Antiepileptics

Management of pediatric seizure patients

2022 Akron Children's Hospital

APRN/PA Pediatric Pharmacology & Law Conference

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Objectives

- Evaluation of pediatric patient presenting with spells/abnormal movements/behavior
- Identification of pediatric seizure types and diagnosis of epilepsy
- Discuss the pharmacologic and non-pharmacologic treatment for pediatric epilepsy patients

Disclosures: None

What is a seizure?

ILAE (International League Against Epilepsy) defines a seizure as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain"[1,2]

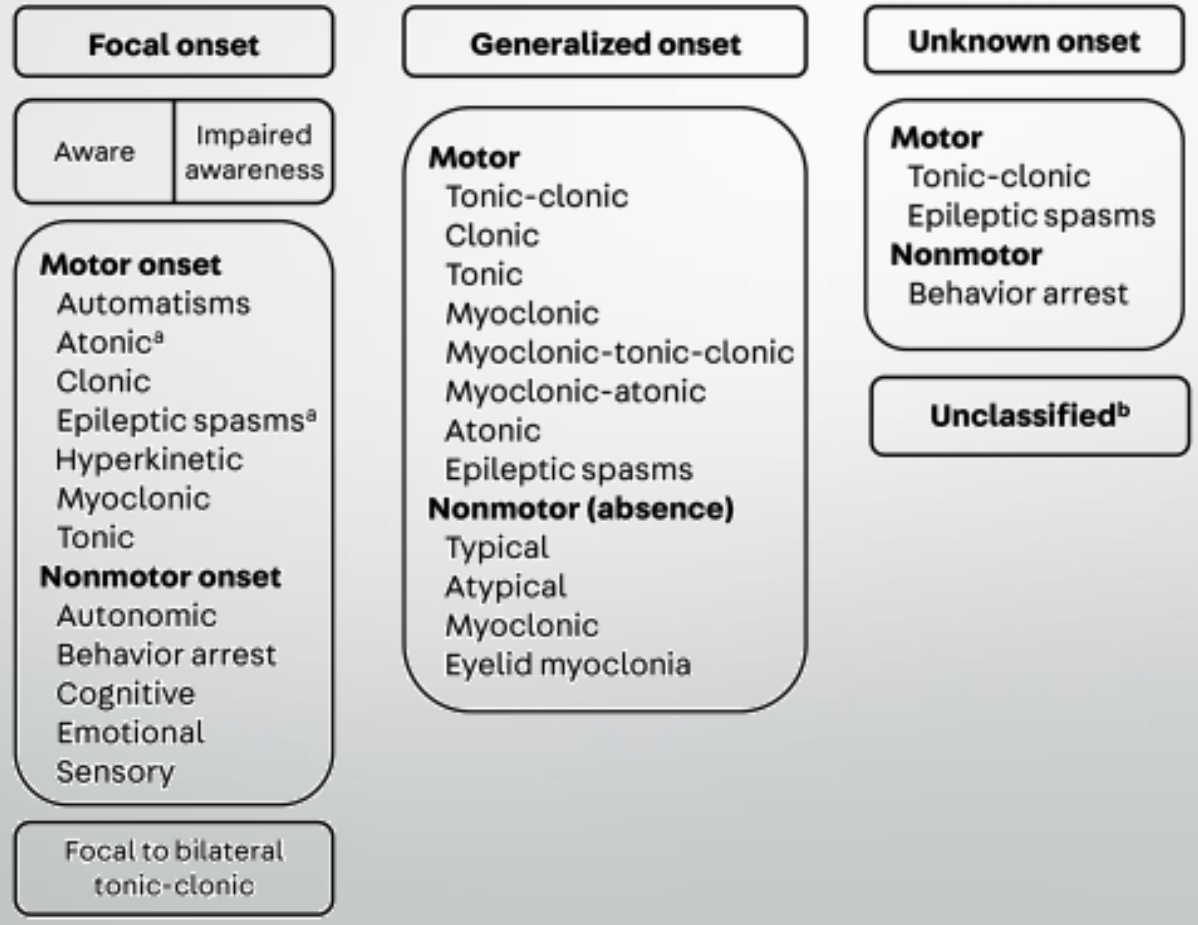


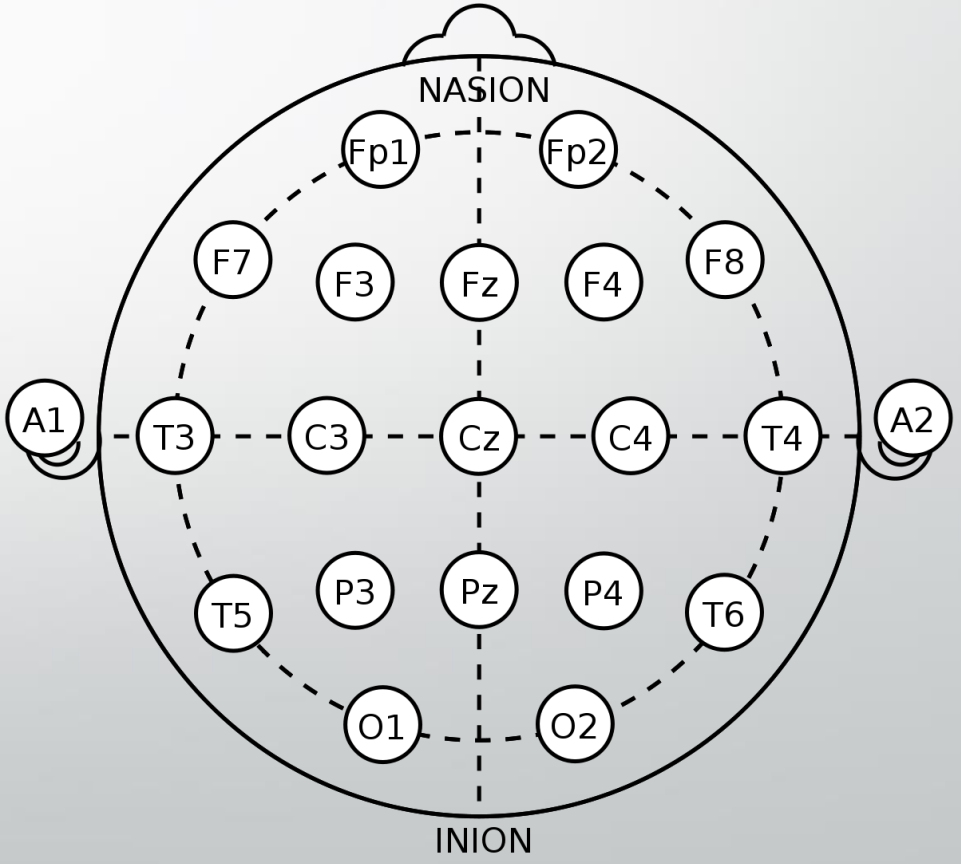
Image: Wirrell E. Evaluation of First Seizure and Newly Diagnosed Epilepsy. *Continuum (Minneap Minn)*. 2022;28(2):230-260. doi:10.1212/CON.0000000000001074

What else can look like a seizure?[2]

- Benign sleep myoclonus
- Jitteriness
- Shuddering attacks
- Benign infantile myoclonus
- Breath holding spells
- Sandifer's Syndrome/GERD
- Stereotypies
- Cardiac event
- Benign paroxysmal vertigo
- Tics
- Psychogenic non-epileptic events (PNEE)*
- Syncope
- Migraine
- Parasomnias
- ADHD (staring spells)

How do we evaluate these children?[2]

- HISTORY, HISTORY, HISTORY
  - Description of event – before, during and after
  - Triggers? Temporal pattern? Duration?
  - PMH – what other conditions does this child have? Any epilepsy risk factors?
- Electroencephalogram (EEG)



What is epilepsy?

- ILAE defines epilepsy as "*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]:
  - (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?[3]

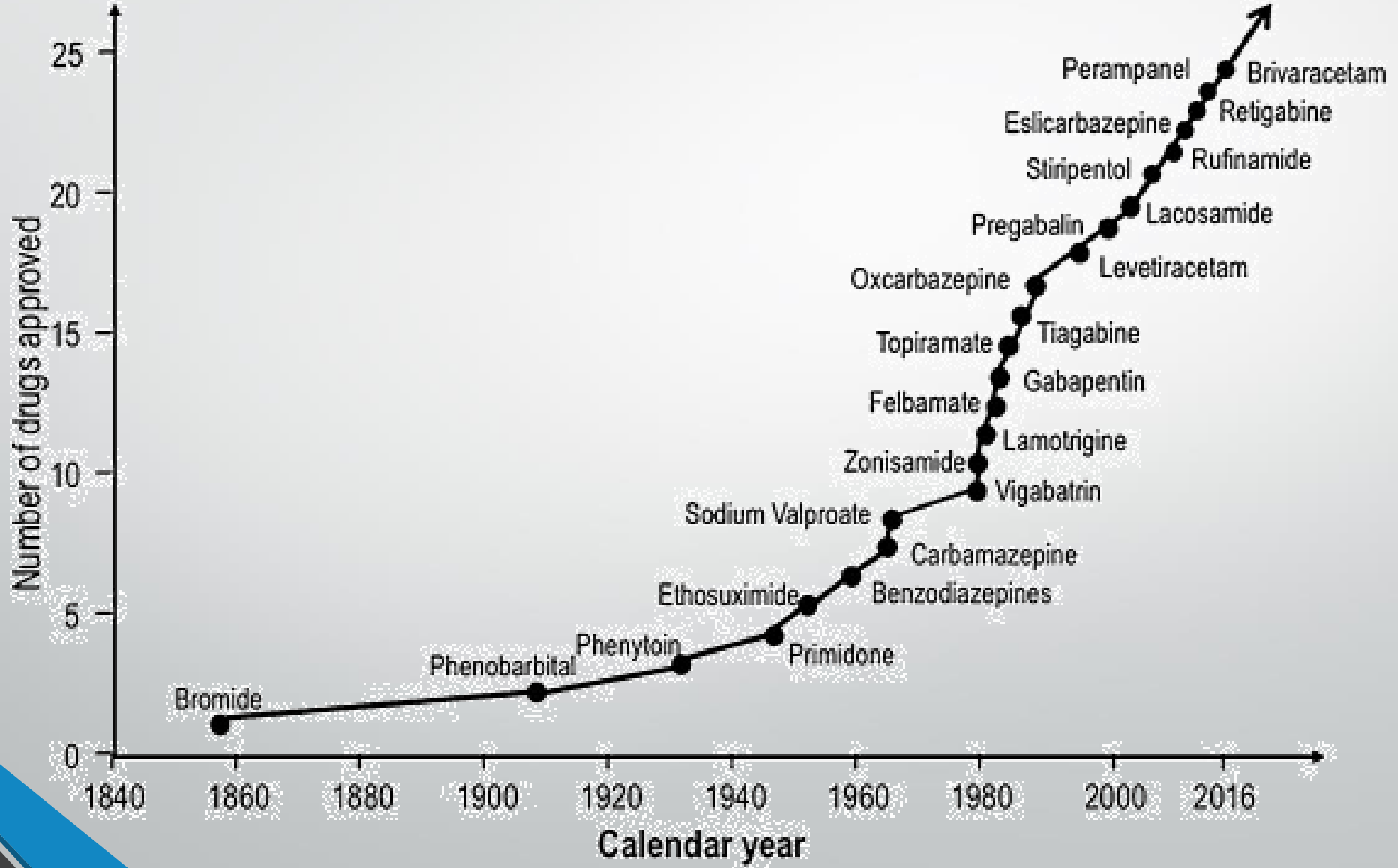
- Daily AEDs
  - Diagnosis of epilepsy (increased risk for recurrent seizures)
  - Other patients without epilepsy
    - Recurrent/prolonged febrile seizures
    - Provoked seizures (short term)
    - "Seizure prophylaxis"
- Seizure Rescue Medication
  - Any child > 2 years of age that has had an event clinically concerning for a seizure

How to choose treatment?[3]

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

Approximately 70% of children with epilepsy will have seizure freedom with appropriate AED therapy[3]

What are the AED options to choose from?[4,5]



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
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

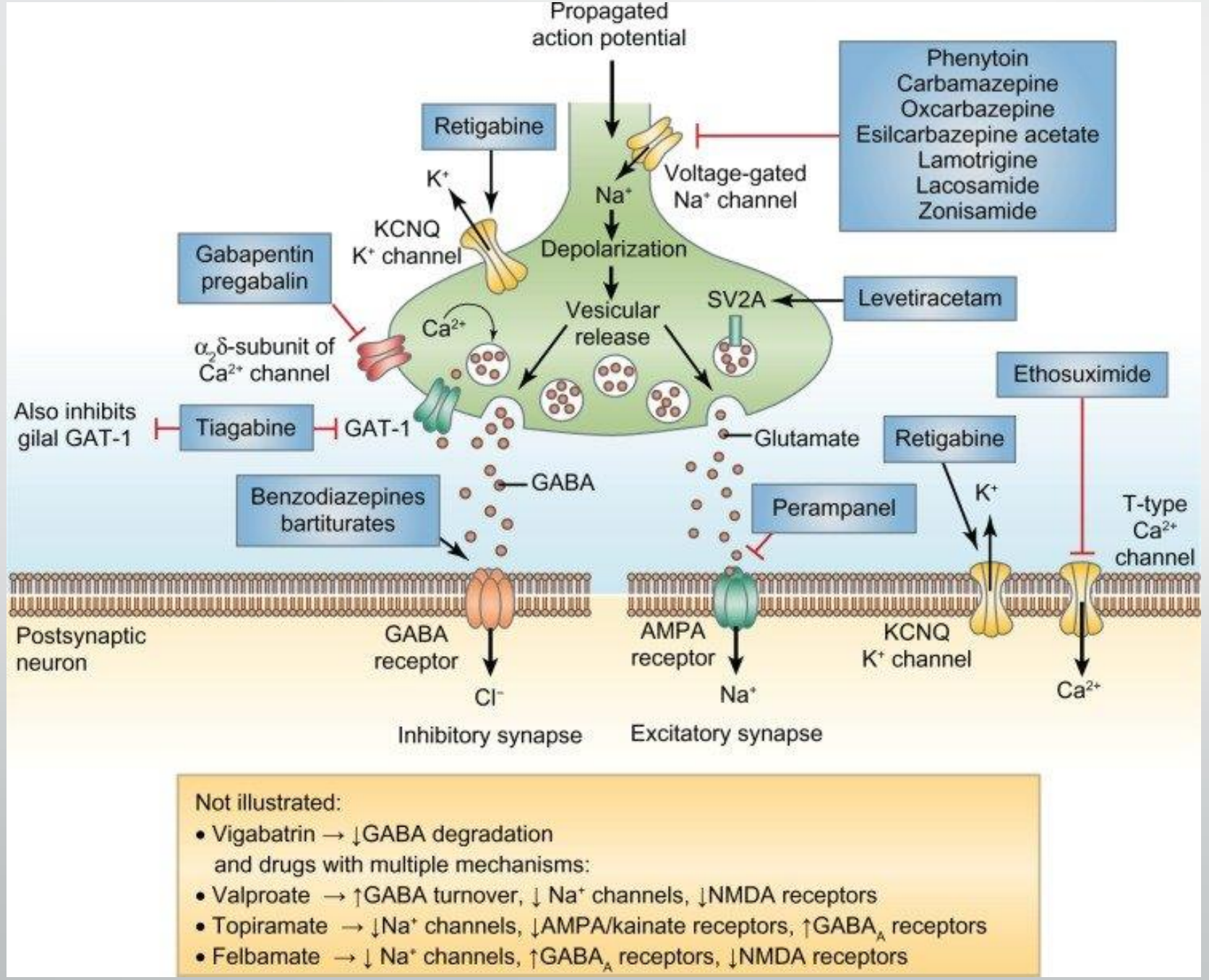
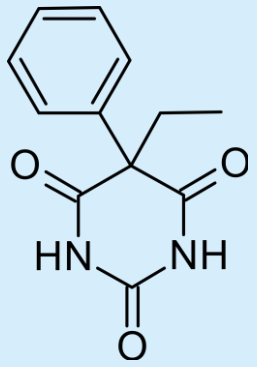


Image: Shih JJ, Tatum WO, Rudzinski LA. New drug classes for the treatment of partial onset epilepsy: focus on perampanel. *Ther Clin Risk Manag*. 2013;9:285-293. doi:10.2147/TCRM.S37317

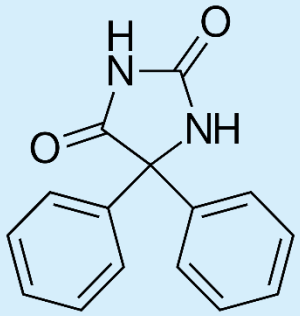
Phenobarbital



- **Indications**
  - All seizure types other than absence
  - Neonatal seizures
  - Status epilepticus
- **Mechanism of Action**
  - Binds $GABA_A$ receptor → prolongs opening of chloride channel → enhances GABA inhibition
- **Metabolism/Interactions**
  - Liver metabolized
  - CYP_{450} enzyme inducer = MANY interactions
- **Dose:**
  - Pediatric: 4 - 6 mg/kg/day (once daily or 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

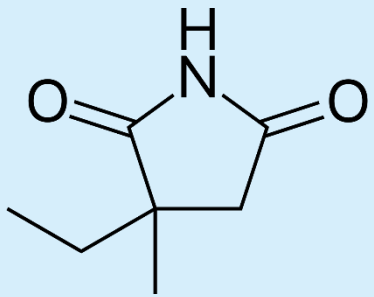


- **Indications**
  - Most seizure types (not absence or myoclonic)
  - Status epilepticus (IV)
- **MOA**
  - Binds to sodium channels → reduces high frequency firing
- **Metabolism/Interactions**
  - Potent enzyme inducer (CYP450) – many interactions
  - Non-linear pharmacokinetics
- **Dose**:
  - Pediatric: 5 – 8 mg/kg/day (can go up to 10 mkd, 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

Ethosuximide

Zarontin

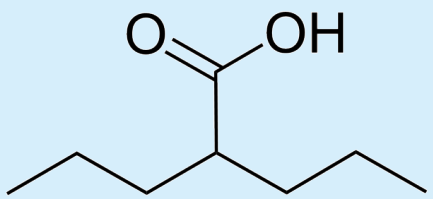


- **Indications:**
  - ABSENCE SEIZURES
- **MOA**
  - Not well understood
  - Blocks t-type calcium channels
- **Metabolism/Interactions**
  - Can affect levels of VPA and primidone
  - Can be affected by VPA, phenobarbital, phenytoin, stiripentol, carbamazepine, rifampicin and isoniazid
- **Dose**:
  - Pediatric: 5 – 10 mg/kg/day → 20 – 30 mg/kg/day ÷ BID
  - Adult: 500 – 1500 mg/day
- **Side Effects**
  - GI upset
  - Irritability, fatigue, bone marrow reactions
- **Monitoring**
  - Minimal: CBC, +/- levels as needed (40-100 mg/L)

Remember… absence, absence, absence

Valproate

Depakote

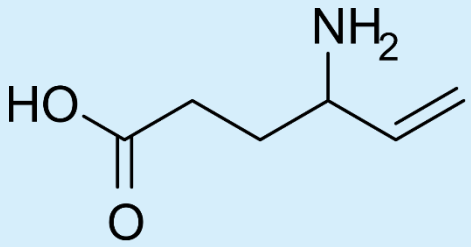


- **Indications**
  - Multiple seizure types including absence seizures
  - Status epilepticus
  - Non-epilepsy uses – bipolar disorder, migraine prophylaxis
- **MOA** (variety)
  - Increases GABA
  - Blocks voltage gated sodium channels
  - Activate Ca-dependent potassium conductance
- **Metabolism/Interactions**
  - 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, hypocarnitinemia, 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)

Remember… broad spectrum, no babies, limit females, labs

Vigabatrin

Sabril, Vigadrone

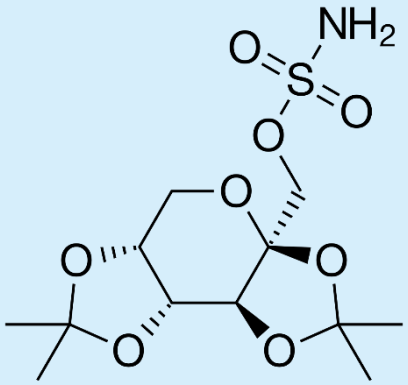


- **Indications**
  - INFANTILE SPASMS
  - Adjunct treatment for refractory focal seizures
- **MOA**
  - Binds GABA transaminase → permanent inactivation → increase GABA
- **Metabolism/Interactions**
  - May interact with felbamate, carbamazepine, phenytoin and rufinamide
- **Dose (in infants):**
  - 50 mg/kg/day x 3 days → 100 mg/kg/day x 3 days → 150 mg/kg/day (max is 200 mg/kg/day)
  - Powder pack has to be mixed with water, then discarded after each dose
- **Side Effects**
  - Risk of permanent peripheral vision loss
  - Sedation
  - Dizziness, headache, ataxia, cognitive disturbance
- **Monitoring**
  - Ophthalmology examination within 3 months of starting medication

Remember… infantile spasms and ophthalmology

Topiramate

Topamax

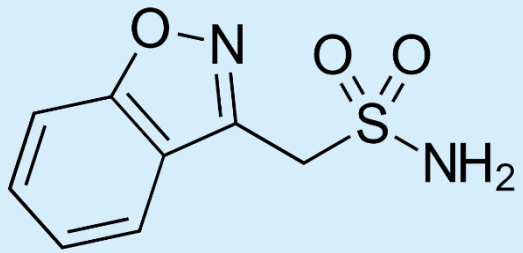


- **Indications**
  - ALL seizure types
  - Non-epilepsy uses – migraine prophylaxis, PTSD, bipolar disorder, IIH, binge eating disorder, neuropathic pain etc.
- **MOA**
  - Enhances GABA
  - Inhibits voltage-dependent sodium channels
  - Decrease glutamate excitation (AMPA antagonism)
  - Carbonic anhydrase 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, parethesias
  - Oligohydrosis, metabolic acidosis, nephrolithiasis
- **Monitoring**
  - Periodic BMP – sodium bicarb levels
  - Levels: 5 – 20 mg/L

Remember… broad spectrum, cognition, hydration

Zonisamide

Zonegran

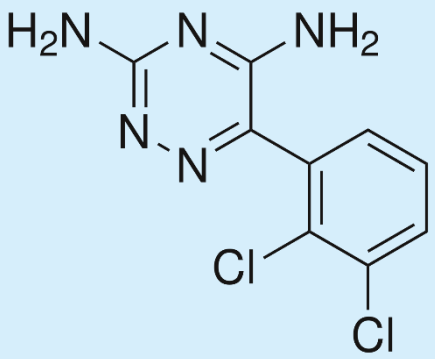


- **Indications**
  - ALL seizure types
  - Non-epilepsy uses: binge-eating disorder, bipolar disorder, migraine, neuropathic pain
- **MOA**
  - Partially block sodium channels
  - Block t-type calcium channels
  - Increase extracellular dopamine and serotonin
  - Carbonic anhydrase inhibition
- **Metabolism/Interactions**
  - Carbamazepine, phenobarbital, phenytoin, risperidone
- **Dose**:
  - Pediatric: 1-2 mg/kg/day → 5-8 mg/kg/day (up to 12)
  - Adult: 100 – 600 mg/day
- **Side Effects**
  - Cognitive slowing, fatigue, anorexia/weight loss, behavioral changes, ataxia
  - Metabolic acidosis, hypohydrosis, rash, nephrolithiasis
- **Monitoring**
  - Periodic BMP – sodium bicarb levels
  - Levels: 10 – 40 mg/L

Remember… broad, like Topamax

Lamotrigine

Lamictal

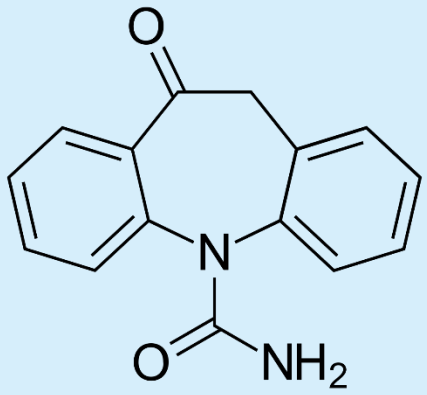


- **Indications**
  - Most seizure types
  - *May* worsen myoclonic seizures
  - Non-epilepsy uses: Bipolar disorder, migraine, neuropathy, cluster headaches etc
- **MOA**
  - Modulates sodium channels
  - Inhibits glutamine release
- **Metabolism/Interactions**
  - Various AEDs (especially valproate)
  - OCPs
  - Lamotrigine + Topiramate and Lamotrigine + vigabatrin may be synergistic
- **Dose**:
  - Goal pediatric dose = 2-8 mg/kg/day
  - SLOW titration – 0.4 mkd x 2 weeks → 0.8 mkd x 2 weeks → increase by 0.8 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

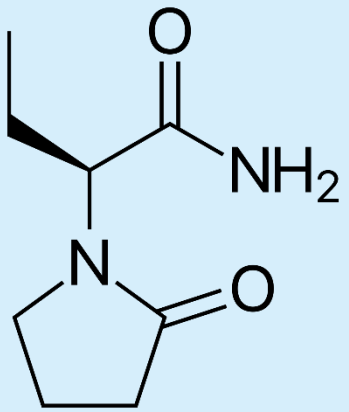


- **Indications**
  - Focal seizures ONLY
  - Other: bipolar disorder, trigeminal neuralgia
- **MOA**
  - Blocks sodium channels
- **Metabolism/Interactions**
  - Carbamazepine, lacosamide, perampanel, phenobarbital, phenytoin
  - OCPs
- **Dose**:
  - Pediatric: 10 mg/kg/day → 20 – 40 mg/kg/day (max 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

Levetiracetam

Keppra

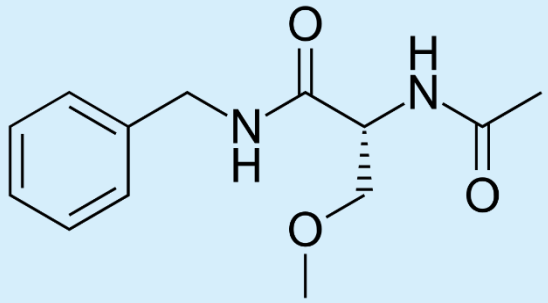


- **Indications**
  - ALL seizures types
  - Status epilepticus
- **MOA**
  - SV2A binding → disrupts synaptic vesicle exocytosis
- **Metabolism/Interactions**
  - Minimal interactions
  - Renal excretion – may need to renally dose if renal impairment
- **Dose**:
  - Pediatric: 10 – 20 mg/kg/day → 60 – 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

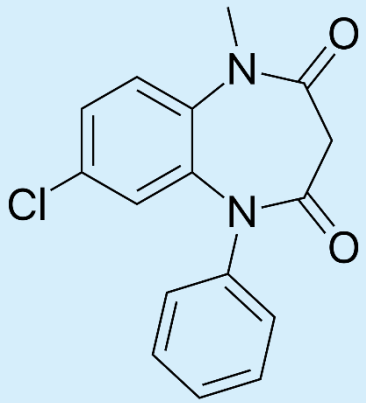


- **Indications**
  - Focal seizures
  - Focal status epilepticus (IV)
- **MOA**
  - Enhances inactivation of sodium channels → stabilizes neuronal membranes
- **Metabolism/Interactions**
  - Avoid co-medicating with other similar sodium channel medications
- **Dose**:
  - Pediatric: 3 mg/kg/day → 6-8 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

Remember… focal, IV, EKG first

Clobazam

Onfi

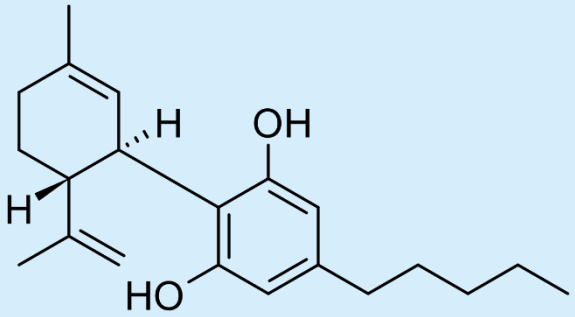


- **Indications**
  - Adjunctive treatment for focal and generalized seizures
  - Catamenial epilepsy and Lennox-Gastaut syndrome
  - Non-convulsive status epilepticus
- **MOA**
  - Enhances GABA
  - Benzodiazepine
- **Metabolism/Interactions**
  - Longer half life (36-46 hours in kids)
  - Can potentiate effects of other CNS depressants
  - Phenytoin, primidone, stiripentol, cannabidiol, valproate* etc.
- **Dose**:
  - Pediatric: 0.25 mg/kg/day → 1 mg/kg/day (up to 2)
  - 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

Remember… sedation, refractory epilepsy

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

Steroids[7]

Adrenocorticotropin hormone (ACTH)
IV methylprednisolone
Oral prednisone

- **Indications**
  - ACTH = infantile spasms
  - Methylprednisolone = infantile spasms, ESES
  - Oral prednisone = infantile spasms , ESES
- **MOA**
  - ACTH – stimulates adrenal secretion of cortisol, suppresses CRH which is a proconvulsant neuropeptide
  - Oral steroids: act on glucocorticoid and mineralocorticoid receptors in the brain (anticonvulsant effects unclear)
- **Metabolism/Interactions**
  - No drug interactions
  - ACTH must be IM as it is inactivated in GI tract
- **Dose**:
  - IM ACTH: 150unit/m2/day divided twice a day → taper
  - Oral prednisolone: Start Day 1-14: 9mg QID (36mg/day) → taper
  - IV methylprednisolone: 30 mg/kg/day 3-5 days → oral taper
- **Side Effects:**
  - Hypertension, hyperglycemia, weight gain, cardiomyopathy, immunosuppression
  - Irritability, insomnia, cushingoid features
- **Monitoring**
  - Before ACTH: BP/vitals, skin TB test, CXR, UA, CBC, electrolytes
  - During ACTH: BP, urine glucose, weight, stool guaiac, CBC and electrolytes
  - ALWAYS prescribe H_2 blocker!!!

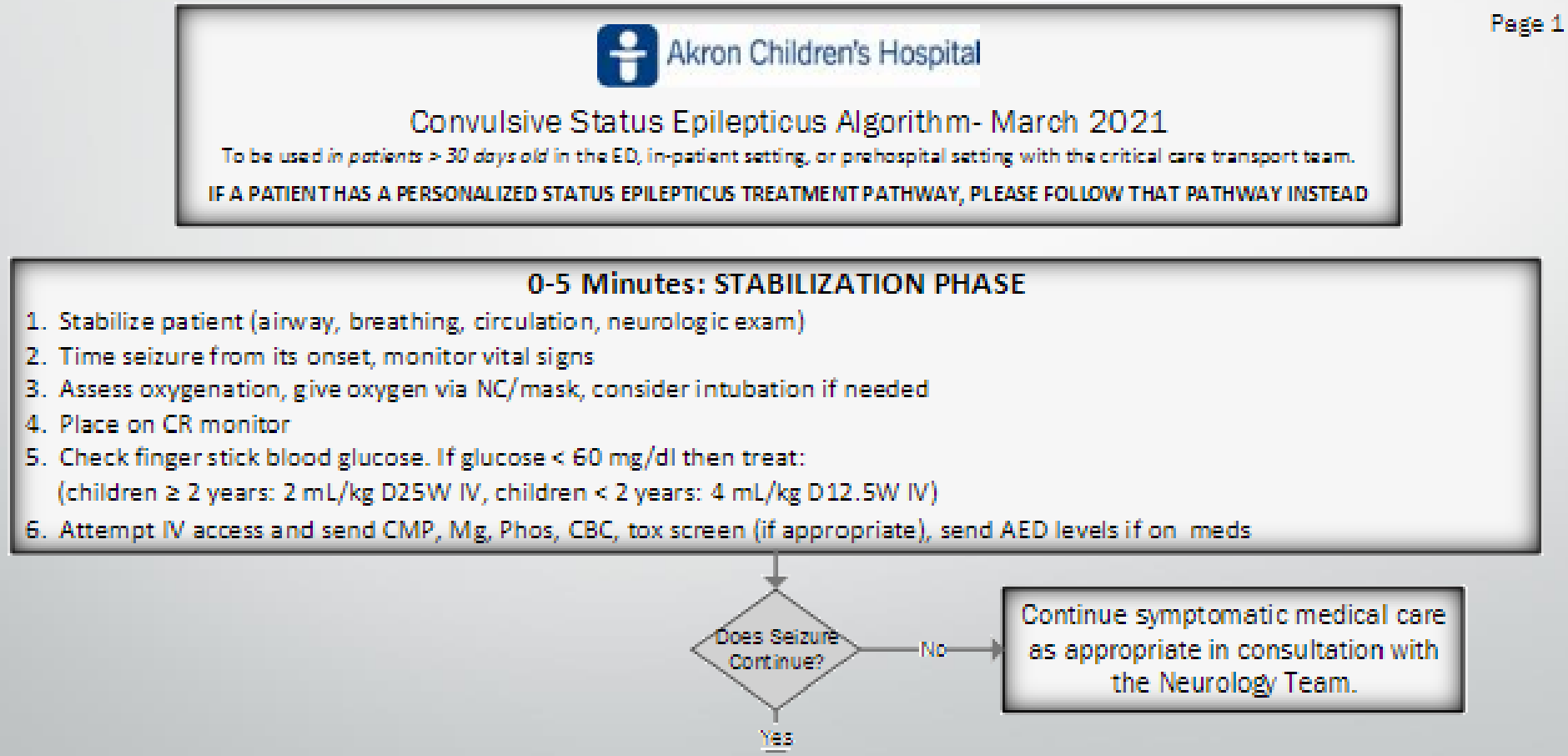
Remember… Infantile spasms, ESES, monitor

What is status epilepticus?[1,8]

- 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 t_1). It is a condition that can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures*."

- Initiate treatment at t_1 (5 minutes)
- Concern for brain damage begins at t_2 (30 minutes)

How do I manage status epilepticus?[9]



Page 1

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

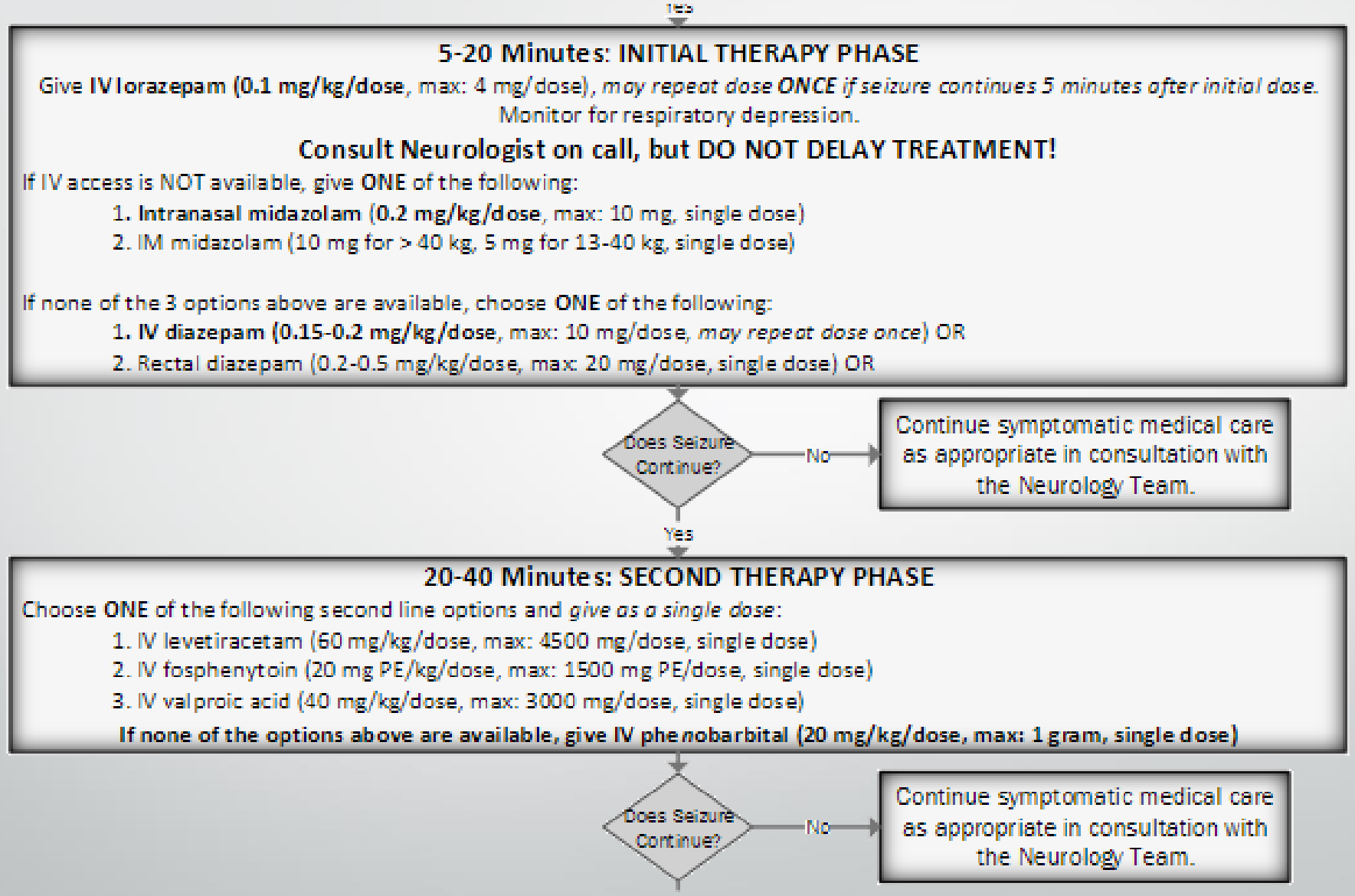
0-5 Minutes: STABILIZATION PHASE

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 ≥ 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


Yes
5-20 Minutes: INITIAL THERAPY PHASE
Give IV lorazepam (0.1 mg/kg/dose, max: 4 mg/dose), may repeat dose ONCE if seizure continues 5 minutes after initial dose.
Monitor for respiratory depression.
Consult Neurologist on call, but DO NOT DELAY TREATMENT!
If IV access is NOT available, give ONE of the following:
1. Intranasal midazolam (0.2 mg/kg/dose, max: 10 mg, single dose)
2. IM midazolam (10 mg for > 40 kg, 5 mg for 13-40 kg, single dose)
If none of the 3 options above are available, choose ONE of the following:
1. IV diazepam (0.15-0.2 mg/kg/dose, max: 10 mg/dose, may repeat dose once) OR
2. Rectal diazepam (0.2-0.5 mg/kg/dose, max: 20 mg/dose, single dose) OR
Does Seizure Continue?
No
Continue symptomatic medical care as appropriate in consultation with the Neurology Team.
Yes
20-40 Minutes: SECOND THERAPY PHASE
Choose ONE of the following second line options and give as a single dose:
1. IV levetiracetam (60 mg/kg/dose, max: 4500 mg/dose, single dose)
2. IV fosphenytoin (20 mg PE/kg/dose, max: 1500 mg PE/dose, single dose)
3. IV valproic acid (40 mg/kg/dose, max: 3000 mg/dose, single dose)
If none of the options above are available, give IV phenobarbital (20 mg/kg/dose, max: 1 gram, single dose)
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.

Benzodiazepines

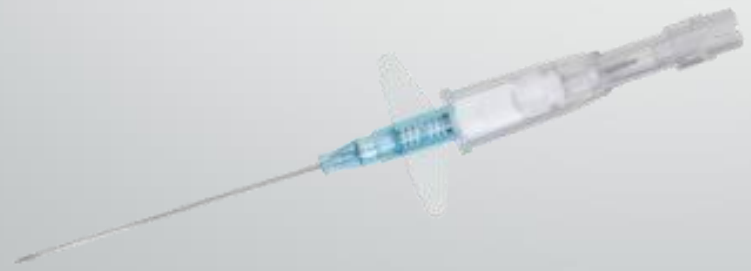
Clobazam
Clonazepam
Diazepam
Lorazepam
Midazolam

- **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 use of benzodiazepines[5,10]

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 or continuous infusion
  - IN = 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)

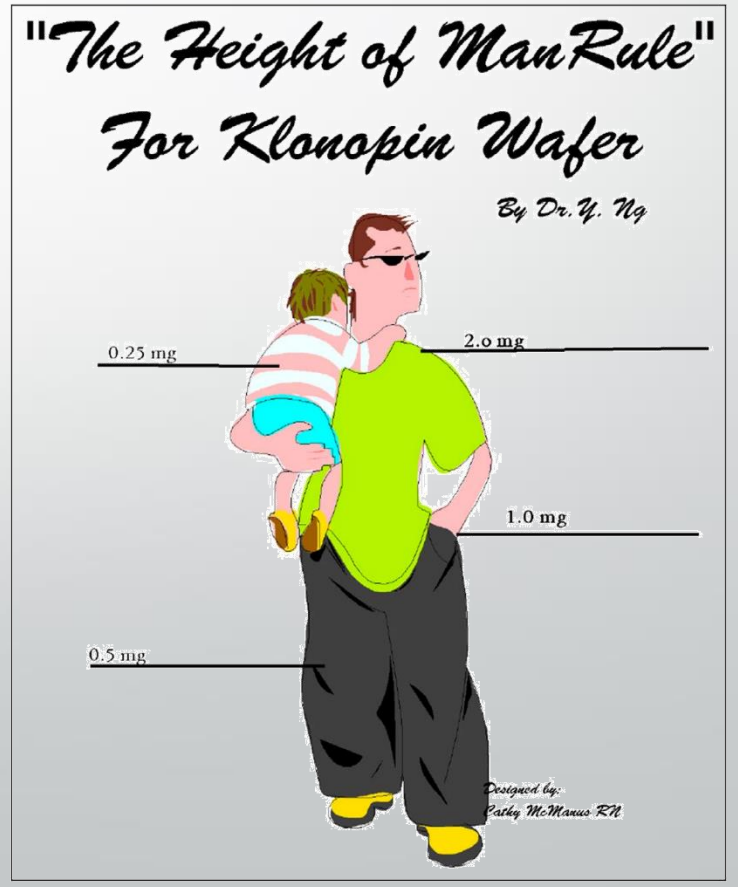
Home use of benzodiazepines[5,10]

- **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

Image: Diastat.com

- **Clonazepam ODT** (Klonopin)



Home use of benzodiazepines (cont.)[5,10]

Valtoco® (Diazepam nasal spray)

Specific, individualized VALTOCO nasal spray dosing[1]

- Individualized dosing based on age and weight[1]
- Available in 4 treatment doses: 5 mg, 10 mg, 15 mg, 20 mg[1]
- A second dose may be given at least 4 hours after initial dose, if needed[1]
- Each single dose is ready to use, no assembly required[1]

6-11 years (0.3 mg/kg)

Weight (kg)	Weight (lb)	Dose (mg)	Given As
10-18	22.0-39.7	5	One **5 mg** nasal spray device in one nostril
19-37	41.9-81.6	10	One **10 mg** nasal spray device in one nostril
38-55	83.8-121.3	15	Two **7.5 mg** nasal spray devices, one in each nostril
56-74	123.5-163.1	20	Two **10 mg** nasal spray devices, one in each nostril

12+ years (0.2 mg/kg)

Weight (kg)	Weight (lb)	Dose (mg)	Given As
14-27	30.9-59.5	5	One **5 mg** nasal spray device in one nostril
28-50	61.7-110.2	10	One **10 mg** nasal spray device in one nostril
51-75	112.4-165.3	15	Two **7.5 mg** nasal spray devices, one in each nostril
76 and up	167.6 and up	20	Two **10 mg** nasal spray devices, one in each nostril

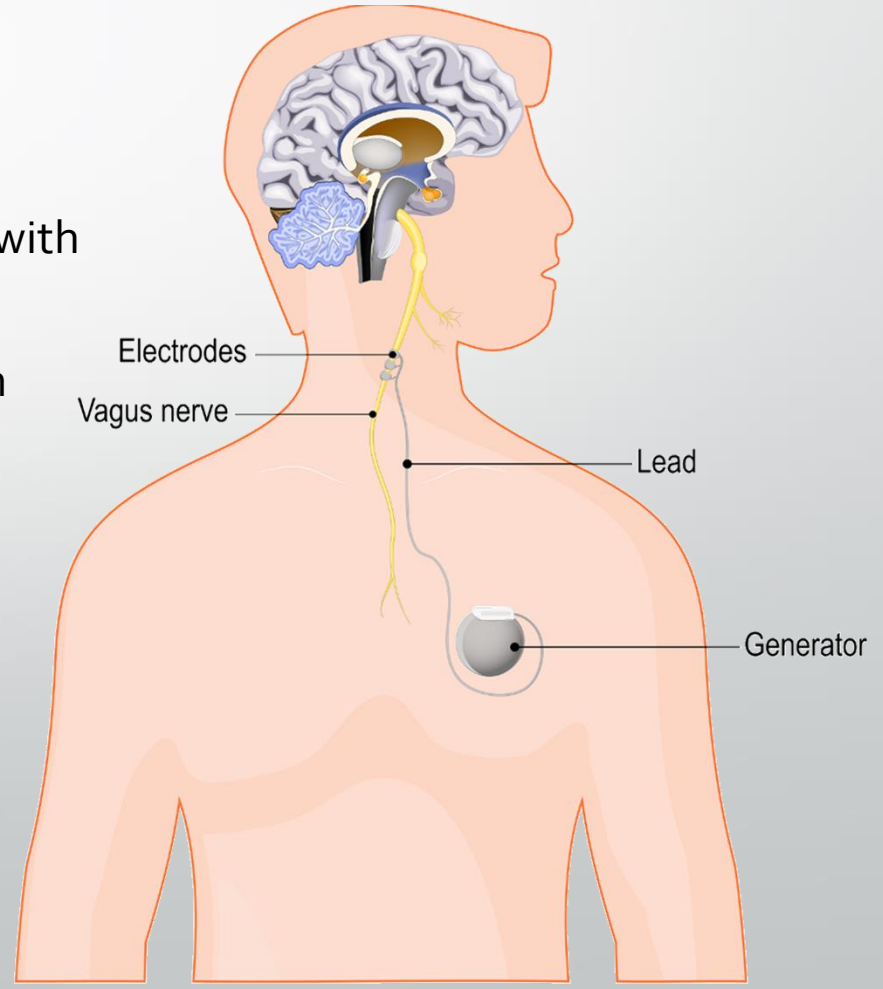
Image: Valtocohcp.com

Nayzilam® (Midazolam nasal spray)

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

What are the non-pharmacologic treatments for epilepsy?[11]

- Surgery
  - Vagus Nerve Stimulator (VNS)
    - Inhibits the development of seizure kindling associated with noradrenaline
    - Increase cerebral blood flow to certain areas of the brain
    - Increases level of GABA
  - Resection of seizure focus
  - Corpus Callosotomy
  - Hemispherectomy



Ketogenic Diet[11,12]

- Indications
  - Specific metabolic diseases - Glucose Transporter Protein 1 (GLUT-1) deficiency syndrome and Pyruvate Dehydrogenase Deficiency
  - Refractory/Intractable epilepsy
- High fat, low protein, very low carb diet
- Ketone bodies are used at primary energy source of brain in place of glucose
- Side effects: dehydration, hypoglycemia, lethargy, metabolic acidosis, and gastrointestinal symptoms (constipation)
- Requires various blood monitoring before and during treatment

References

1. Fisher RS, van Emde Boas W, Blume W, et al. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia 2005;46(4):470-472. doi:10.1111/j.0013-9580.2005.66104.x
2. Wirrell E. Evaluation of First Seizure and Newly Diagnosed Epilepsy. *Continuum (Minneap Minn)*. 2022;28(2):230-260. doi:10.1212/CON.0000000000001074
3. Moosa ANV. Antiepileptic Drug Treatment of Epilepsy in Children. *Continuum (Minneap Minn)*. 2019;25(2):381-407. doi:10.1212/CON.0000000000000712
4. Abou-Khalil BW. Update on Antiseizure Medications 2022. Continuum (Minneap Minn). 2022;28(2):500-535. doi:10.1212/CON.0000000000001104
5. Patsalos PN, St. Louis EK. *The Epilepsy Prescriber's Guide to Antiepileptic Drugs*. 3rd ed. Cambridge University Press; 2018.
6. Shih JJ, Tatum WO, Rudzinski LA. New drug classes for the treatment of partial onset epilepsy: focus on perampanel. Ther Clin Risk Manag. 2013;9:285-293. doi:10.2147/TCRM.S37317
7. Grinspan ZM, Knupp KG, Patel AD, et al. Comparative Effectiveness of Initial Treatment for Infantile Spasms in a Contemporary US Cohort [published online ahead of print, 2021 Jul 15]. Neurology. 2021;97(12):e1217-e1228. doi:10.1212/WNL.0000000000012511
8. Trinka E, Cock H, Hesdorffer D, et al. A definition and classification of status epilepticus--Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia. 2015;56(10):1515-1523. doi:10.1111/epi.13121
9. Raimer P, Besunder J, Gunkelman S, Zawadzki L, Ruggles C. Akron Children's Hospital Convulsive Status Epilepticus Algorithm. 2021. Adapted from: Glauser T, Shinnar S, Gloss D, et al. Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society. *Epilepsy Curr*. 2016;16(1):48-61. doi:10.5698/1535-7597-16.1.48
10. Samanta D. Rescue therapies for seizure emergencies: current and future landscape. Neurol Sci. 2021;42(10):4017-4027. doi:10.1007/s10072-021-05468-9
11. Alqahtani F, Imran I, Pervaiz H, et al. Non-pharmacological Interventions for Intractable Epilepsy. Saudi Pharm J. 2020;28(8):951-962. doi:10.1016/j.jsps.2020.06.016
12. D'Andrea Meira I, Romão TT, Pires do Prado HJ, Krüger LT, Pires MEP, da Conceição PO. Ketogenic Diet and Epilepsy: What We Know So Far. Front Neurosci. 2019;13:5. Published 2019 Jan 29. doi:10.3389/fnins.2019.00005

[illegible]. Perucca P, Scheffer IE, Kiley M. The management of epilepsy in children and adults. *Med J Aust*. 2018;208(5):226-233. doi:10.5694/mja17.00951

Piña-Garza JE, James KC. *Fenichel's Clinical Pediatric Neurology : A Signs and Symptoms Approach*. 8th ed. Elsevier; 2019.

Thank you!

- Questions?
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