Seizures and Epilepsy

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Disclosures

- None

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Objectives

- Definitions
- Differential diagnosis for epilepsy
- Diagnostic work up
- Seizure classification
- Epilepsy classification
- Management options
- Comorbidities
- Status epilepticus

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SEIZURE	EPILEPSY
Sign or symptom of disorder	The disorder

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Case

26 y/o female who presents to the ED for new onset seizure.

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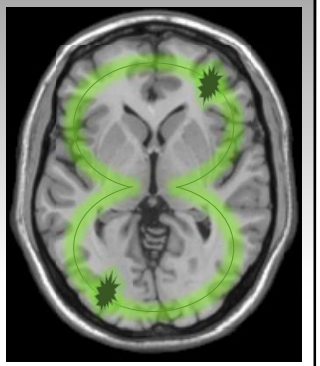
Definitions

Seizure –
Transient occurrence of signs and / or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.



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Seizure classification

Focal Onset

Aware | Impaired Awareness

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

Non-Motor 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

Non-Motor (absence)
- typical
- atypical
- myoclonic
- eyelid myoclonia

Unknown Onset

Motor
- tonic-clonic
- epileptic spasms

Non-Motor
- behavior arrest

Unclassified [3]

1 Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary of terms

2 Degree of awareness usually is not specified

3 Due to inadequate information or inability to place in other categories

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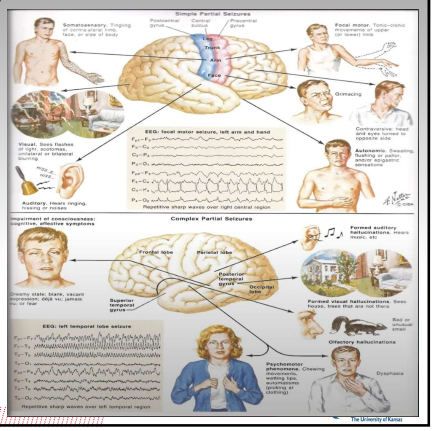
Focal Seizures



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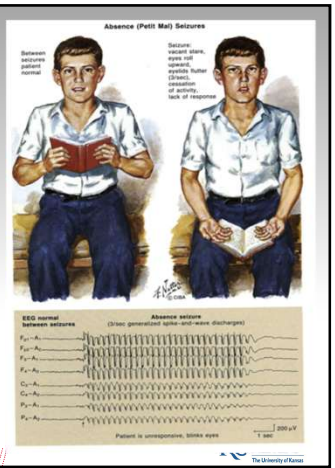
Generalized seizure



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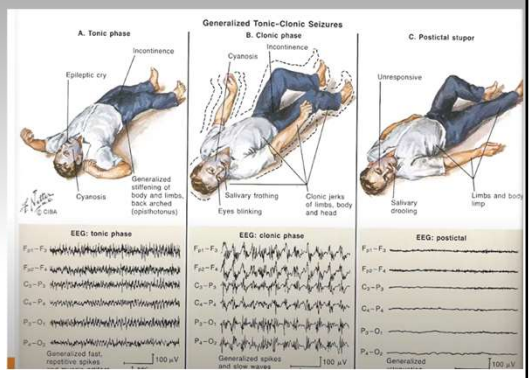
Tonic Clonic Seizure



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Definitions

Provoked seizure –
Occurs in context of an acute brain insult or systemic disorder.
Underlying etiology can be treated or reversed.
Does not increase risk of developing epilepsy.

Unprovoked seizure –
Occurs in absence of an acute exacerbating factor.
Higher risk of developing epilepsy

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Common causes of provoked seizures

- Alcohol withdrawal
- Electrolyte abnormalities -

Hypo / Hypernatremia
Hypocalcemia
Hypomagnesemia
Hypo or Hyperglycemia

- Recreational drug use
- Adverse effect to Bupropion or tramadol
- Acute intracranial bleeding
- Acute TBI

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Definitions

- Epilepsy –

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

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Definitions

Epilepsy is a disease of the brain defined by any of the following conditions

- Atleast two unprovoked seizures occurring >24 h apart
- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
- Diagnosis of an epilepsy syndrome

- Do NOT use 'SEIZURE DISORDER'.

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History – New onset seizure

- Does the patient remember the event
- Any warning signs / feelings aka aura prior to the event.
- What happened before, during and after the event – collateral information is the key.
- Incontinence / lateral tongue or cheek biting.
- Previous use of anti seizure medication.
- Any new medications or obvious triggers

Epilepsy risk factors

- H/o childhood / febrile seizures,
- H/o of significant head trauma,
- CNS infections
- Family h/o seizures
- H/o tumor or stroke

Epilepsy is a clinical diagnosis

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Epidemiology

1 in 26 people in the US will have a seizure at some point in their lifetime.
Lifetime risk of epilepsy is 1.5 – 3.5 %

Seizure recurrence if cause unknown –
1 year → 10%
3 years → 24 %
5 years → 29%

Seizure recurrence if risk factor present –
1 year → 26 %
3 year → 41 %
5 years → 48 %

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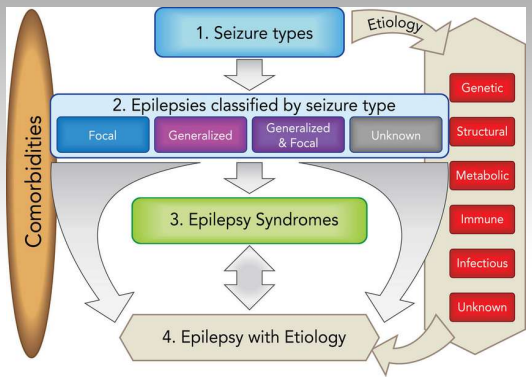
Epilepsy classification



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Differential diagnosis

- Convulsive syncope
- Migraine
- Transient ischemic attacks
- Transient global amnesia
- Vertigo
- Sleep disorders / parasomnia
- Other movement disorders
- Psychogenic spells – panic attacks / anxiety / conversion disorders

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Differentiate from Non epileptic events

- Aura
- Duration
- Start and stop
- Abnormal posturing
- Post ictal confusion
- Amnesia for the event
- Events arising from sleep
- Eyes open during the seizure

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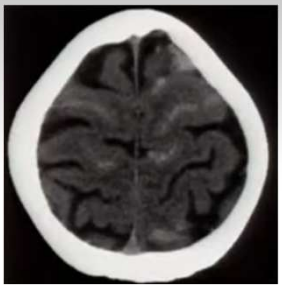
Diagnostic work up

Urgent assessment for first seizure in acute settings –
CT Head to identify acute neurologic injury.
Rapid, widely available and cost effective.
But can only pick up 20 % lesion associated with epilepsy.



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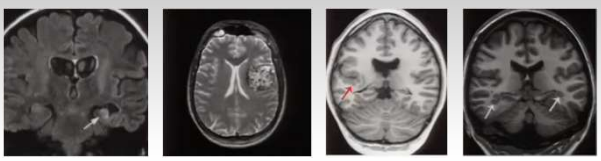
Diagnostic work up

MRI brain
About 50 % of the time imaging may not reveal an obvious cause.



Mesial temporal sclerosis | AVM / cavernous malformation | Focal cortical dysplasia | Heterotopia

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Diagnostic work up

• EEG

Not a very sensitive test –
Normal test does not change your outlook / clinical diagnosis.

Very specific test –
Abnormal test is helpful

Poor temporal co relation but good spatial co relation.

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Diagnostic work up - EEG

Reasons to get EEG -
Spell characterization
Classification of seizure / epilepsy
Evaluate for status epilepticus
Surgical evaluation

Types of EEG –
Routine 20 – 60 minute recordings.
Ambulatory EEG – 48 – 72 hrs recordings
Continuous monitoring with or without video
Invasive monitoring.
Ceribell

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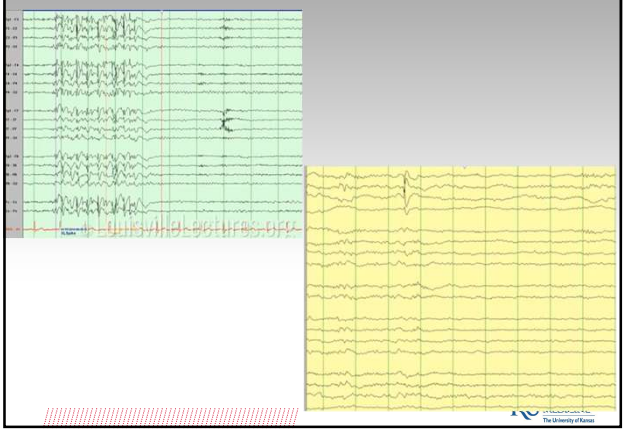

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Case…….

- You assess the patient which is groggy but awake and answers questions appropriately. She has never had a seizure before. She cannot think of anything out of ordinary and has no risk factors for seizures. Her muscles ache and she bit her tongue. She reports event occurred out of sleep and does not know what happened. She woke up with her husband and EMS around and was confused. Her husband reports violent shaking of the bed which woke him up lasting nearly 1-2 minutes.
- Her vitals and labs look normal except for some WBC count elevation, lactic acid elevation and prolactin elevation.
- She has an EEG and MRI brain in the ER which comes back normal.

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Case …..

History – No risk factors

Exam – Normal

Work up – Normal

How do you counsel the patient next….

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Seizure precautions

Driving restriction

No unattended swimming or surfing

No unattended baths (showers are acceptable).

Do not stand over open flames or bonfires

Do not get high on ladders or roof

Do not operate heavy machinery or power tools or farms tools.

Avoid sleeping in prone position

Family members help with child care

Do not sleep with baby in bed

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- Numbers for discussion on starting asm vs not

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Case continued.....

- The patients comes back to the clinic 5 weeks later and says that her husband reports another shaking event in her sleep. Once when he was out, she woke up confused and had urinary incontinence.
- She is now diagnosed with epilepsy and started on a daily anti seizure medication.
- She is on an oral contraceptive agent for birth control.

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Treatment

GOAL of treatment is improvement in Quality of LIFE and seizure freedom.

Treatment choice is based on several factors -

Seizure type – Focal v/s generalized

Side effect profile – Good v/s bad

Drug drug interactions and adherence

Special considerations – pregnancy

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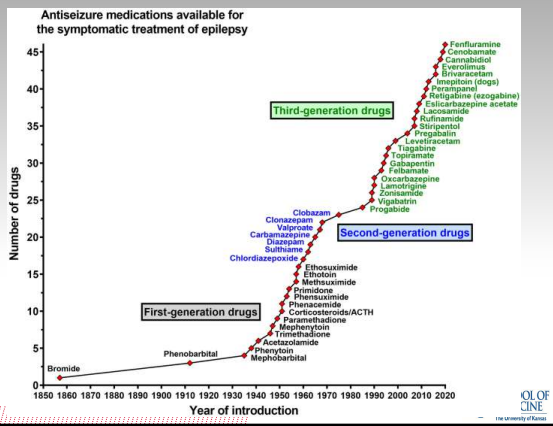
Evolution of Anti Seizure Medications



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Treatment

Broad spectrum	Narrow spectrum
Lamotrigine	Phenytoin
Leveteriacetam	Pregabalin
Topiramate	Gabapentin
Zonisamide	Carbamazepine
Valproate	Vigabatrin
Clobazam	Oxcarbezepine
Felbamate	Eslicarbezepine
Primidone	Tiagabine
Phenobarbital	Rufinamide
Perampanel	Cenobamate
Lacosamide	

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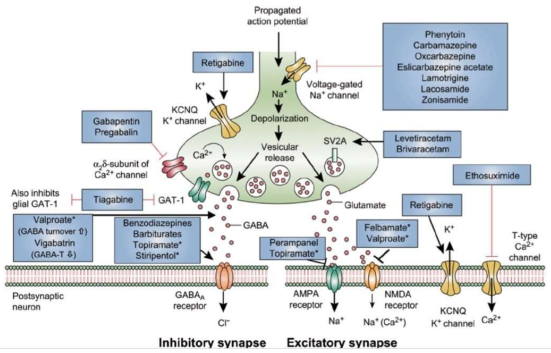
Treatment



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Treatment – Synergistic effect

Condition	Use
Anxiety	PB, LM, PGB, GBP
Bipolar Affective Disorder/mood stabilization	VPA, LM, CBZ, OXC, TPM
Obesity/T2DM	TPM, ZN (FB)
Migraines	VPA, TPM
Insomnia	GBP, PGB, PB
Painful neuropathy	GBP, PGB, CBZ, OXC
Trigeminal Neuralgia	OXC, CBZ
Fibromyalgia	PGB (GBP)
Restless leg syndrome	CBZ, GBP, PGB
Essential Tremor	Primidone

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Treatment – Antagonistic effect

Condition	Avoid
Behavioral/mood problems	LEV, PMP
Obesity (+OSA)	VPA, PGB, GBP
Cognitive issues	TPM, PB
Renal Stones	TPM, ZN
Osteoporosis	PB/PM, CBZ, PHT; (VPA)
Diabetes	VPA
Elderly on diuretics/ ACE inhibitors (↓ Na)	OXC, CBZ, ESL (?)
Glaucoma	TPM

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Treatment

Side Effect	AEDs
Rash/allergy/SJS	PHT,PB,CBZ,OXC,LMT, CLB
Marrow suppression	CBZ (aplastic anemia), PHT, FB, ZN, VPA (platelets)
Hepatitis/↑ LFTs	VPA (+pancreatitis), CBZ, PHT, ZN,
Cognition	TPM, PB,CBZ
Psychiatric --	LEV, PB (depression), EZG, PMP, CLB
Weight Gain	VPA, GBP, PGB, VGB
Weight Loss	TPM, ZN, FB, CBD (?)
PCOS, DM,	VPA
↓ Na	CBZ, OXC, ESL
Renal Stones	TPM, ZN
Teratogenicity	VPA, PB, TPM, PHT
Osteoporosis	PB, PHT, CBZ, VPA
Neuropathy/cerebellar atrophy	PHT, CBZ (neuropathy)

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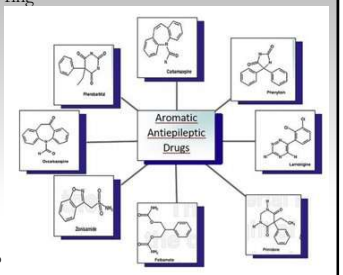
ASM hypersensitivity syndrome

Rash, systemic involvement: SJS,TNE,DRESS
Arene oxide intermediates – aromatic ring
Cross-reactivity
Phenytoin
Phenobarbital
Carbamazepine
Oxcarbazepine
Lamotrigine



Rash: 15%
HLA-A*1502 in Han Chinese: 9-10%
HLA-A*3101 in Japanese : 15% population prevalence
Europeans: 2-5% prevalence

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Treatment – Enzyme induction

Enzyme inhibitor
Valproate

Enzyme inducer
Carbamazepine
Oxcarbazepine
Phenytoin
Phenobarbital
Primidone
Topiramate
Felbamate

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Treatment - Effect on the EKG

Increase PR interval -
Carbamazepine
Lacosamide
Lamotrigine

Increase QT interval – Exogabine
Decrease QT interval - Rufinamide

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Treatment – Contraception

Enzyme inducers can lower effectiveness of OC pills

Lamotrigine can reduce effectiveness of oral contraceptive and vice versa.

IUDs are safest in terms of no significant interaction with AEDs.

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Treatment - Women with epilepsy

Teratogenicity -

Risk of major fetal malformation in general population is 1- 2 %

Risk for women with epilepsy on ASM is 2 – 9%

All drugs are category C or D

None of these are category X

Avoid valproic acid

Add folic acid 1 mg OD; in pregnancy 4 mg

Risks of seizures outweighs risks of medications

Encourage breast feeding.

Bone health screening

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Co morbidities

- Cognitive impairment – Attention, executive function, memory
- Depression – 50 % of medically refractory
- Anxiety – 20 %
- Psychosis
- Suicide – 25x general population
- Migraine
- OSA
- Increased mortality – 2x general population

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SUDEP - Sudden unexpected death in epilepsy

0 – 4 % risk
Incidence of 0.4 - 9.3/1000 person years

Risk factors -
Males
Epilepsy > 15 yrs
Early onset seizures.
Frequent tonic clonic seizures.
Intractable seizures

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Case continued.....

- You have been following your patient for about 2 yrs now and she has continued to have seizures on additional medications which were appropriately chosen and at therapeutic dosages.

- What now??

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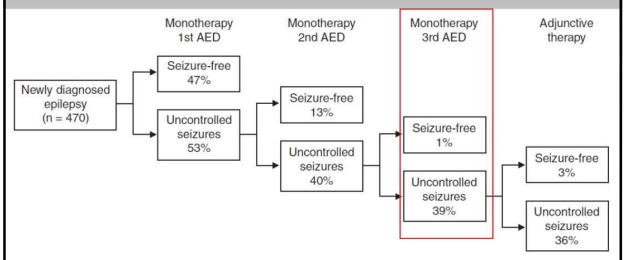
What happens with ASM treatment



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Refractory / treatment resistant epilepsy

Ascertain diagnosis -

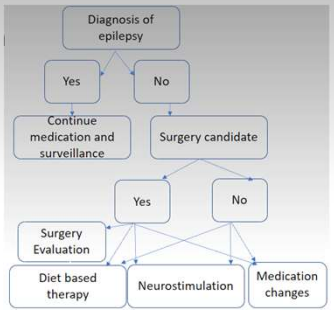
25 % of patients previously diagnosed with epilepsy may not have epilepsy and were inappropriately diagnosed.

Consider non medication approach -

Diet therapy

Surgical resection

Neuromodulation



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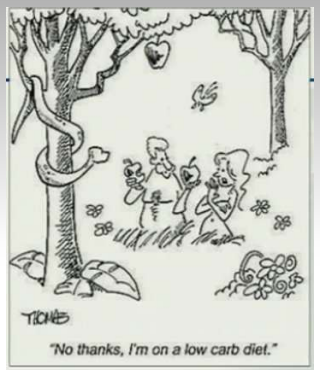
Diet therapy



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Classic Ketogenic diet –

5 studies, 47 patients

15 (32%) responders

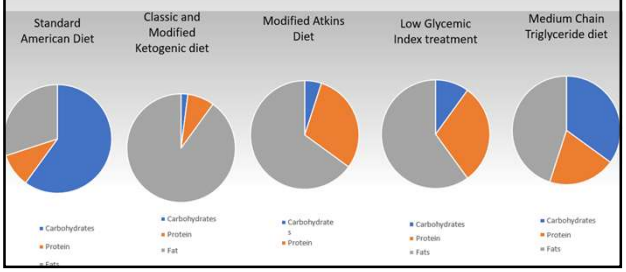
4 (9%) > 90 % seizure reduction

Modified Atkins Diet –

5 studies, 85 patients

24 (28%) responders

7 (8%) > 90 % seizure reduction



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Surgical interventions

Lesionectomy

Lobectomy

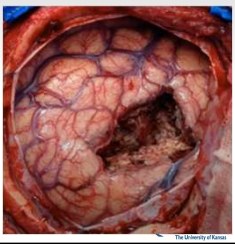
Thermal ablation (LITT)

Radiofrequency ablation

Corpus callosotomy

Functional hemispherectomy

Multiple subpial transections



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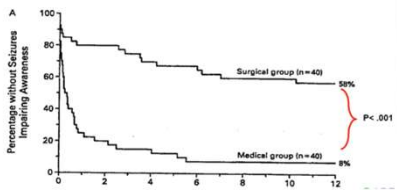
Evidence for surgical treatment

1st Randomized Controlled Trial for temporal lobectomy
Seizure Freedom



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Temporal lobe surgery

Published in final edited form as:
JAMA. 2012 March 7; 307(9): 922–930. doi:10.1001/jama.2012.220.

Early Surgical Therapy for Drug-Resistant Temporal Lobe Epilepsy:
A Randomized Trial

Jerome Engel Jr, MD, PhD, Michael P. McDermott, PhD, Samuel Wiebe, MD, John T. Langfitt, PhD, John M. Stern, MD, Sandra Dewar, RN, Michael R. Sperling, MD, Irenita Gardiner, RN, Giuseppe Erba, MD, Itzhak Fried, MD, PhD, Margaret Jacobs, BA, Harry V. Vinters, MD, Scott Mintzer, MD, Karl Kieburtz, MD, MPH, and for the Early Randomized Surgical Epilepsy Trial (ERSET) Study Group

0 % in medical therapy seizure free

85 % in surgical group seizure free

Odds ratio – Infinity.

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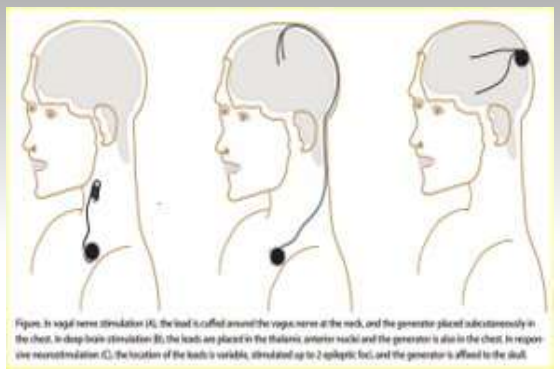
Neuromodulation



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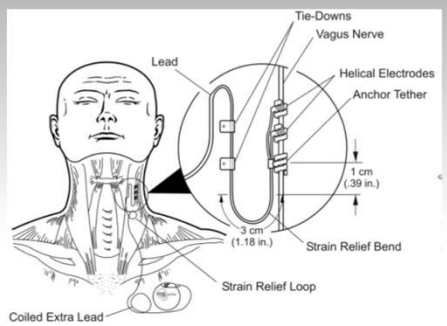
Vagal Nerve Stimulator (VNS)



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Deep Brain Stimulation (DBS)

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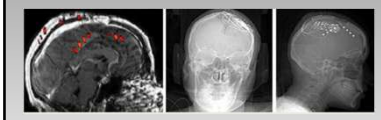
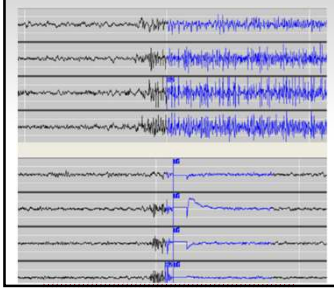
Responsive Neuro Stimulation (RNS)





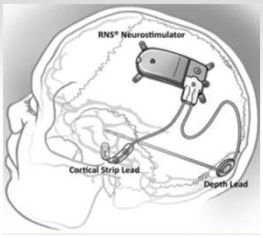


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TABLE. NEUROSTIMULATION DEVICES FOR TREATMENT OF MEDICALLY-REFRACTORY EPILEPSY

	Vagal nerve stimulation	Deep brain stimulation	Responsive neurostimulation
Target and parameters	Left vagus nerve is stimulated intermittently in an open-loop system or, in a closed-loop system, in response to tachycardia or by patient/caregiver with a magnet in response to seizure	Bilateral thalamic anterior nucleus stimulation intermittently scheduled by physician in open loop system	Epileptogenic focus or foci are stimulated in reponse to interictal abnormalities in a closed-looped system
Indication	Generalized or focal epilepsy in people age 4 years or more	Focal epilepsy in adults (age 18 yrs or more)	Focal epilepsy in adults with ≤2 foci
Response to treatment	At 5 years, > 50% seizure reduction experienced by 60% of people treated	At 5 years, median seizure reduction = 68%	At 9 years, median % seizure reduction = 66%; at 5 years, seizure reduction > 50% is seen in 65% of people with mesial temporal epilepsy who were treated and 70% of people with neocortical epilepsy who were treated
Seizure freedom	At 5 years, 8.25% were seizure free for at least 6 months	At 6 months, 16% had at least 3 seizure-free months; overall, 5.4% with 2 years of seizure freedom	At 6 months, 30% were seizure free; at 12 months, 19% were seizure free for at least 3 months
Postimplant MRI	Yes, with safety coil (except few models)	Yes, with safety coil	Contraindicated
Complications	Infection, left vocal cord paralysis	Infection, misplaced leads, parasthesias	Infection, hemorrhage
Side effects	Cough, dyspnea, hoarseness, and pain		Dysesthesia, muscle twitching, parasthesias, photopsia
SUDEP risk[a]	2.47-4.1/1,000 patient years	2.5-2.8/1,000 patient years	2/1,000 patient years
Neuropsychologic effects	May improve word recognition. Subjective improvement in verbal concentration reported. Independent effect on mood has been seen.	No objective change; subjective worsening of memory and depression.	With mesial temporal lobe stimulation, improvement in cognitive flexibility, visuospatial abilities, and mood; with stimulation of other areas, improvement in language, verbal ability, and cognitive flexibility

[a]SUDEP incidence is measured per 1000 patient years, and rates increase proportionally to severity of epilepsy: 0.9-2.3 in all people with epilepsy, 3.2-5.9 in medically refractory epilepsy and 6.3-9.3 in those who are surgical candidates. Abbreviation: SUDEP, sudden unexpected death in epilepsy

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Status Epilepticus

Continuous seizure activity lasting > 5 minutes or
2 or more sequential seizures without regaining consciousness.

Tonic clonic seizure – 5 minute
Focal status epilepticus with impaired awareness – 10 minutes
Absence status epilepticus – 10 –15 minutes

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Etiology - Cleveland Clinic ICU experience

Etiologies	n	EEG +	% with Sz
Acute stroke	120	20	16.7
Remote Stroke	64	18	28.1
Intracranial hemorrhage (SAH / SDH/ ICH / IPH)	206	40	46.4
Extra axial tumor	31	13	41.9
Intra axial tumor	106	35	33
Hypoxic ischemic injury	101	27	26.7
CNS infection (Abscess)	10	1	10%
CNS infection (Meningitis / encephalitis)	51	15	29.4%
Metabolic (Liver, kidney, sepsis)	160	18	11.3%
Transplant	15	3	20%
Epilepsy	127	15	11
Convulsions NOS	104	1	1
Overall	1123	215	19.1

Christopher Newey et al.

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Etiology on cEEG - Columbia

Claassen et al 2004

Table 2 *Primary admission diagnoses and frequency of seizures*

		CEEG findings		
Admission diagnoses	n	Any seizure	NCS	NCSE
Epilepsy-related seizures	51	17 (33)	16 (31)	10 (20)
CNS infection	35	10 (29)	9 (26)	6 (17)
Brain tumor	43	10 (23)	10 (23)	5 (12)
Post neurosurgery	13	3 (23)	3 (23)	1 (8)
Hypoxic–ischemic encephalopathy	25	5 (20)	4 (16)	3 (12)
Subarachnoid hemorrhage	108	20 (19)	19 (18)	14 (13)
Traumatic brain injury	51	9 (18)	9 (18)	4 (8)
Toxic–metabolic encephalopathy	38	7 (18)	8 (21)	3 (8)
Unexplained decrease in LOC*	105	17 (17)	16 (15)	5 (5)
Intracerebral hemorrhage	45	6 (13)	6 (13)	4 (9)
Ischemic stroke	56	6 (11)	5 (9)	4 (7)
Overall	570	110 (19)	105 (18)	59 (10)

Data are given as n (% of patients with this admission diagnosis).

* Although cEEG monitoring was initiated for the detection of subclinical seizures or unexplained decrease in level of consciousness in all 570 patients, unexplained decrease in level of consciousness was the primary admission diagnosis in these 105 patients.

cEEG = continuous EEG; NCS = nonconvulsive seizure; NCSE = nonconvulsive status epilepticus; LOC = level of consciousness.

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How long should I monitor

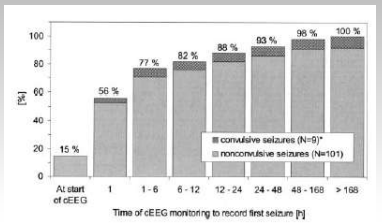

*Figure 1. Time elapsed between start of continuous EEG (cEEG) monitoring and detection of the first seizure (n = 110). *Three of these nine patients had nonconvulsive seizures as well.*

Detection of electrographic seizures with continuous EEG monitoring in critically ill patients J. Claassen et al. Neurology 2004

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How long should I monitor

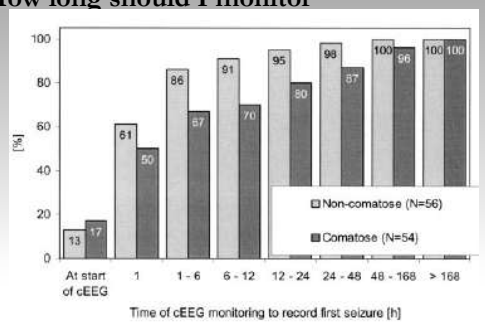

Figure 2. Time to record the first seizure, comparing noncomatose and comatose patients. cEEG = continuous EEG.

Detection of electrographic seizures with continuous EEG monitoring in critically ill patients J Claassen et al. Neurology 2004

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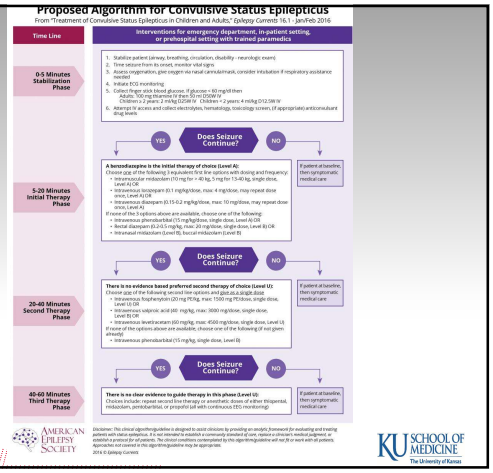

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Take home points

- First time seizure work up
- Patients with atleast 2 seizures have epilepsy
- Goal is seizure freedom and quality of life improvement.
- Reconsider diagnosis if clinical improvement is not apparent.
- Consider surgical evaluation and candidacy if 2 appropriately chosen AEDs fail to control seizures.
- Co manage co morbidities
- Treat status epilepticus with appropriate doses and rate

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