

Strengthen & Enhance Epilepsy Knowledge (SEEK) Training

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NATIONAL
COORDINATING
CENTER *for* EPILEPSY

American Academy of Pediatrics
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EPILEPSY TREATMENT AND SUDDEN UNEXPECTED DEATH IN EPILEPSY (SUDEP)



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DISCLOSURES

- We have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this activity.
- This program will address some medications that are used off-label as rescue therapies.



OBJECTIVES

- Describe the different treatments for epilepsy (ie, special diets, devices, and surgery).
- Recognize risk factors for Sudden Death in Epilepsy (SUDEP) and outline prevention measures.
- Recognize activities and/or conditions at home or school that may pose a risk to those living with epilepsy.



EPILEPSY BACKGROUND

- There are approximately 13.5 million children and youth with special health care needs (CYSHCN) in the United States.¹
 - Included among the CYSHCN are 470,000 children aged birth to 18 years living with epilepsy, the most common childhood neurologic condition in the US.²
- Epilepsy is a brain disorder where a person has recurring seizures.³
 - Seizures are sudden events that cause temporary changes in physical movement, sensation, behavior, or consciousness; they are caused by abnormal electrical and chemical changes in the brain.³



EPILEPSY BACKGROUND

- Epilepsy is a condition that requires complex, coordinated systems of primary and specialty care.⁴
 - A lack of awareness of the treatment options by providers can significantly affect a patient's quality of life.⁵
 - However, only roughly one-third of children with epilepsy have access to comprehensive health care.⁶
 - Nationally, the number of pediatric neurologists is at least 20% below the need, resulting in limited access to care for CYE, especially in rural and medically underserved areas/populations (MUA/Ps).^{4,7}
 - Approximately 20% of Americans live in rural areas, while only 9% of the nation's physicians practice in these areas.⁴



Epilepsy Background References

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3. S. Russ, K. Larson, N. Halfon. A National Profile of Childhood Epilepsy and Seizure Disorder. *Pediatrics*. February 2012. 129 (2) 256-264. <https://doi.org/10.1542/peds.2010-1371>.
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Epilepsy Treatment

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REPRESENTATIVE CASE

- 8-year-old girl with history of focal seizures for 2 years.
 - Her seizures start with a vague sensation of old memories, then proceed to facial flushing, pupillary dilation, then stiffening of her right arm.
 - She rarely has a convulsive seizure.
 - These initially were occurring once per month, but now, despite being on 3 antiseizure medications, occur 3-5 times per week.



REPRESENTATIVE CASE

- 8-year-old girl with history of focal seizures for 2 years.
 - We did a surgical evaluation:
 - Captured seizures on EEG which looked right temporal at onset.
 - MRI normal.
 - PET showed abnormal signal in right temporal lobe.
 - Presented her data formally and everyone agreed she should have a right temporal lobectomy.



Image Source: Mcnamara, N. Positron Emission Tomography (PET)/Magnetic Resonance Imaging (MRI) Scan. 2022

REPRESENTATIVE CASE

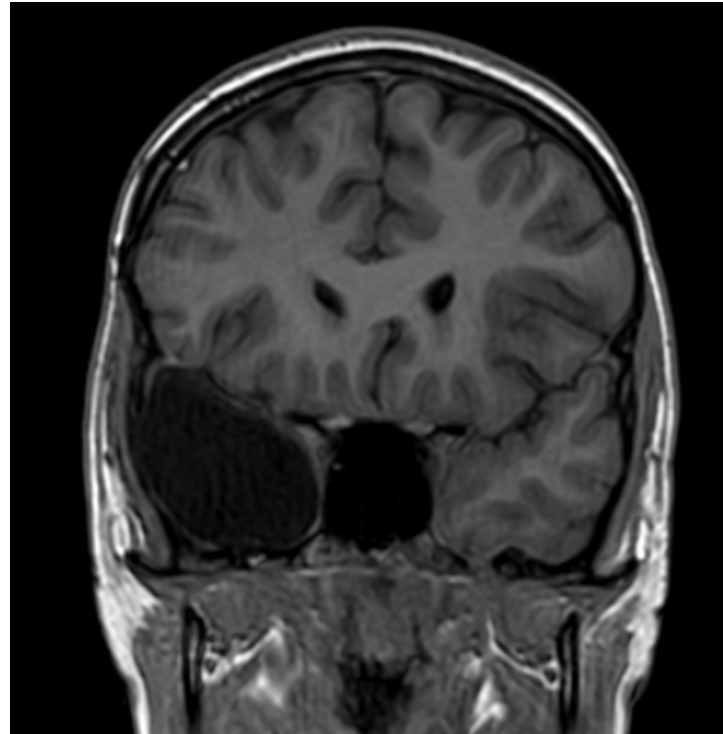


Image Source: Mcnamara, N. Positron Emission Tomography (PET)/Magnetic Resonance Imaging (MRI) Scan. 2022

Follow up:

- Seizure free for 4 years.
- Off all 3 antiseizure medications for 3 years.

TREATMENT OF EPILEPSY

- Once a patient has more than 1 unprovoked seizure, or 1 unprovoked seizure and increased risk for seizures (ex: abnormal EEG), a daily antiseizure medication is started.
- This medication is chosen based on:
 - Side effect profile
 - Type of seizures (if known)
- About 50% of the time, the patient will become seizure free on this first medication, though uptitration may need to occur.



EPILEPSY MEDICATION TREATMENT

- Epilepsy > 1 unprovoked seizure

Chances of seizure
freedom with first
medication - 50%



EPILEPSY MEDICATION TREATMENT

- Epilepsy > 1 unprovoked seizure
- Most people have seizure control with the first or second medication chosen, though it may have to be titrated up.

Chances of seizure freedom with first medication - 50%

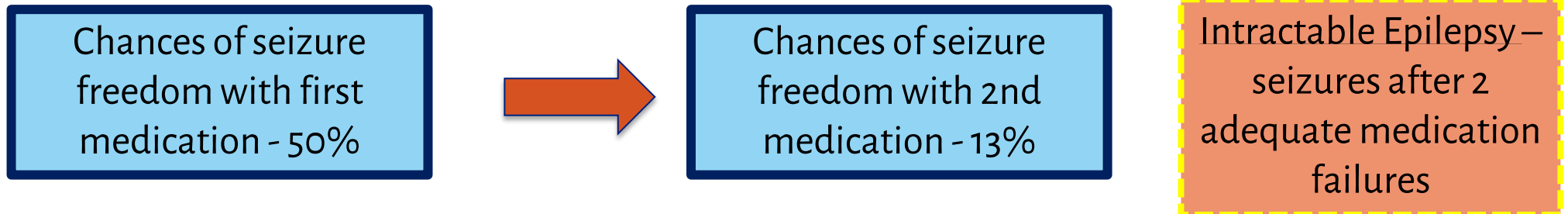


Chances of seizure freedom with 2nd medication - 13%



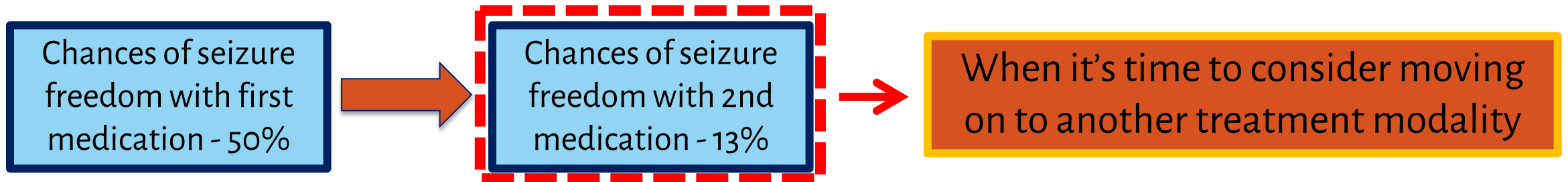
EPILEPSY MEDICATION TREATMENT

- Epilepsy > 1 unprovoked seizure
- Most people have seizure control with the first or second medication chosen, though it may have to be titrated up.



INTRACTABLE EPILEPSY TREATMENT OPTIONS

- Epilepsy > 1 unprovoked seizure
- Intractable Epilepsy – seizures after 2 adequate medication failures



ANTISEIZURE MEDICATIONS OVER THE YEARS

First generation antiseizure medications (1850-1960s):

- Bromides
- Borax
- Phenobarbital
- Phenytoin
- Primidone
- Ethosuximide

Second generation antiseizure medications (1960-1980s):

- Valproate
- Carbamazepine
- Sulthiamine
- Clobazam

Third generation antiseizure medications (1980s-):

- Levetiracetam
- Topiramate
- Gabapentin
- Felbamate
- Oxcarbazepine
- Zonisamide
- Lamotrigine
- Vigabatrin
- Rufinamide
- Stiripentol

Source: England MJ. Health care: Quality, Access, and Value. In: Committee on the Public Health Dimensions of the Epilepsies, Board on Health Sciences Policy, Institute of Medicine, ed. *Epilepsy Across the Spectrum: Promoting Health and Understanding*. National Academies Press; 2012; 169

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INTRACTABLE SEIZURES: WHEN MEDICATIONS DON'T WORK

- Ketogenic Diet²
 - A distinct high-fat, low-carbohydrate diet that helps to control seizures in some people with epilepsy.
- Neuromodulation: Vagus Nerve Stimulation (VNS)¹
 - An approved add-on therapy by the U.S. Food and Drug Administration (FDA) for adults and children 4 years and older to treat focal or partial seizures that do not respond to seizure medications.
- Surgery

1. Shafer PO, Dean PM. Vagus Nerve Stimulation (VNS) Therapy. Epilepsy.com. Updated on March 12, 2018. Accessed August 29, 2022. <https://www.epilepsy.com/treatment/devices/vagus-nerve-stimulation-therapy>.

2. Kossoff, E. Ketogenic Diet. Epilepsy.com. Updated on October 25, 2017. Accessed August 29, 2022. <https://www.epilepsy.com/treatment/dietary-therapies/ketogenic-diet>.



DIETARY THERAPY: KETOGENIC DIET, MODIFIED KD, & MODIFIED ATKINS DIET

- High fat, moderate protein, low carb
- Highly effective
- Strictly regimented
- Requires inpatient hospitalization for initiation



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KETOGENIC DIET: DOES IT WORK?

- On average there is a ~ 50% seizure reduction after 4 months on the KD (in comparison to no change/seizure worsening in children treated “as usual”)
 - 10-15% of patients are seizure-free after 6-months
- Positive side effects: Children see an increase learning and cognitive function
- Negative side effects: GI symptoms (like constipation)



NEUROMODULATION: VAGUS NERVE STIMULATION (VNS)

- FDA approved for children ≥ 4 years old
- Implanted stimulator device placed under the skin in the chest with wire around vagus nerve
- Regular mild pulses of electrical current delivered to the brain via the vagus nerve
- Mechanism of action is incompletely understood
- May improve seizures overtime



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EPILEPSY SURGERY: CANDIDACY

- Intractable focal epilepsy whose seizures cause an adverse impact on their lives.
- Should not be considered as “last resort.”



BRAIN SURGERY OPTIONS

- Resective surgery
 - Must identify epileptogenic zone
 - Typically, do not resect eloquent cortex
- Hemispherectomy (*Hemispherotomy*)
 - Removal/disconnection of 1 hemisphere
- Palliative options
 - Corpus callosotomy (used for atonic seizures)
- Laser ablation
 - Can be used in special situations



Source: Mcnamara, N. Positron Emission Tomography (PET)/Magnetic Resonance Imaging (MRI) Scan.
2022

Example of hemispherotomy: Patient had large left hemispheric perinatal stroke and intractable left hemispheric seizures and right sided hemiparesis.

Seizures stopped and there were no new deficits after hemisphere was disconnected.

Sudden Unexpected Death in Epilepsy (SUDEP)

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WHAT IS SUDDEN UNEXPECTED DEATH IN EPILEPSY?

- Sudden Unexpected Death in Epilepsy (SUDEP)
 - Deaths in people with epilepsy that are not caused by other known causes¹
 - Death occurs during or immediately after a seizure
 - Often person is found lying face down
 - Annual incidence rate of SUDEP is 1 in 4,500 children with epilepsy²
 - Significantly higher incidence in special populations such as Dravet syndrome

1. Wicker E, Cole JW. Sudden Unexpected Death in Epilepsy (SUDEP): A Review of Risk Factors and Possible Interventions in Children. *J Pediatr Pharmacol Ther.* 2021;26(6):556-564. doi:10.5863/1551-6776-26.6.556

2. Harden C, Tomson T, Gloss D, et al. Practice Guideline Summary: Sudden Unexpected Death in Epilepsy Incidence Rates and Risk Factors: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Epilepsy Curr.* 2017;17(3):180-187. doi:10.5698/1535-7511.17.3.180



WHAT ARE THE MECHANISMS OF SUDDEN UNEXPECTED DEATH IN EPILEPSY?

- Exact reasons and mechanisms are unknown:
 - Dysregulation of cardiac, respiratory, or autonomic nervous system suspected
 - Abnormal breathing during a seizure: apnea, hypoxia
 - Abnormal heart rhythm: arrhythmia, cardiac arrest
 - Abnormal brain function: brainstem dysfunction
- Genetic factors may also play a role



WHAT ARE THE MECHANISMS OF SUDDEN UNEXPECTED DEATH IN EPILEPSY?

- Respiratory
 - Pulmonary edema
 - Dysregulated breathing during or after seizure
- Cardiac
 - Primary, or secondary to autonomic dysfunction
 - Dysrhythmia
 - Myocyte hypertrophy, Myofibrosis
- Autonomic Dysfunction
 - Decreased serotonin levels
 - Cardiac dysregulation
 - Brainstem dysfunction, impaired CO₂ arousal responses



RISK FACTORS OF SUDEP

- **Frequent tonic-clonic (convulsive) seizures (≥ 3 per year)**
- Medication noncompliance
- Nocturnal seizures
- Onset of seizures at an early age
- Long duration of epilepsy (>15 years)
- Developmental disabilities

1. Devinsky O. Sudden, unexpected death in epilepsy [published correction appears in *N Engl J Med*. 2011 Dec 22;365(25):2441]. *N Engl J Med*. 2011;365(19):1801-1811. doi:10.1056/NEJMra1010481
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PREVENTING SUDEP

- Medication/therapy compliance
 - Reduce seizure burden, reduce tonic-clonic seizures
 - Consideration of epilepsy surgery and/or neurostimulation devices for refractory epilepsies
- Avoidance of prone position while sleeping
- Avoidance of alcohol
- Avoidance of seizure triggers (eg, sleep deprivation or stress)



PREVENTING SUDEP

- Consider seizure alert/detection devices, particularly for nocturnal seizures.
- Consider sharing a room with someone trained in seizure first aid (ie, siblings, roommate, etc).
- Ensure caregivers know seizure first aid and CPR.



DISCUSSING SUDEP WITH PATIENT AND CAREGIVER(S)

- Acknowledge the existence of Sudden Unexpected Death in Epilepsy
 - Timing? Variable
 - Literature suggests most families prefer to be informed about the risk of SUDEP at the time of their child's diagnosis of epilepsy or soon thereafter.
 - No consensus guidelines on optimal timing or setting, address on a case-by-case basis.



DISCUSSING SUDEP WITH PATIENT AND CAREGIVER(S)

- Always address SUDEP if/when asked and consider discussing with the child/youth not in the room.
- Validate and empathize while tailoring discussion to the patient's specific risk factors.
 - Overall incidence of SUDEP in children is low, however, there is a higher prevalence in children with refractory epilepsy.
- Emphasize prevention and empower caregivers with information regarding all available known preventive measures.
 - Provide written literature and websites as resources.



CONSIDERATIONS FROM LIVED EXPERIENCE

- Patients and caregivers should understand that risk factors for potential seizures at home can include video games, TV, and movies for those with photosensitive epilepsy.
- Physicians should also discuss different anticonvulsant medications and their respective advantages and disadvantages.
 - Consider providing families with a cheat sheet about the different types of seizure medications, the side effects, doses, and efficacy.



CONSIDERATIONS FROM LIVED EXPERIENCE

- As physicians, when providing epilepsy treatment be mindful that it may be best to build up to the use of invasive approaches in consideration of patients' and caregivers' comfort levels with the procedures.
 - Note that eligibility for certain treatments is dependent upon age (eg, vagus nerve stimulation can be too large for some younger children like deep brain stimulation implants)
- Families should be encouraged to contact their provider(s) with any questions or concerns as researching epilepsy via the internet may be harmful as some things may be applicable to a different type of epilepsy compared to what a patient is living with.



SUMMARY

- Medication is the main treatment for patients with epilepsy.
- When patients develop intractable epilepsy (> 2 antiseizure medications have been tried), other treatment options include dietary therapy or epilepsy surgery.
 - Neuromodulation is also an option.
- SUDEP is a rare cause of death in patients with epilepsy. There are actions that can be taken to reduce the risk, including optimal medication compliance.



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AAP RESOURCES

- [National Coordinating Center for Epilepsy](#)
 - [National Coordinating Center for Epilepsy – Treating Pediatric Epilepsy](#)
 - While there is no one definitive treatment or cure for pediatric epilepsy, there are medicines and other treatment options that can help keep seizures under control. Finding the right treatment plan can help children and youth with epilepsy (CYE) thrive.
 - [National Coordinating Center for Epilepsy – Sudden Unexpected Death in Epilepsy \(SUDEP\)](#)
 - For some children and youth living with epilepsy, the risk of Sudden Unexpected Death in Epilepsy (SUDEP) is an important concern. SUDEP refers to death in a person living with epilepsy whose death isn't caused by another illness or injury. Parents and caregivers can lower their child's risk of SUDEP by taking steps to keep seizures under control.



RESOURCES

- American Academy of Neurology
 - [Practice Guideline: Sudden Unexpected Death in Epilepsy Incidence Rates and Risk Factors](#)
- [Centers for Disease Control and Prevention: Seizure First Aid](#)
- [Centers for Disease Control and Prevention: SUDEP Information for Parents of Children with Epilepsy](#)
- [Epilepsy Foundation](#)



QUESTIONS?

If you have any questions regarding the presentation, please feel free to contact The National Coordinating Center for Epilepsy (epilepsy@aap.org).

