

# Epilepsy Medication

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# Outline

- Antiepileptic Drugs (AEDs) & Seizures
  - Definitions
  - Why start AED treatment?
  - How AEDs work
  - Side effects
  - Picking the right medication
- Specific AEDs
  - Commonly used AEDs

# Epileptic Seizures

- Seizures are abnormal (surge) patterns of brain electrical activity which disrupt normal function
- There are different types of epileptic seizures
  - May arise from part of the brain
  - May arise from the whole brain

# Epileptic Seizures

- Behavior often has certain characteristic qualities
- EEG (electroencephalography) measures brain electrical activity, noninvasively
- Other non-epileptic behaviors often look like epileptic seizures

# Epilepsy

- Recurring seizures
  - Usually requires 2 unprovoked seizures
- Implies continued risk of further seizures
  - Usually leads to medication treatment

# Why start a medication?

- Prevent negative effects of seizures
  - For example, injuries due to loss of awareness
  - May reduce restrictions of seizure precautions
    - For example, driving

# Why not start a medication?

- There are consequences to being on a medication
  - Cost of effort, time and money
  - All medications have potential for side effects
  - Stigma associated with taking medications for seizures

# Ideal AED medication (\*imaginary)

- Prevents all future seizures
  - Thus, no further consequence from seizures
- One time treatment
  - Minimal effort and time requirement
- Cheap
  - Minimal cost
- No side effect
  
- *“No Seizures, No Side Effects”*



# When to start a medication?

- When having clear recurrent epileptic seizures
  - May be the result of other tests, such as
    - EEG
    - Imaging (e.g., MRI)
    - History
- When concerned about future seizures
  - Estimates for next seizure after one unprovoked seizure:
    - 25% within 6 months
    - 30% within 1 year
    - 40% within 2 years
    - 50% within 5 years

# How do AEDs work?

- Electrical activity in the brain requires certain chemicals and structures for it to work
- Seizures can be thought of as hyperactive brain activity
- Therefore, medications which reduce the chance of having seizures tend to change the amount of chemicals or structures that direct brain activity
  - They may decrease or increase concentrations

# How do AEDs work?

- Different AEDs work on different groups of chemicals
  - Often affect multiple chemicals
  - May be delivered to the brain through different paths
  - All these factors determine how AEDs work and their side effects
- There is no best medication for all of epilepsy

# Side effects

- If seizure medications try to reduce the abnormal excessive brain activities of seizures, then those functions which depend on brain firing may be affected
  - Thinking
  - Wakefulness
  - Emotions
- Other side effects may be due to how the medication is processed
  - Interactions with other medications
  - Monitoring of liver function (metabolism)

# Toxicity

- The amount of medication in the body can often be measured via blood draws
- “Recommended” drug levels are based on studies across patients
  - Effective & toxic levels vary across individuals
  - We treat the PATIENT and NOT just the Lab Values
    - Dosage depends on seizure control and side effects
  - May be useful to know if levels are very low or if someone is/will be pregnant

# Generic versus Brand medications

- In theory, there should not be a significant difference
- However, recall that
  - Effective & toxic levels vary across individuals
- In general, the more economical generic medication should be tried and failure documented before Brand options are requested

# Different Formulations of AEDs

- Medications can vary by
  - Frequency required (e.g., once a day)
  - Form of medication (e.g., tablets, liquid, IV, etc.)
- Some formulations of a medication may be non-formulary (have limitations of use within the VHA)

# How to start an AED medication

- Which medication to start?
  - Again, there is no universal best AED
  - May be influenced by type of seizure
    - “Focal” versus “primary generalized”
  - Convenience
    - For example, method or frequency of administration
  - Cost and availability
  - Possible side effects
    - For example, mental status, weight, job, other meds, etc.
  - Experience and comfort
- How to start that medication
- What if a medication fails?



# How to start an AED medication

- Which medication to start?
- How to start that medication
  - *“Start low and go slow”*
    - People are different
    - Increase single medication until seizures stop or medication not tolerated
- What if a medication fails?

# How to start an AED medication

- Which medication to start?
- How to start that medication
- What if a medication fails?
  - Most common cause of breakthrough seizures is not taking the medication
    - Let your practitioner know if you do not tolerate a medication or often forget to take them
  - Minimize number of medications taken at same time
    - However, there is often an overlap period for transition
  - Sometimes, a combination of AEDs is helpful
  - Most people (>60%) can have their seizures controlled with AEDs, but for those who fail three or more AEDs, surgery should be considered

# List of common AEDs (Brand)

- Phenobarbital<sup>1912</sup>
- Phenytoin (Dilantin)<sup>1938</sup>
- Valproate (Depakote)<sup>1978</sup>
- Carbamazepine (Tegretol)<sup>1974</sup>
- Oxcarbazepine (Trileptal)<sup>1999</sup>
- Ethosuximide (Zarontin)<sup>1960</sup>
- Benzodiazapines
- Levetiracetam (Keppra)<sup>2000</sup>
- Lamotrigine (Lamictal)<sup>1995</sup>
- Lacosamide (Vimpat)<sup>2008</sup>
- Pregabalin (Lyrica)<sup>2005</sup>
- Gabapentin (Neurontin)<sup>1994</sup>
- Topiramate (Topamax)<sup>1996</sup>
- Zonisamide (Zonegran)<sup>2000</sup>
- 1<sup>st</sup> Generation
- 2<sup>nd</sup> Generation
- 3<sup>rd</sup> Generation

# List of less common AEDs

- Clobazam (Onfi) <sup>2011</sup>
- Ezogabine (Potiga) <sup>2011</sup>
- Perampanel (Fycompa) <sup>2013</sup>
- Felbamate (Felbatol) <sup>1993</sup>
- Rufinamide (Banzel) <sup>2008</sup>
- Vigabatrin (Sabril) <sup>2009</sup>
- Tiagabine (Gabitril) <sup>1997</sup>
- Primidone (Mysoline) <sup>1954</sup>
- Eslicarbazepine
- Breviracetam

# Medication (Brand name)

- Seizure-type indication
- Metabolism (how it is processed)
- Some possible side effects
  
- Comments

# Phenobarbital

- Broad spectrum
  - Avoid in absence & myoclonic seizures
- Enzyme inducer (liver metabolism) & long half-life
- **Somnolence**/cognition & behavioral (dose)
- Long term effects on bone health
  
- Wean down slowly
- Used less frequently now than previously

# Phenytoin (Dilantin)

- Usually used with partial seizures
- Levels nonlinear (hard to control) & enzyme inducer
- Toxic: Dizziness, coordination, sedation/cognition
- Long term: Osteoporosis, gingival hyperplasia, cerebellar syndrome
  
- IV form available, generic, common

# Valproate (Depakote)

- Broad spectrum (e.g., absence, myoclonic)
- Inhibits metabolism
- Somnolence/cognition (ammonia), weight gain, hair loss, tremor
- Liver & pancreas toxicities, low platelets, teratogen
- IV form available, generic, common



# Carbamazepine (Tegretol)

- Partial seizures
- Enzyme inducer
- Coordination, diplopia, somnolence, nausea
- Rash (HLA-B Asians), blood reactions, low sodium, liver toxicity, osteoporosis
  
- Generic, common

# Oxcarbazepine (Trileptal)

- Partial seizures
  - Pro-drug of carbamazepine, often better tolerated
- Not self-inducing, but still involved liver metabolism
- Dizziness, diplopia, rash, low sodium
  
- Recently was non-formulary

# Levetiracetam (Keppra)

- Partial (and generalized) seizures
- Minimal drug interactions
- Mood disturbance (irritability), somnolence
- Relatively easy to use

# Lamotrigine (Lamictal)

- Partial and generalized seizures
  - Except for severe myoclonic
- May be affected by enzyme-inducers/inhibitors
- **Rash**, & some dizziness, mild tremor, less sedation
- Slow titration up; increase in pregnancy

# Lacosamide (Vimpat)

- Partial (& generalized) seizures
- Minimal drug interactions
- Dizziness, gait difficulties, nausea
- Watch if history of EKG abnormalities (PR increase)
- **Non-formulary**, still brand-only

# Gabapentin (Neurontin)

- Partial seizures
- Minimal drug interactions
- Peripheral edema (weight gain), somnolence, dizziness
- Used often for chronic pain & neuropathy

# Pregabalin (Lyrica)

- Partial seizures
- Minimal drug interactions
- Edema/weight gain, dizziness/somnolence
- Similar to gabapentin, but **non-formulary**

# Topiramate (Topamax)

- Partial and generalized seizures
- Some hepatic induction
- **Cognition/somnolence**, weight loss
- Kidney stones, glaucoma, metabolic acidosis



# Zonisamide (Zonegran)

- Partial (& generalized) seizures
- Cognition, weight loss, kidney stones, rash
- Recently was non-formulary

# Special cases

- Because of relative lack of drug interactions, lamotrigine and levetiracetam are commonly used in elderly patients
- For women of child-bearing age, valproate is typically avoided. Lamotrigine, levetiracetam and zonisamide are commonly used.

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  - Commonly used AEDs
  - Benefits versus Risks

# Take Home Point

- Work with your practitioner
  - Let them know how things are going
    - Seizure frequency and side effects
  - Please let them know if you cannot take a medication

# Questions?

- For more information: <http://www.epilepsy.va.gov/>
- Thank you