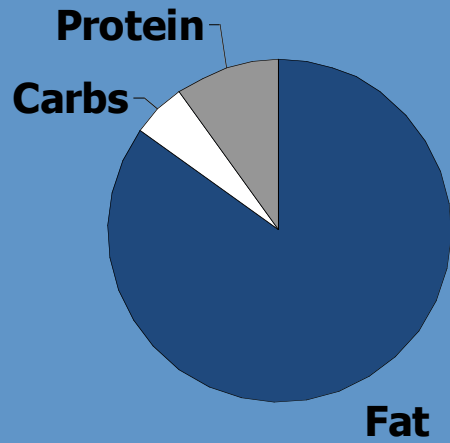
- High fat, adequate protein and carbohydrate diet which induces ketosis in those who consume it.
- Fasting as treatment: Hippocrates, Old Testament
- Wilder (1921): ketogenic diet to mimic fasting state
- Introduction of phenytoin in 1930's
- Resurgence 17 yrs ago with treatment of pt at JHU

# Diet “Prescription”

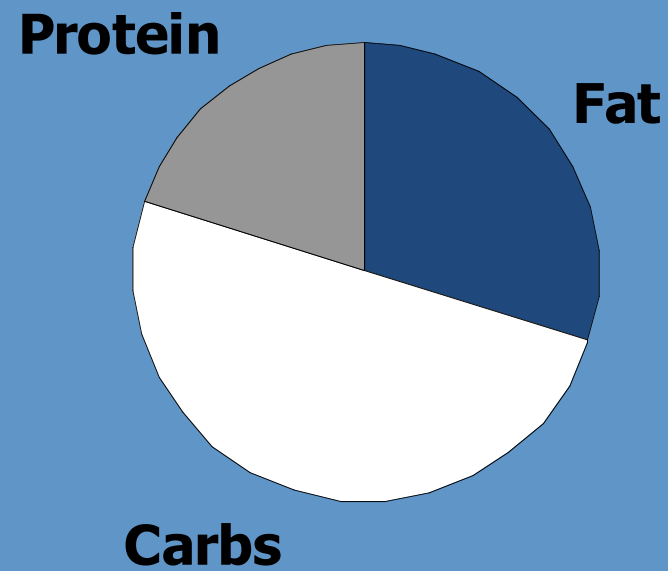
- Ratio (fat: carb+protein)
  - 4:1 more strict
  - 3:1 for infants, adolescents
- Infants: ketogenic formula
- Children:



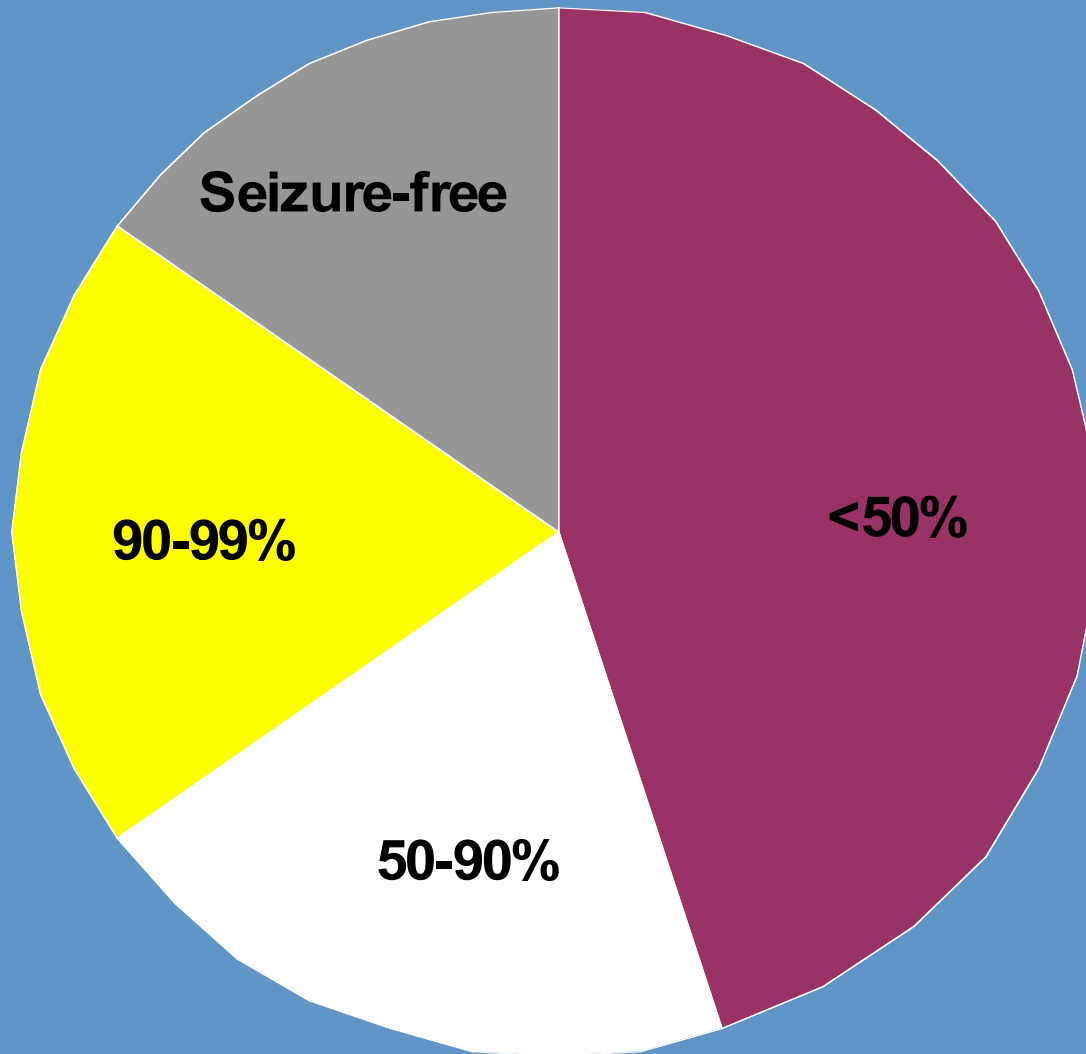
# Ketogenic Diet



# “American” Diet



## Seizure Reduction from Ketogenic Diet



# Common and Occasional Side Effects

- Constipation
- Slowed weight gain
- Acidosis (with illness)
- Vitamin deficiency (if unsupplemented)
  
- Renal stones
- Growth slowing
- Dyslipidemia

# Neurostimulation

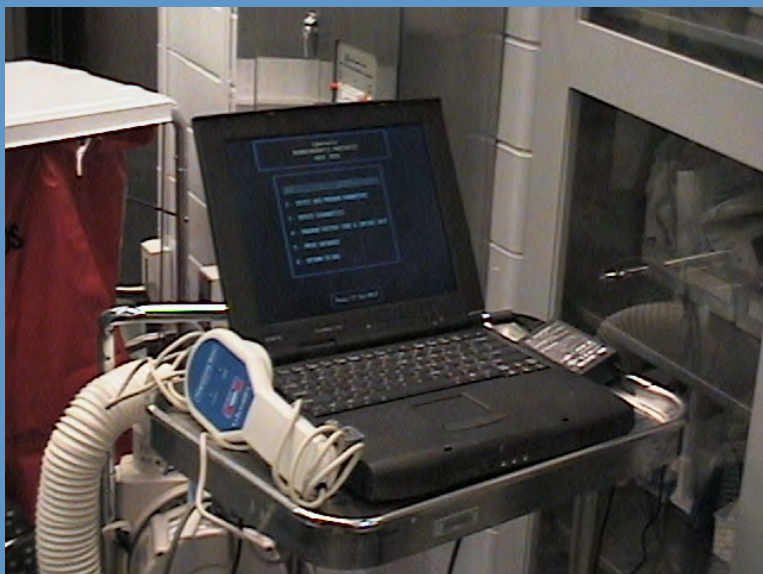
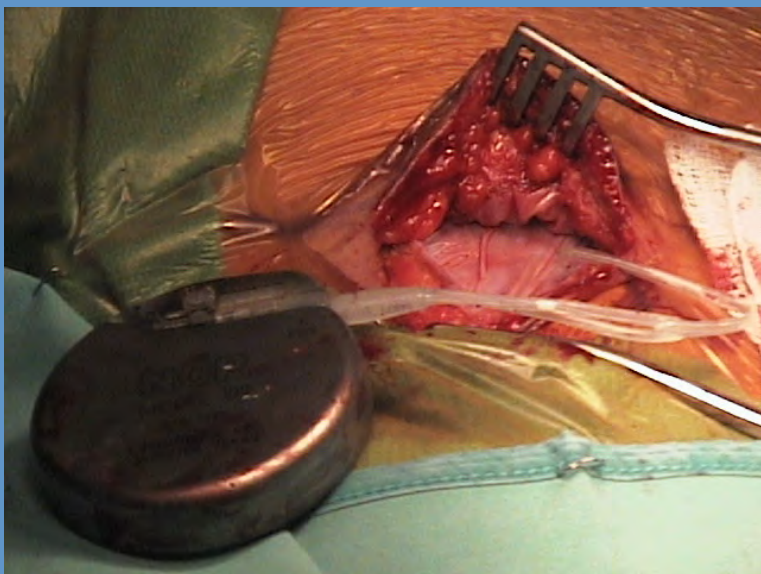
- Vagus Nerve Stimulator
- Responsive Neurostimulator (Neuropace)
- Deep Brain (Thalamic) Stimulation

# Vagus Nerve Stimulation

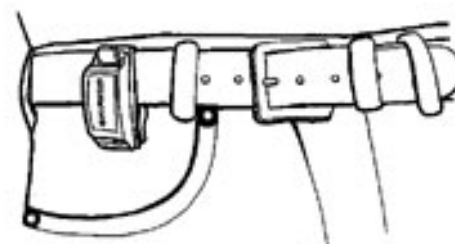
- Implantable device – constant stimulation
- FDA indicated for patients >12 since 1997
- Day surgery procedure
- 35,000 patients implanted (8,000 in <18)







*This special VNS magnet is worn on the wrist.*



*The VNS magnet can also be clipped to a belt, like a pager.*

# Mechanism of Action

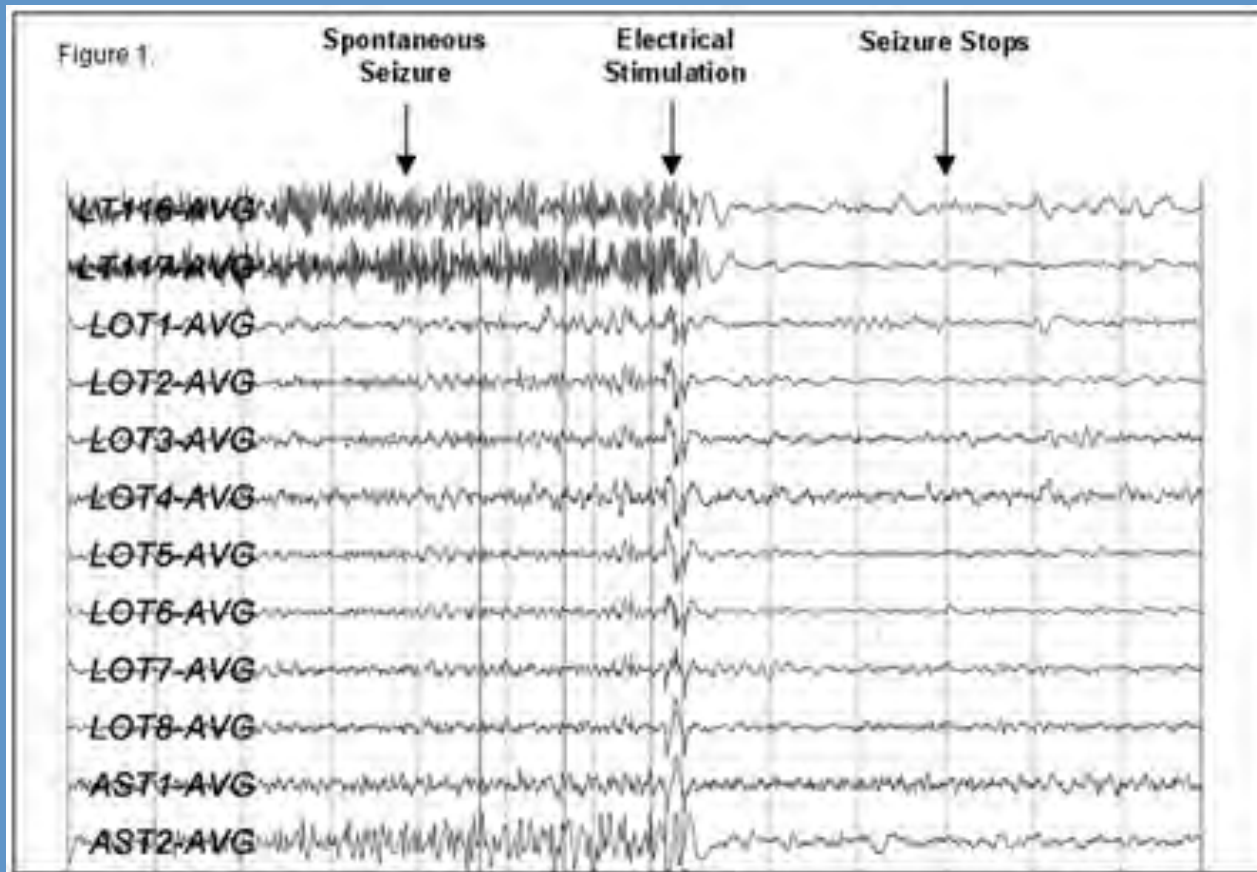
- Unclear
- Clear thalamic inhibition
- May activate the dorsal midbrain to reduce cortical excitability
- Multiple pathways potentially involved

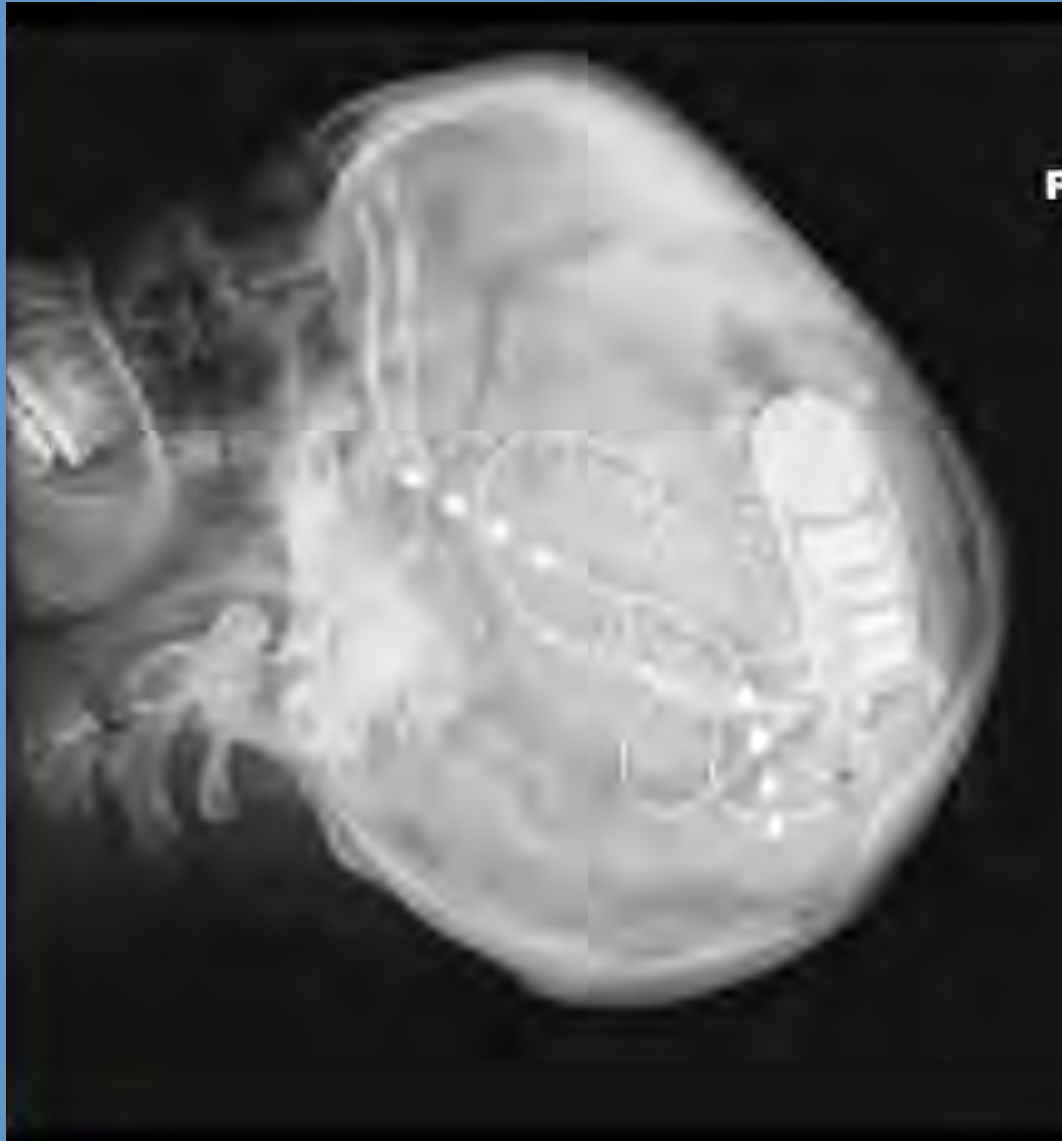
# Efficacy

- 35% with >50% seizure reduction at 12 months
  - 20% with >75%
- Similar to new AEDs

# NeuroPace

- Responsive neurostimulation





## NeuroPace Pilot Trial:

Safety preliminary efficacy of the Responsive Neurostimulator in Adults:

During the preliminary evaluation period, the responder rate was:

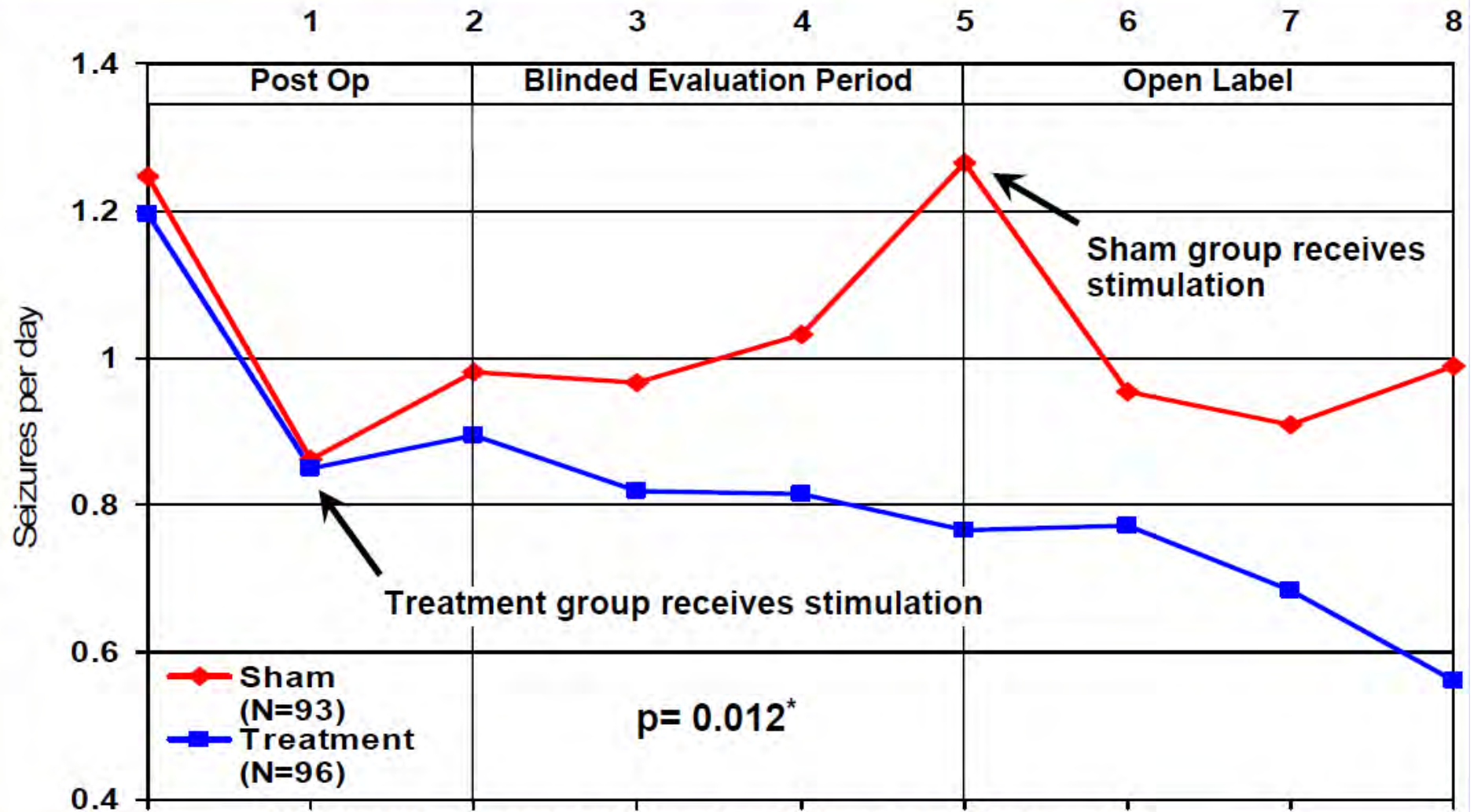
- 32% for complex partial seizures
- 63% for generalized tonic clonic seizures



# Pivotal RNS Trial

- 240 patients enrolled
  - 191 implanted
- 18-70 years of age
- Intractable seizures
- 3 seizures/28 day period

# Mean of Disabling Seizures by Month



\*GEE controlling for onset zone, number of seizure foci, and prior surgery

Investigational Device. Limited by US law to investigational use only.



# Deep Brain Stimulation

- SANTE: Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy
  - At two years:
    - Median 57% reduction from baseline seizure frequency
    - Responder rate 54%
    - 12.7% seizure-free for at least 6 months
    - Improvement in quality of life scores

# Summary

- 1/3 of children with epilepsy have intractable seizures (1/2 of these will not be surgical candidates)
- Other options
  - KD: probably the best chance for improved seizure control in patients that are not epilepsy surgery candidates
  - VNS
  - RNS
  - DBS
  - Herbal remedies

- Thanks to Eric Kossoff, MD, Johns Hopkins Hospital for many slides used in this presentation.