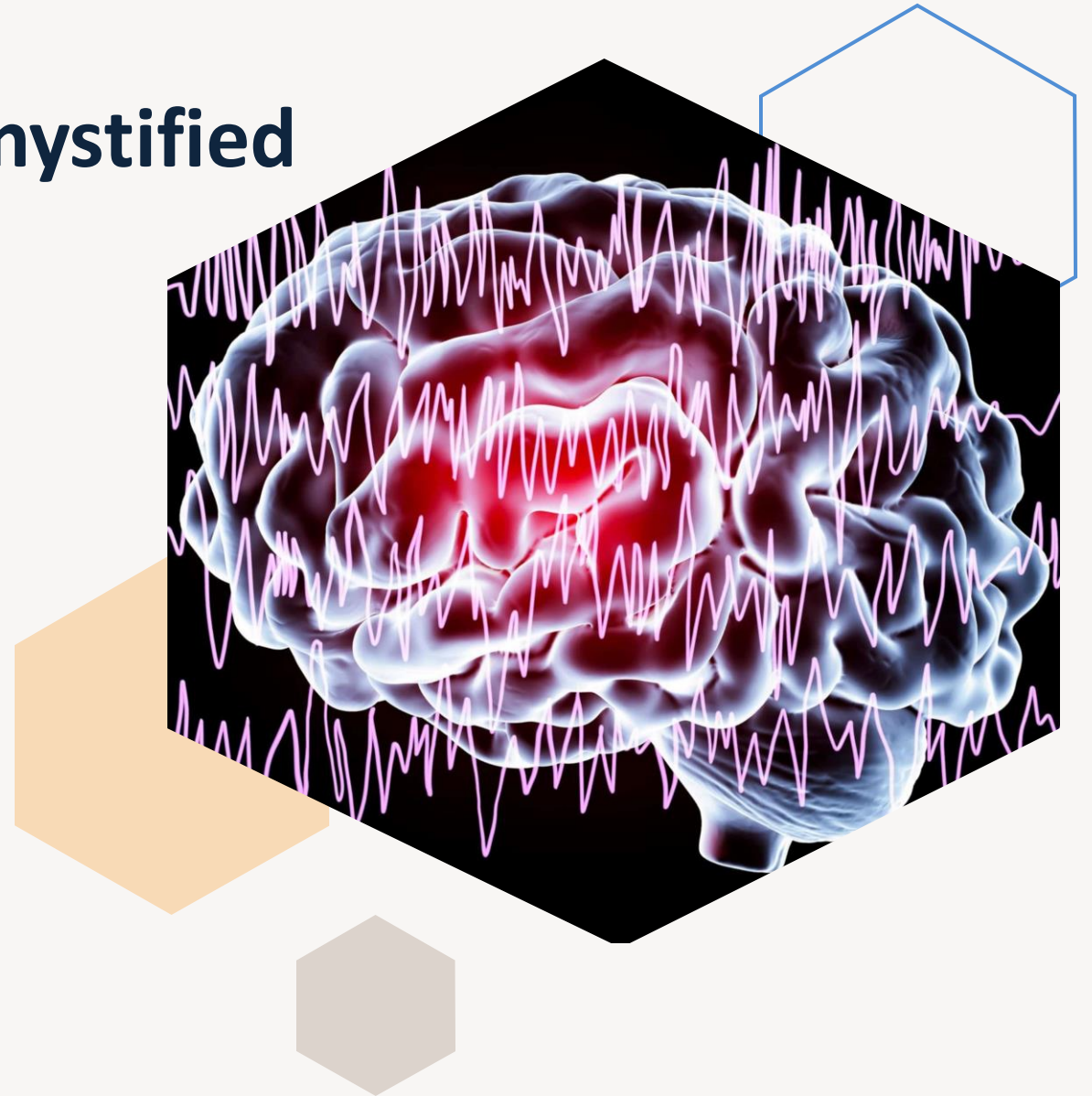


SEIZE CONTROL

Antiseizure Medications Demystified

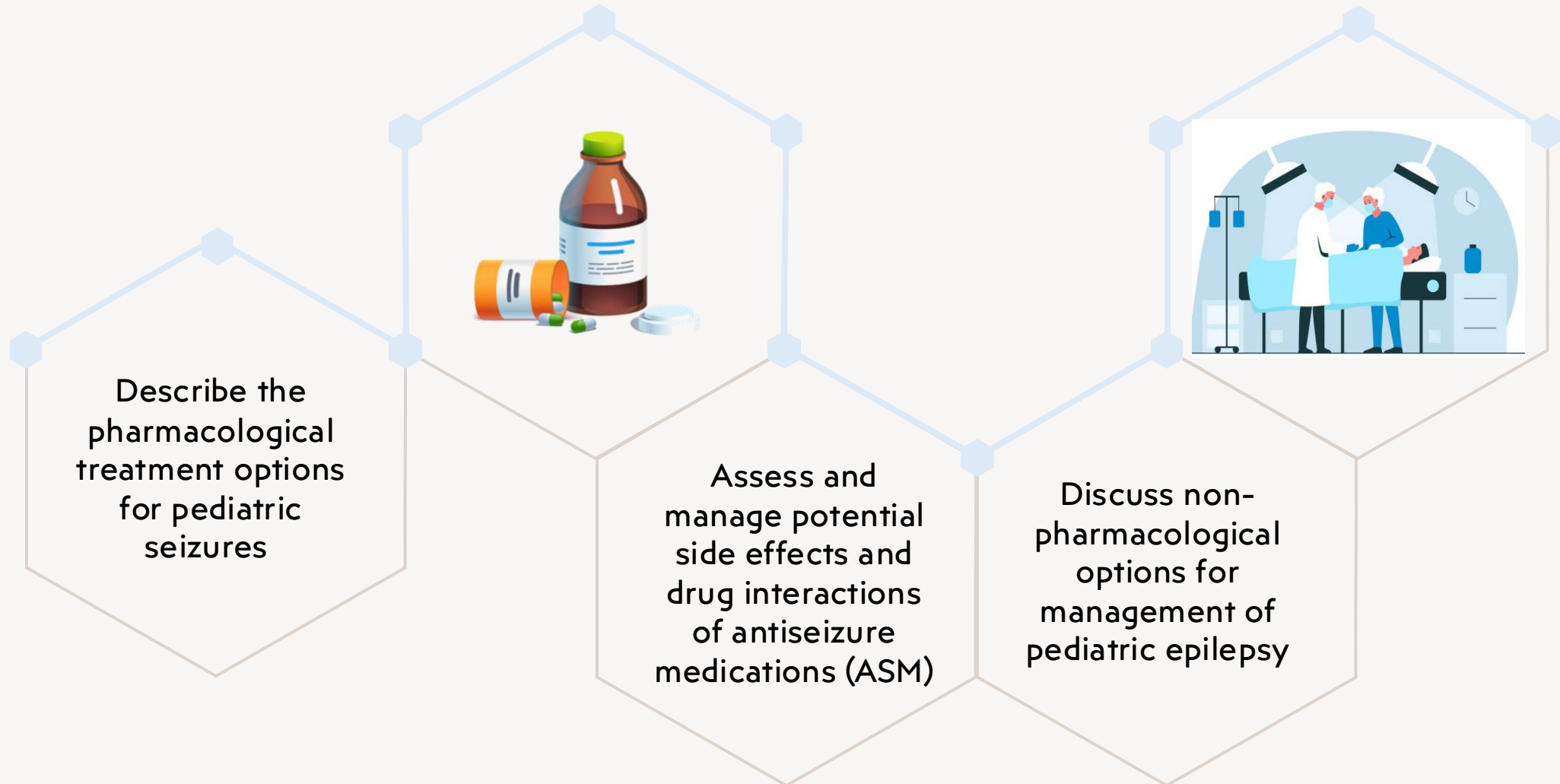
2025 Akron Children's APRN/PA
Pharmacology Conference
September 17, 2025

Francesca Shick, MSPAS, PA-C
Neurodevelopmental Science Center
Neurodevelopmental Science Center
Francesca Shick, MSPAS, PA-C



Akron Children's

Objectives





Definitions¹

Seizure

ILAE (International League Against Epilepsy)
definition:¹

“a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain”

Generalized Seizure

- Generalized Tonic Clonic (GTC)
- Myoclonic
- Tonic
- Atonic
- Absence
- Etc.

Focal Seizure

- Focal preserved consciousness seizure (FPC)
- Focal impaired consciousness seizure (FIC)
- Focal-to-bilateral tonic-clonic seizure (FBTC)

Unknown whether focal or generalized

Unclassified

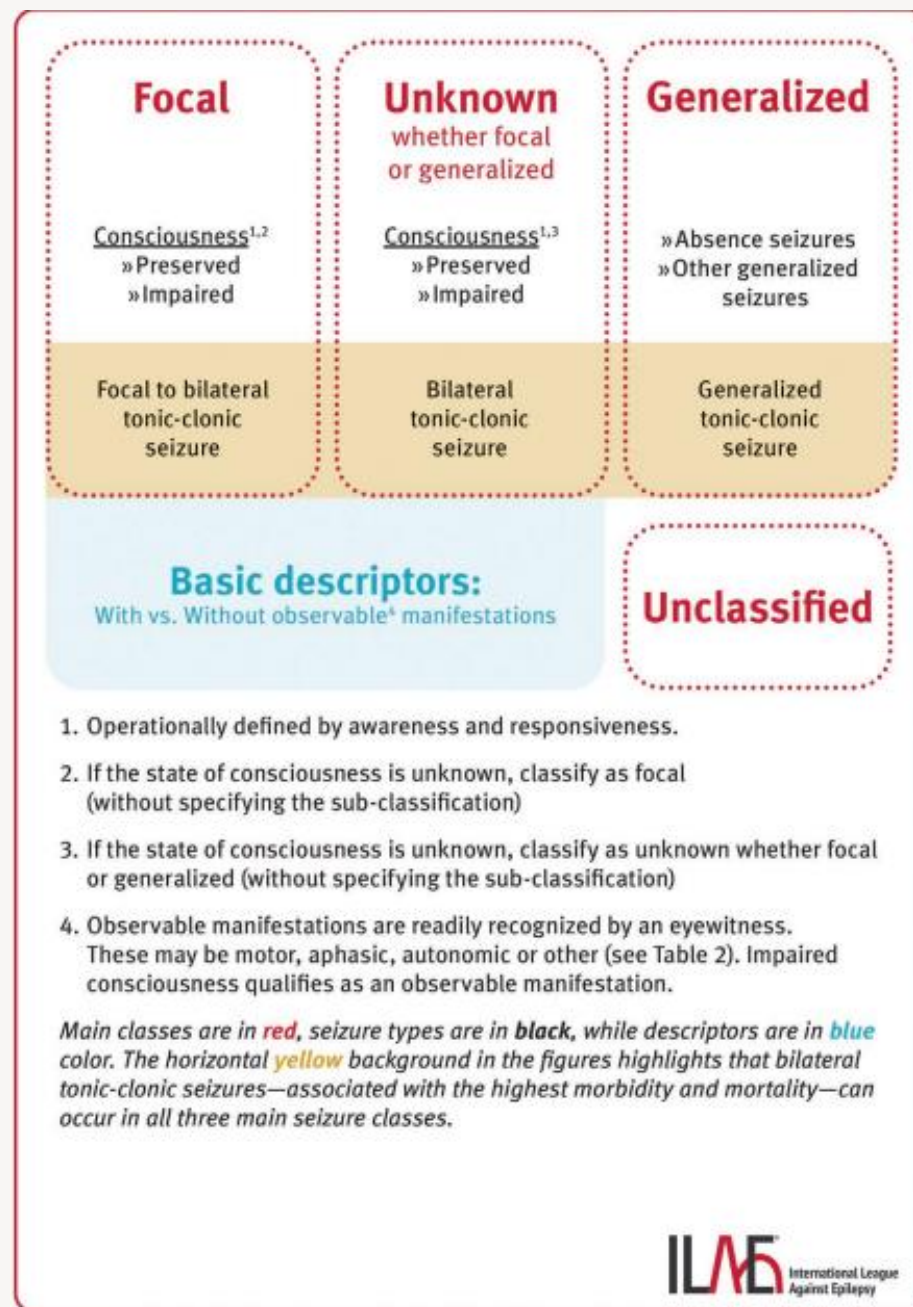
Epilepsy

ILAE definition:

“a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.”¹

Clinical definition:

(1) at least two unprovoked (or reflex) seizures occurring more than 24 hours apart
(2) 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, or
(3) diagnosis of an epilepsy syndrome



Who needs treatment?



Maintenance/Daily ASM

- Epilepsy Diagnosis
- Recurrent/prolonged febrile seizures
- Provoked seizures in acute setting
- Seizure "prophylaxis"

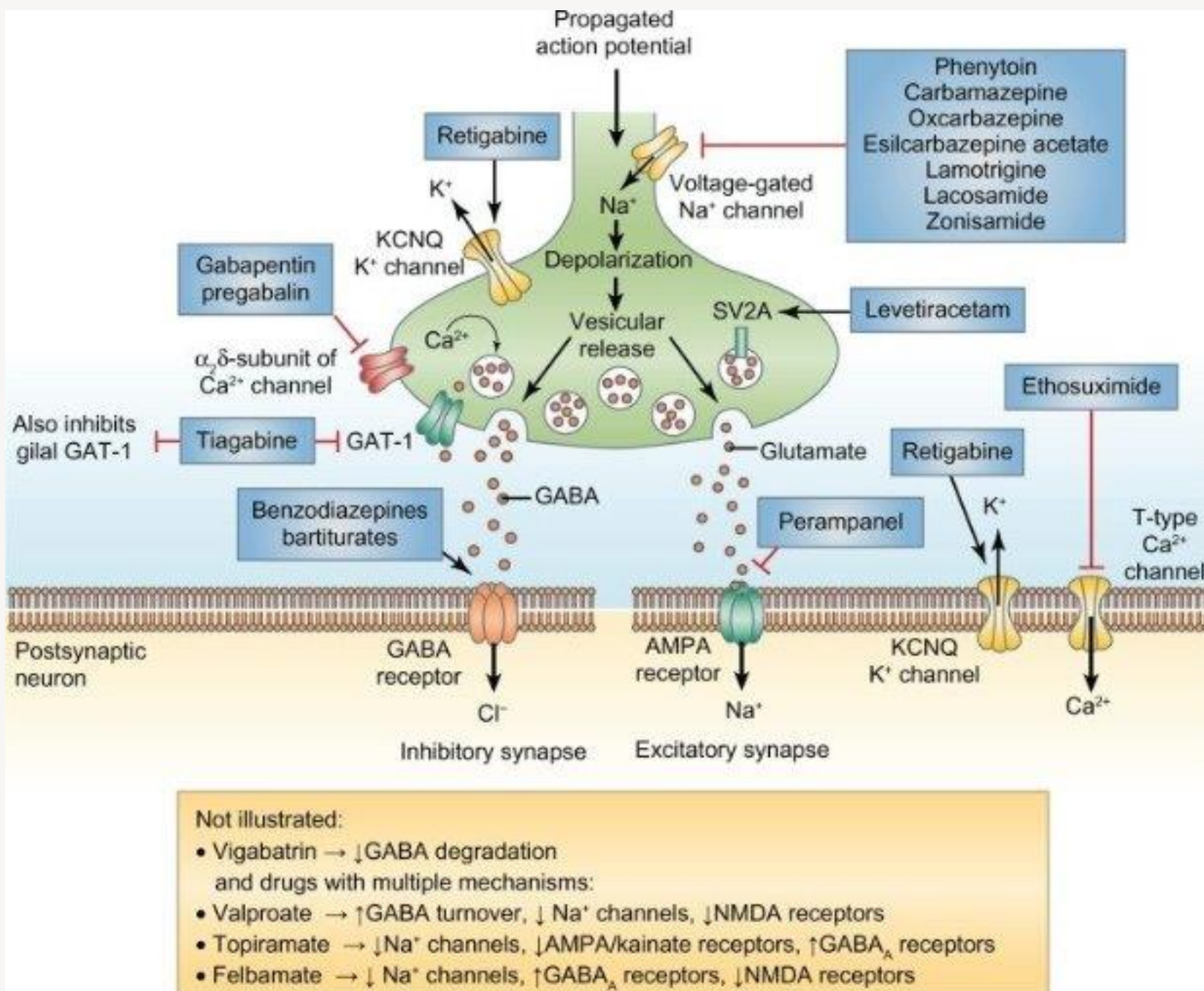


Seizure Rescue medications

- Home Rescue: Any child > 2 years of age that has had an event clinically concerning for a seizure
- Healthcare Setting: any patient having event clinically concerning for seizure last > 5 minutes OR recurrent seizures

Choosing Treatment²

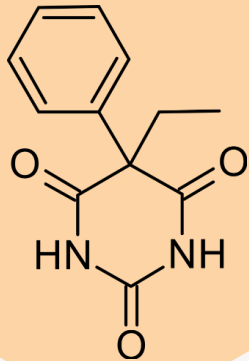
Epilepsy Characteristics	Patient Characteristics	ASM Characteristics	Side effects	Other
• Seizure type • Epilepsy syndrome • Seizure frequency	• Age • Sex/pregnancy • Comorbidities • Medications/Allergies • Ethnicity/genomics	• Indications • Efficacy • Forms – IV, tablet, liquid • Titration	• SE profile • Drug interactions • Half-life • Teratogenic risk	• \$\$\$/insurance • Availability • Personal choice



Generic	Brand	MOA
Brivaracetam	Briviact	Binds SV2A
Carbamazepine	Tegretol	Block Na channels
Cannabidiol	Epidiolex	Enhance GABA, modulate Ca
Cenobamate	Xcopri	Block Na channels
Clobazam	Onfi	Enhance GABA
Eslicarbazepine acetate	Aptiom	Block Na channels
Ethosuximide	Zarontin	Block t-type Ca channels
Felbamate	Felbatol	Various mechanisms
Fenfluramine	Fintepla	Enhance serotonin
Gabapentin	-----	Binds Ca channel subunit
Ganaxolone	Ztalmy	Enhance GABA
Lacosamide	Vimpat	Block Na channels
Lamotrigine	Lamictal	Block Na channels
Levetiracetam	Keppra	Binds SV2A

Generic	Brand	MOA
Oxcarbazepine	Trileptal	Block Na channels
Perampanel	Fycompa	AMPA antagonist
Phenobarbital	-----	Enhance GABA
Phenytoin	Dilantin	Block Na channels
Pregabalin	Lyrica	Binds Ca channel subunit
Primidone	-----	Enhance GABA
Rufinamide	Banzel	Block Na channels
Stiripentol	Diacomit	Enhance GABA
Tigabaine	Gabatril	Enhance GABA
Topiramate	Topamax	Block Na channel, APMA antagonism, enhance GABA
Valproate	Depakote	Block Na channel, enhance GABA, block t-type Ca channels
Vigabatrin	Sabril	Enhance GABA
Zonisamide	Zonegran	Block Na channel, block t-type Ca channels

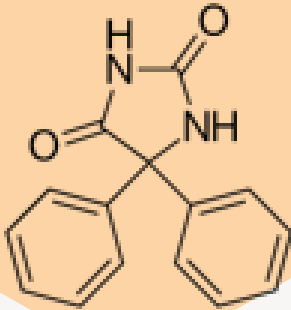
Phenobarbital



- **Indications**
 - All seizure types
 - Neonatal seizures
 - Status epilepticus
- **Mechanism of Action**
 - Binds GABA_A receptor → prolongs opening of chloride channel → enhances GABA inhibition
- **Metabolism/Interactions**
 - Liver metabolized
 - CYP450 enzyme inducer = MANY interactions
- **Dose**
 - Pediatric: 4 - 6 mg/kg/day (divided BID)
 - Adult: 1.5 – 4 mg/kg/day
- **Side Effects**
 - Sedation, hyperactivity (children), ataxia, dysarthria
 - Cognitive impairment
 - Decreased bone mineral density (BMD)
- **Monitoring**
 - Levels: 10-40 mg/L
 - Vitamin D, liver enzymes, other AED levels

Remember... IV, neonates, interactions, sedating

Phenytoin (Fosphenytoin) Dilantin

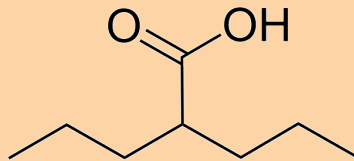


- **Indications**
 - Most seizure types (not absence or myoclonic)
 - Status epilepticus (IV)
- **MOA**
 - Binds to sodium channels → reduces high frequency firing
- **Metabolism/Interactions**
 - Potent enzyme inducer (CYP450) – many interactions
 - Non-linear pharmacokinetics
- **Dose**
 - Pediatric: 5 – 8 mg/kg/day (can go up to 10 mg/kg, use levels)
 - Status: IV loading dose of 20 mg/kg
 - Adult: 200 – 400 mg/day
- **Side Effects**
 - Ataxia, nystagmus, slurred speech, discoordination
 - Toxic hepatitis, gingival hyperplasia, decreased BMD
 - Rare/severe: SJS, hematologic (pancytopenia, aplastic anemia etc.)
- **Monitoring**
 - Levels (10-20 mg/L)
 - CMP, folate, vitamin D (q 6-12 months)

Remember... status epilepticus, levels, cerebellar SE

Valproate

Depakote*

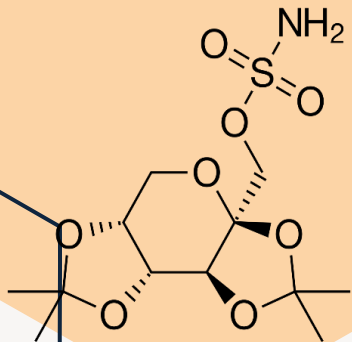


Remember... broad, no babies, limit females, labs

- **Indications**
 - Multiple seizure types including absence seizures
 - Status epilepticus
 - Other: bipolar disorder, migraine prophylaxis
- **MOA (variety)**
 - Increases GABA
 - Blocks voltage gated sodium channels
 - Activate Ca-dependent potassium conductance
- **Metabolism/Interactions**
 - MANY interactions – especially Lamictal
- **Dose**
 - Pediatric: 10 – 15 mg/kg/day → 20 – 40 mg/kg/day
 - Caps (BID), tabs (BID), sprinkles (BID), liquid (TID), IV (QID)
 - Adult: 500 – 2500 mg/day
- **Side Effects**
 - Tremor, drowsiness, dizziness
 - Weight gain, alopecia, hirsutism/PCOS
 - Teratogenic (neural tube defects)
 - GI upset, pancreatitis
 - Hepatotoxicity*, hyperammonemia, bone marrow suppression
 - Mood stabilization (beneficial “side effect”)
- **Monitoring**
 - CBC, LFTs – 1-2 months after initiation → q6 months
 - Vitamin D, ammonia (especially if AMS)
 - Levels (50 -100 mg/kg/day)

Topiramate

Topamax



- **Indications**

- ALL seizure types
- Other: migraine prophylaxis, PTSD, bipolar disorder, IIH, binge eating disorder, neuropathic pain etc.

- **MOA**

- Enhances GABA
- Inhibits voltage-dependent sodium channels
- Decrease glutamate excitation (AMPA antagonism)
- Carbonic anhydrase inhibition

- **Metabolism/Interactions**

- May interact with AEDs, cardiac meds, amitriptyline, sumatriptan etc.
- Do not use in conjunction with other carbonic anhydrase inhibitors
- OCPs

- **Dose**

- Pediatric: 1 mg/kg/day → 3-8 mg/kg/day
- Adult: 100 – 600 mg/day

- **Side Effects**

- Cognitive slowing, anorexia/weight loss, sedation, blurry vision, impaired memory, paresthesia
- Oligohydrosis, metabolic acidosis, nephrolithiasis

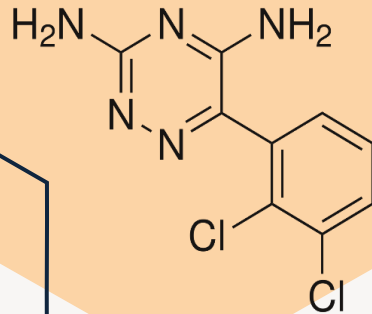
- **Monitoring**

- Periodic BMP – sodium bicarb levels
- Levels: 5 – 20 mg/L

Remember... broad spectrum, cognition, hydration

Lamotrigine

Lamictal

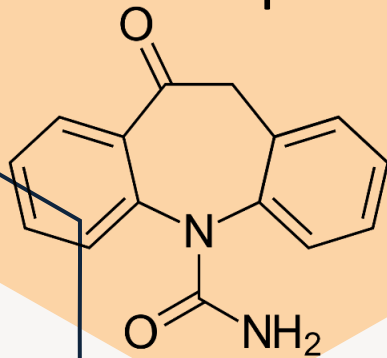


- **Indications**
 - Most seizure types
 - *May* worsen myoclonic seizures
 - Other: Bipolar disorder, migraine, neuropathy, cluster headaches etc
- **MOA**
 - Modulates sodium channels
 - Inhibits glutamine release
- **Metabolism/Interactions**
 - Various AEDs (especially valproate)
 - OCPs
 - Lamotrigine + Topiramate and Lamotrigine + vigabatrin may be synergistic
- **Dose**
 - Goal pediatric dose = 2-8 mg/kg/day
 - SLOW titration – 0.4 mg/kg x 2 weeks → 0.8 mg/kg x 2 weeks → increase by 0.8 mg/kg q 2 weeks
 - Goal adult dose: 100 – 200 mg/day (500 mg/day max)
- **Side Effects**
 - Rash – drug eruption versus SJS
 - Dizziness, headache, GI upset, tremor
 - Mood stabilization (benefit)
- **Monitoring**
 - Yearly liver function and CBC
 - Levels: 3-15 mg/L

Remember... mood stabilizer, SJS, slow titration

Oxcarbazepine

Trileptal

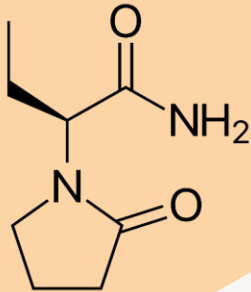


- **Indications**
 - Focal seizures ONLY
 - Other: bipolar disorder, trigeminal neuralgia
- **MOA**
 - Blocks sodium channels
- **Metabolism/Interactions**
 - Carbamazepine, lacosamide, perampanel, phenobarbital, phenytoin
 - OCPs
- **Dose**
 - Pediatric: 10 mg/kg/day → 20 – 40 mg/kg/day (max 1800 mg/day)
 - Adult: 600 – 2400 mg/day
- **Side Effects**
 - Fatigue, dizziness, headache, vertigo
 - Nausea, vomiting
 - Rash – eruption versus SJS
 - Hyponatremia
 - Rare hematologic dyscrasias
- **Monitoring**
 - CBC and BMP before and after starting then ~ q12 months
 - Vitamin D
 - Levels: 3-35 mg/L

Remember... focal seizures, hyponatremia, rash

Levetiracetam

Keppra

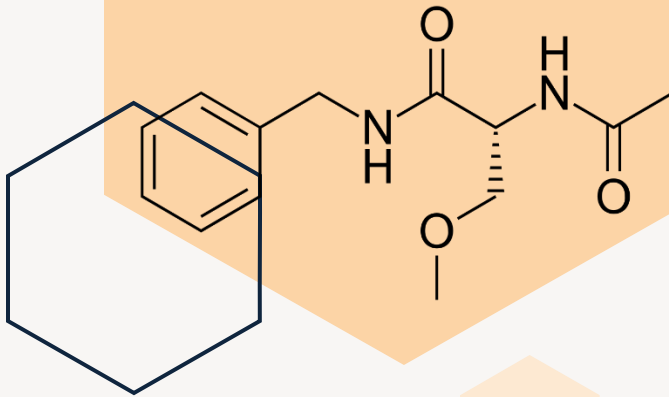


- **Indications**
 - ALL seizures types
 - ALL forms
 - Status epilepticus
- **MOA**
 - SV2A binding → disrupts synaptic vesicle exocytosis
- **Metabolism/Interactions**
 - Minimal interactions
 - Renal excretion – may need to renally dose if renal impairment
- **Dose**
 - Pediatric: 10 – 20 mg/kg/day → 60 – 80 mg/kg/day
 - Adult: 1000 – 3000 mg/day (up to 4,000)
- **Side Effects**
 - Fatigue and behavioral changes
- **Monitoring**
 - None 😊

Remember... when in doubt start with Keppra, behavior

Lacosamide

Vimpat

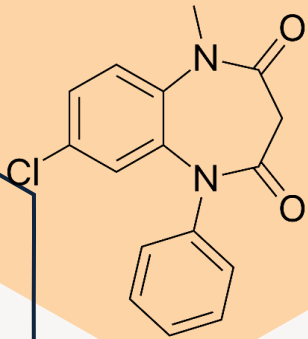


Remember... focal, IV, EKG first

- **Indications**
 - Focal seizures
 - Status epilepticus (IV)
- **MOA**
 - Enhances inactivation of sodium channels → stabilizes neuronal membranes
- **Metabolism/Interactions**
 - Avoid co-medicating with other similar sodium channel medications
- **Dose**
 - Pediatric: 4 mg/kg/day → 6-8 mg/kg/day (max 12)
 - Adult: 200 – 400 mg/day
- **Side Effects**
 - Dizziness, blurred vision, coordination issues, tremor
 - GI upset
 - PR prolongation
- **Monitoring**
 - EKG BEFORE starting due to risk of PR prolongation
 - Levels: 10-20 mg/L
 - CMP q 12 months

Clobazam

Onfi

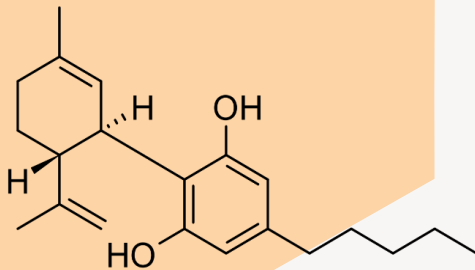


Remember... sedation, 2nd/3rd line

- **Indications**
 - Adjunctive treatment for focal and generalized seizures
 - Catamenial epilepsy and Lennox-Gastaut syndrome
- **MOA**
 - Enhances GABA
 - Benzodiazepine
- **Metabolism/Interactions**
 - Longer half life (36-46 hours in kids)
 - Can potentiate effects of other CNS depressants
 - Phenytoin, primidone, stiripentol, cannabidiol, valproate* etc.
- **Dose**
 - Pediatric: 0.25 mg/kg/day → 1-2 mg/kg/day
 - Adult: 20 – 40 mg/day
- **Side Effects**
 - Sedation/drowsiness, dizziness, rash, increase in secretions
 - Mood changes – hyperactivity, insomnia, depression
 - Respiratory depression and tolerance at higher doses
- **Monitoring**
 - Levels: 30-300 (ng/mL)
 - CMP intermittently

Cannabidiol

Epidiolex

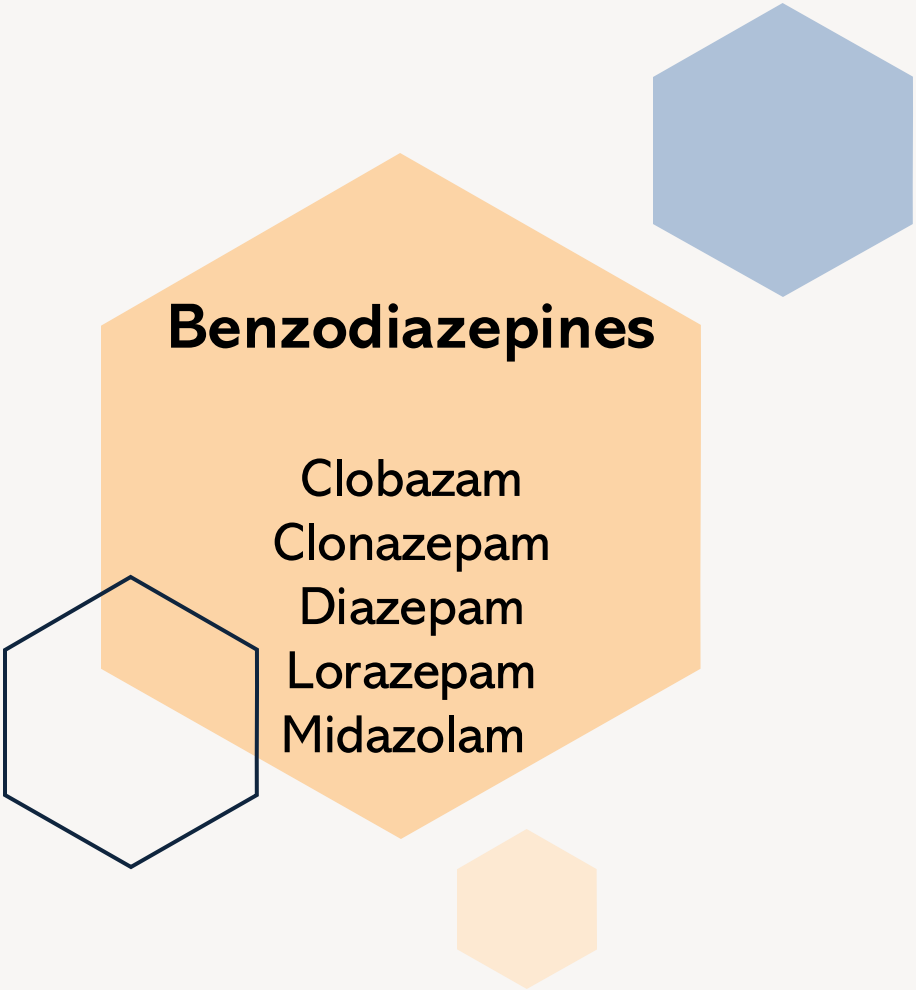


- **Indications**
 - Lennox-Gastaut Syndrome
 - Dravet Syndrome
 - Tuberous Sclerosis
- **MOA***
 - Enhance GABA
 - Modulate intracellular calcium
- **Metabolism/Interactions**
 - Reduces clearance (increases levels) of Onfi
- **Dose**
 - Pediatric: 5 mg/kg/day → 20 mg/kg/day
 - Adult: 3 – 10 mg/kg/day
- **Side Effects**
 - GI upset, sedation
 - Elevated liver enzymes
- **Monitoring**
 - Liver enzymes
 - Other AED levels

Remember... Refractory epilepsy, interactions, liver

Status Epilepticus⁵

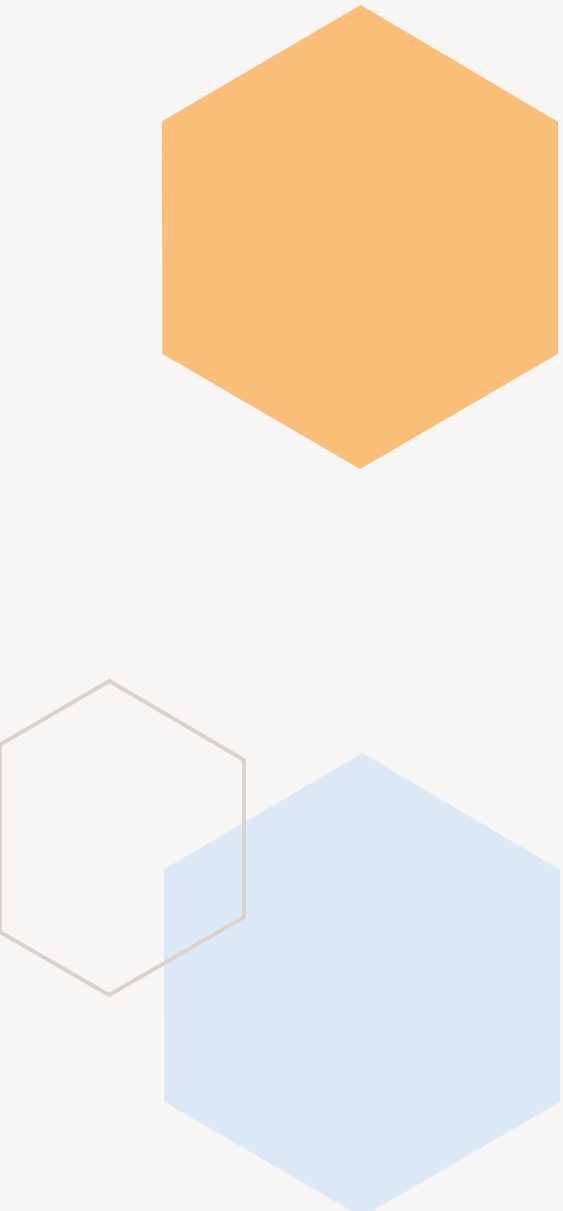
- ILAE defines status epilepticus (SE) as “a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms which lead to abnormally prolonged seizures (after time point t1). It is a condition that can have long-term consequences (after time point t2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.”
- Initiate treatment at t1 (5 minutes)
- Concern for brain damage begins at t2 (30 minutes)



Benzodiazepines

Clobazam
Clonazepam
Diazepam
Lorazepam
Midazolam

- **Indications**
 - Status epilepticus
 - MANY MORE
- **MOA**
 - Binds GABA_A receptor -> enhance inhibitory action of GABA
- **Metabolism/Interactions**
 - Depressive effects worsened when taken with other CNS depression
- **Dose** varies between drugs and formulation
- **Side Effects**
 - Sedation, lethargy, ataxia
 - Respiratory depression
 - Tolerance and withdrawal



Inpatient Benzodiazepines⁶

Lorazepam (Ativan)

- IM, IV, PO
- 0.1 mg/kg (max 2-4 mg)
- Can repeat dose once after 5-10 minutes

Midazolam (Versed)

- IM, IV, PO, Intranasal
- Continuous infusion
- IN/IV = 0.2 mg/kg (max 10 mg)
- Gtts = bolus above dose -> start infusion at 0.1 mg/kg/hr -> escalate with 0.2 bolus and increase by 0.1 (max 2 mg/kg/hr)

Management of Status Epilepticus^{6,7}

KIDSNET "Convulsive Status Epilepticus Algorithm"



Akron Children's Hospital

Convulsive Status Epilepticus Algorithm- March 2021

To be used in patients > 30 days old in the ED, in-patient setting, or prehospital setting with the critical care transport team.

IF A PATIENT HAS A PERSONALIZED STATUS EPILEPTICUS TREATMENT PATHWAY, PLEASE FOLLOW THAT PATHWAY INSTEAD

Page 1

0-5 Minutes: STABILIZATION PHASE

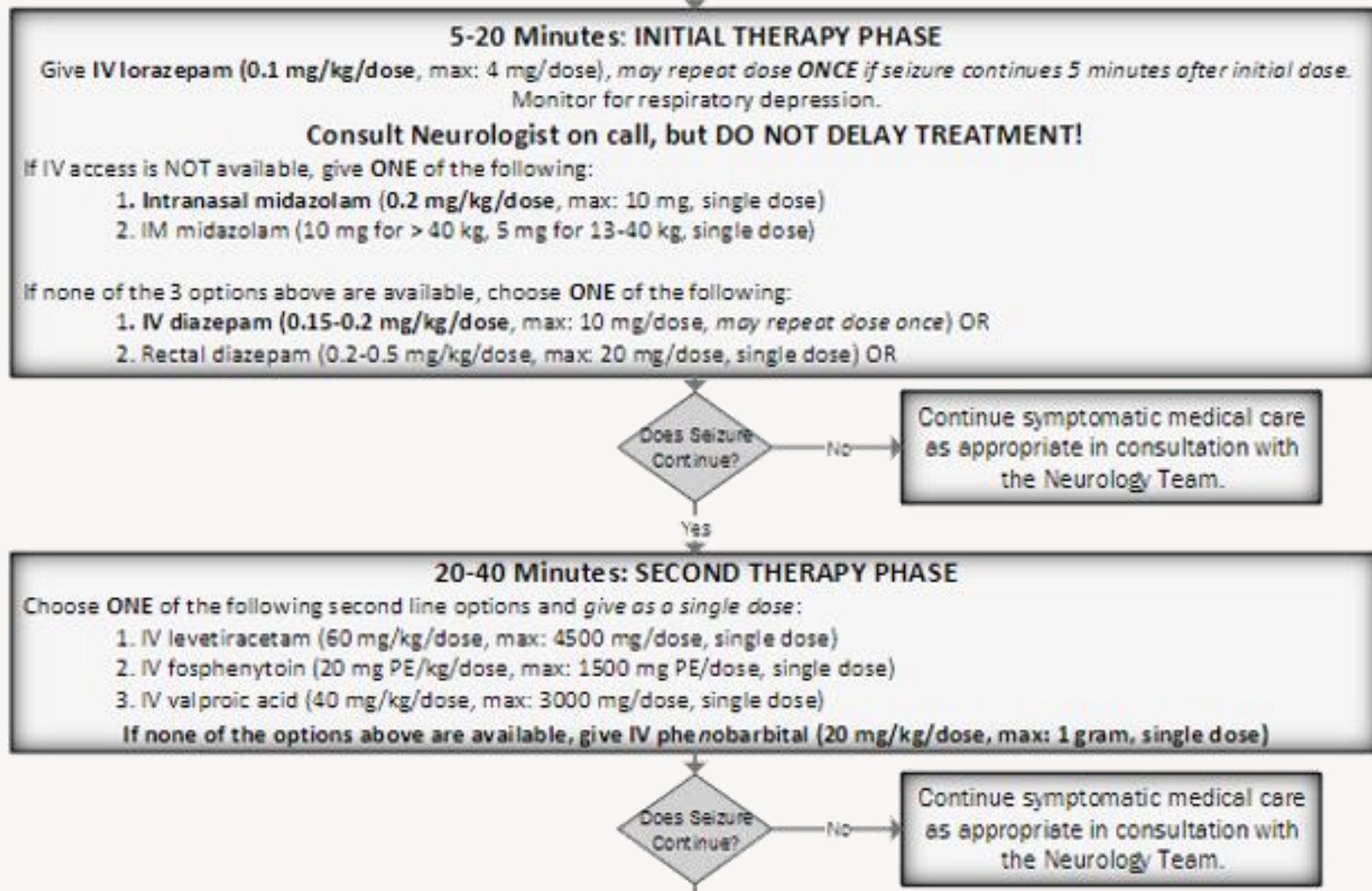
1. Stabilize patient (airway, breathing, circulation, neurologic exam)
2. Time seizure from its onset, monitor vital signs
3. Assess oxygenation, give oxygen via NC/mask, consider intubation if needed
4. Place on CR monitor
5. Check finger stick blood glucose. If glucose < 60 mg/dl then treat:
(children $\geq$ 2 years: 2 mL/kg D25W IV, children < 2 years: 4 mL/kg D12.5W IV)
6. Attempt IV access and send CMP, Mg, Phos, CBC, tox screen (if appropriate), send AED levels if on meds

Does Seizure
Continue?

No

Continue symptomatic medical care
as appropriate in consultation with
the Neurology Team.

Yes



40-60 Minutes: THIRD THERAPY PHASE

If Status Epilepticus (SE) persists, recommend transfer to the PICU. Consider endotracheal intubation. Give an additional **SECOND THERAPY** medication and at the same time order a midazolam infusion.

If the midazolam infusion is available first, OK to skip repeat dose of second line therapy.

Give midazolam bolus (0.2 mg/kg/dose, max: 10 mg/dose) and start infusion at 0.1 mg/kg/hr (max: none). If SE persists after 15 mins, repeat bolus (0.2 mg/kg/dose, max: 10 mg/dose) and increase infusion by 0.1 mg/kg/hr. Repeat bolus and escalation of drip to a max of 2 mg/kg/hr every 15 min if SE persists.

ADDITIONAL WORK-UP

- Suggest low threshold to obtain head CT especially in focal SE, with any focal deficit, with known bleeding disorder, or when concerned about trauma/NAT.
- Consider sending urine drug screen and/or coma panel.
- If there is concern for bacterial or viral infection, perform lumbar puncture once the patient is stable. Do NOT delay antibiotic or antiviral treatment.
- Determine if additional testing is indicated with neurology team.

WHEN TO WEAN

The goal is 24 hours without seizure activity. Once this is achieved, discuss with the neurology and epilepsy teams to determine weaning strategy.

Home Benzodiazepines

Diastat® (Rectal Diazepam)



DIASTAT® AcuDial™ (diazepam rectal gel) Dosing Recommendations (by age and weight)					
2 to 5 years 0.5 mg/kg		6 to 11 years 0.3 mg/kg		12+ years 0.2 mg/kg	
Weight (kg)	Dose (mg)	Weight (kg)	Dose (mg)	Weight (kg)	Dose (mg)
6 to 10	5	10 to 16	5	14 to 25	5
11 to 15	7.5	17 to 25	7.5	26 to 37	7.5
16 to 20	10	26 to 33	10	38 to 50	10
21 to 25	12.5	34 to 41	12.5	51 to 62	12.5
26 to 30	15	42 to 50	15	63 to 75	15
31 to 35	17.5	51 to 58	17.5	76 to 87	17.5
36 to 44	20	59 to 74	20	88 to 111	20

Home Benzodiazepines

Valtoco® (Diazepam nasal spray)



	5 mg	10 mg	15 mg	20 mg
2-5 years (0.5 mg/kg)	6-11 kg (13-24 lb)	12-22 kg (25-49 lb)	23-33 kg (50-73 lb)	
6-11 years (0.3 mg/kg)	10-18 kg (22-40 lb)	19-37 kg (41-81 lb)	38-55 kg (82-121 lb)	56-74 kg (122-163 lb)



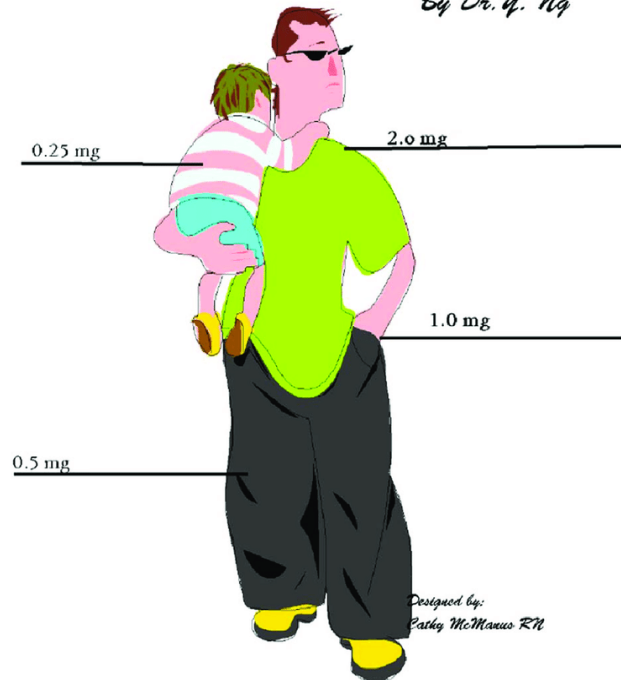
	5 mg	10 mg	15 mg	20 mg
12+ years (0.2 mg/kg)	14-27 kg (30-60 lb)	28-50 kg (61-111 lb)	51-75 kg (112-166 lb)	76 kg and up (167 lb and up)
Majority of adult doses are 15 mg and 20 mg				

Home Benzodiazepines

Klonopin (Clonazepam ODT)

"The Height of Man Rule"
For Klonopin Wafer

By Dr. Y. Ng



Nayzilam® (Midazolam nasal spray)

- One dose = 5 mg
- Can repeat 5 mg dose after 5 minutes



Non-Pharmacologic Treatments for Epilepsy⁸



Metabolic

Ketogenic Diet



Neuromodulation

Vagal Nerve
Stimulator (VNS)

Responsive
Neurostimulation
(RNS)



Surgical Options

Resective
Disconnective

Ketogenic Diet⁹

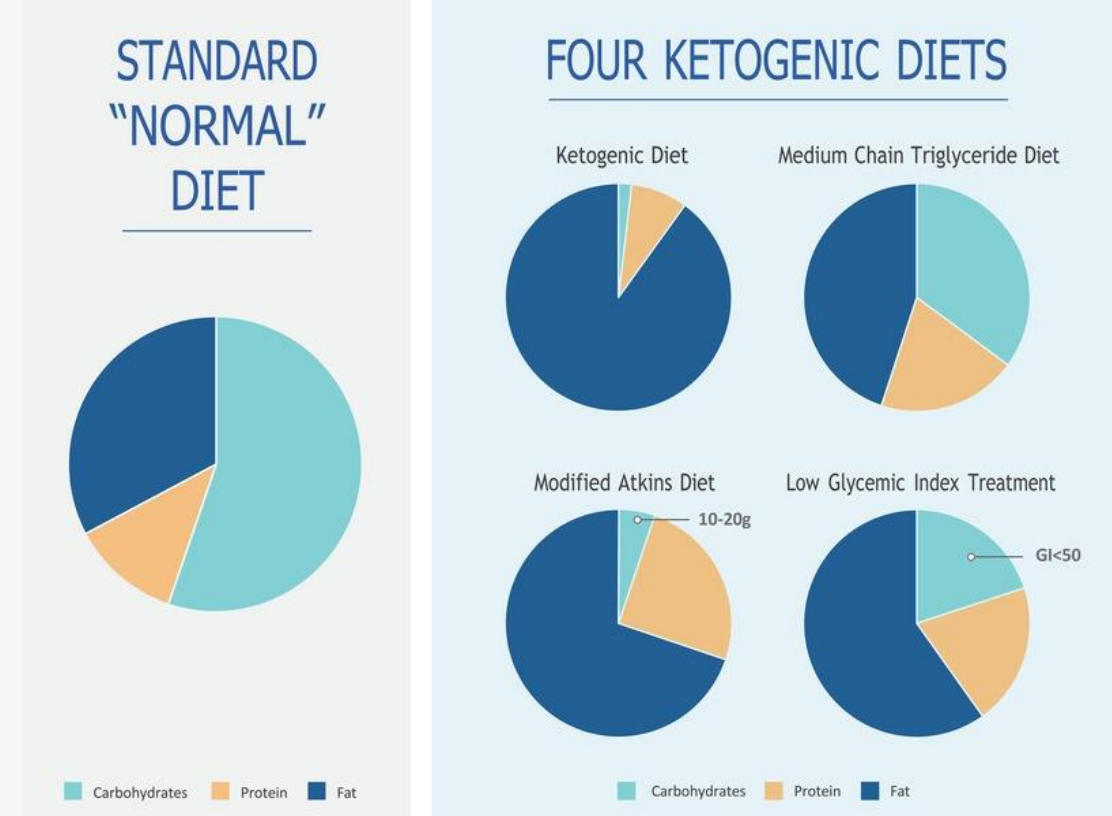
- Indications
 - Specific metabolic diseases - Glucose Transporter Protein 1 (GLUT-1) deficiency syndrome and Pyruvate Dehydrogenase Deficiency
 - Refractory/Intractable epilepsy
 - Dravet syndrome, Doose syndrome, FIRES, TSC
 - *Formula/GT patients

⑩ **High fat**, low protein, very low carb

⑩ Proposed MOA – Mimic fasting state, fats used as primary fuel source creating ketone bodies which have an anticonvulsant effect*

⑩ Side effects: dehydration, hypoglycemia, lethargy, metabolic acidosis, and gastrointestinal symptoms (constipation)

⑩ Requires very close monitoring - blood monitoring before and during treatment, adequate nutritional intake etc.



Epilepsy Surgery⁸

- Overall Goals
 - Seizure reduction
 - Seizure freedom
 - Improve QOL and development
 - Palliation
- Patient Selection
 - Refractory epilepsy
 - Lesional epilepsy – focus clearly identified
 - No other CI
- Significant multidisciplinary discussion and testing process
 - Epilepsy
 - Neurosurgery
 - Neuropsychology
 - Social work

Table 5: Selection criteria for childhood epilepsy surgery

Resective surgery

Seizures arise from a distinct area of the brain

The epileptogenic area is functionally silent

Drug-resistant epilepsy

Hemispherotomy

One-hemispherical structural abnormality

Seizures lateralized to the abnormal hemisphere

Pre-existing neurological deficit due to the underlying cause

Drug-resistant epilepsy

Hypothalamic hamartoma

Children with drug-resistant epilepsy

Progressive cognitive, developmental decline

Corpus callosotomy

Children with disabling drop attacks

Drug-resistant epilepsy

Severe mental retardation

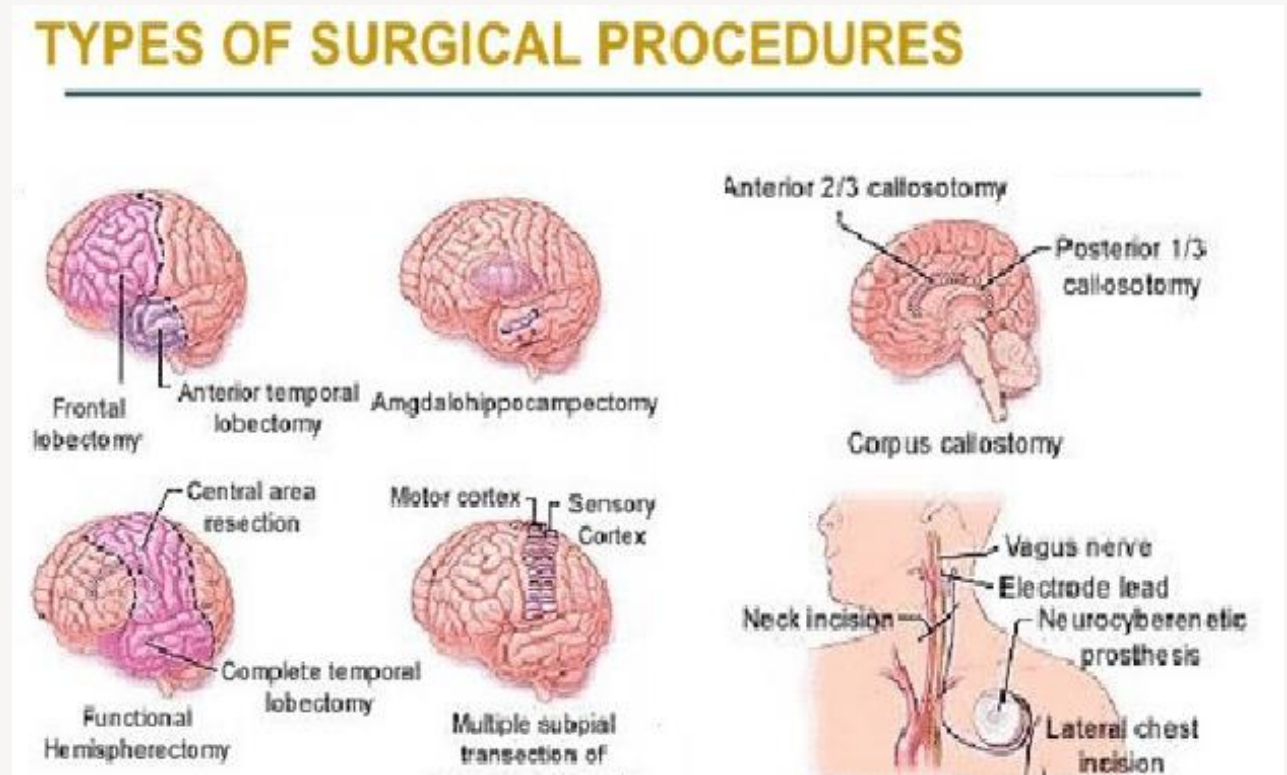
Vagal nerve stimulation

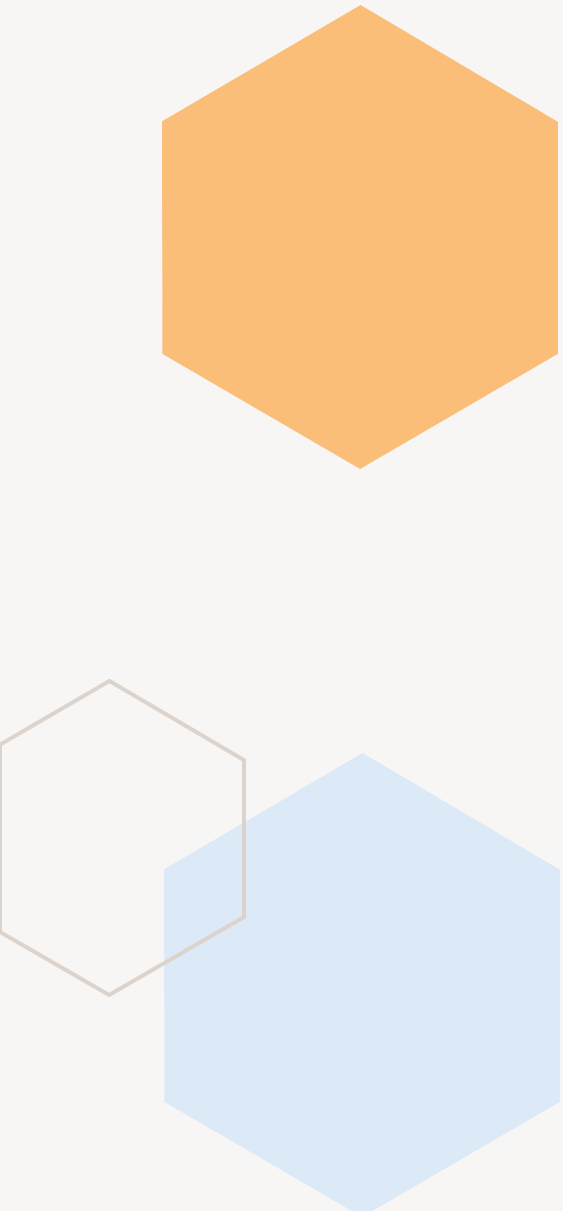
Children with drug-resistant epilepsy who are not candidates for resective epilepsy surgery

Image: Jayalakshmi S, Panigrahi M, Nanda SK, Vadapalli R. Surgery for childhood epilepsy. *Ann Indian Acad Neurol.* 2014;17(Suppl 1):S69-S79. doi:10.4103/0972-2327.128665

Surgical Techniques^{8,10}

- Resection of epileptogenic region/foci
 - Anterior temporal lobectomy
 - Lesionectomy – dysplasia, tumor, gliosis etc.
 - Hemispherectomy
- Interruption of pathways (Disconnective)
 - Corpus Callosotomy
 - Stereotactic ablation
- Decrease brain excitability by stimulating inhibition (neuromodulation)
- Prevent neuronal synchronization – multiple subpial transection





Neuromodulation^{8,11}

Vagal Nerve Stimulator (VNS)

Indications - adjunctive therapy in medically refractory/intractable epilepsy

Surgically implanted neuromodulation device that is used to stimulate the vagus nerve to help stop seizures.

FDA approval: 4 and up

Responsive Neurostimulation (RNS)

Indications – treatment of focal epilepsy (1-2 foci) who have failed 2 or more medical treatments

Closed loop Neuromodulation with device seated in the skull with wires placed directly in the brain to target specific areas

FDA approval: 18 and up

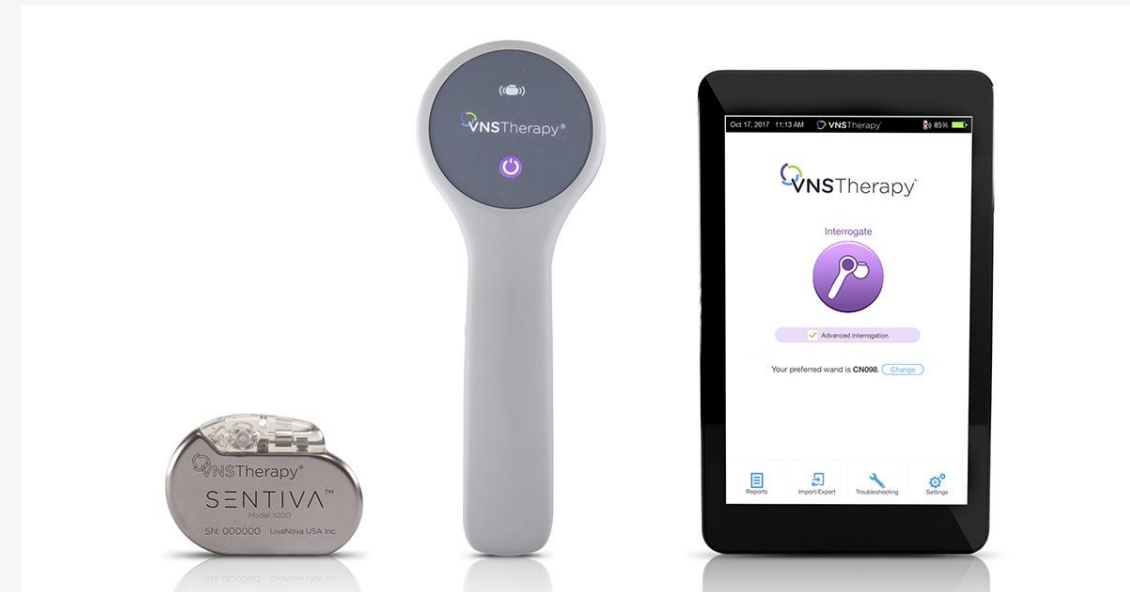
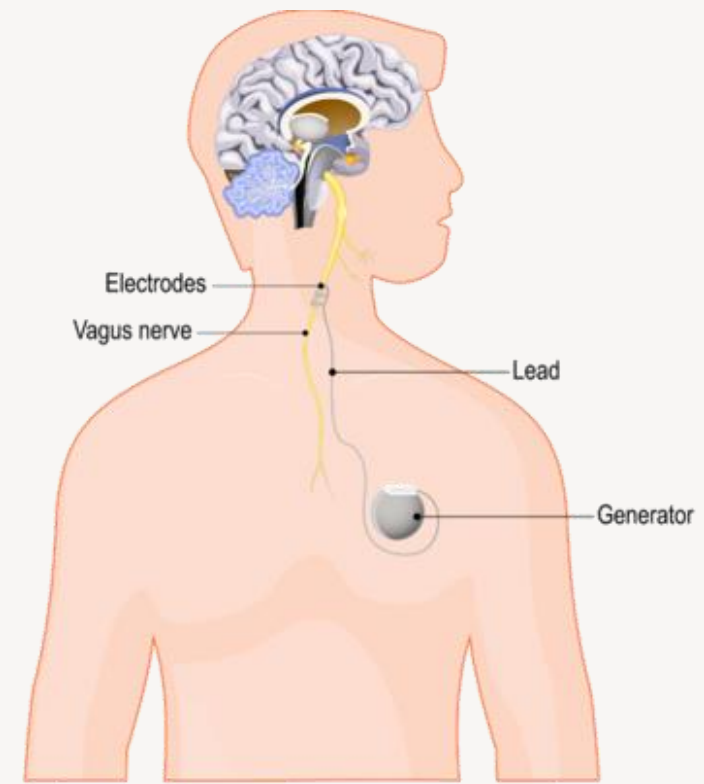
Vagal Nerve Stimulator^{8,11}

Mechanisms

- Inhibits the development of seizure kindling associated with noradrenaline
- Increase cerebral blood flow to certain areas of the brain
- Increases level of GABA
- Immediate and long-term changes

Device

- Implanted electrode coiled around left vagus nerve
- Implanted pulse generator placed left chest wall
- Lead connecting the two
- Magnet – home stimulation
- Tablet/wand – provider use



Responsive Neurostimulation^{11,12}

Mechanisms

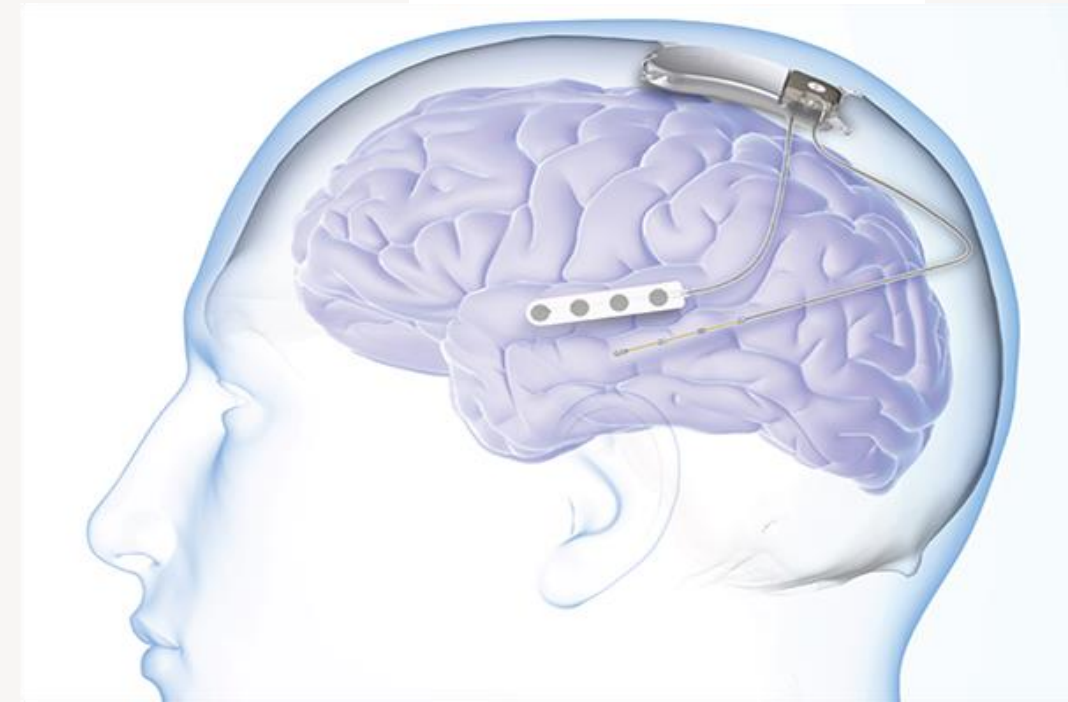
- Continuously monitors brain waves
- Detects pattern of abnormal electrical activity at the source
- Responds – desynchronization with goal of preventing propagation of ictal activity
- Records data over months/years to identify patterns etc

Data

- 75% median seizure reduction at 9 years
- 21% seizure free at end of trial

Device

- Neurostimulator
- Cortical strip lead
- Depth lead
- Remote monitor tablet
- Wand – to place over RNS
- Magnet – home use



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Thank you!

Questions?

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