ANTI-SEIZURE MEDICATION REVIEW

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Objectives

- Understand the basic pathophysiology, classification, and precipitating conditions and causes of seizures.
- Identify medications that can lower seizure threshold
- Demonstrate understanding of available dosage forms and requirements for sterile preparation, compatibility, beyond use dating, and auxiliary labeling for anti-seizure medications
- Describe common side effects of anti-seizure medications
Prevalence

- Epilepsy is the nation’s 4th most common neurological disorder
  - Behind migraine, stroke, and Alzheimer’s
- 2.2 million Americans have epilepsy
- 150,000 new cases are diagnosed in the United States each year
- 1 in 26 people will develop epilepsy in their lifetime
- Epilepsy has an annual direct medical cost in the United States of $9.6 billion
- Around 10% of people worldwide will suffer at least one seizure in their lifetime
Definitions

- **Seizure** = an event
  - an episode of neurologic dysfunction where the abnormal firing of neurons produces motor, sensory, and autonomic dysfunction.

- **Epilepsy** = a disorder/syndrome
  - a condition characterized by recurrent spontaneous seizures as a result of neurological dysfunction.
  - No immediately identifiable cause

- **AED** = Antiepileptic drug

PHYSIOLOGY

Seizures
Brain
Inducing Conditions
Drugs that can lower seizure threshold
Seizure Physiology

- Excitatory and inhibitory signals mediated by ion channels
  - Voltage-gated channels
    - Excitatory: Sodium and Calcium
    - Inhibitory: Potassium
  - Ligand-gated channels
    - Glutamate: primary excitatory neurotransmitter
    - Gamma-aminobutyric acid (GABA):
      - primary inhibitory neurotransmitter
Seizure Physiology

- Balance between neuronal excitation and inhibition is altered
- Rapid firing of repeat action potentials → prolonged depolarization
- Neurons within the brain are activated in an unusual synchronous manner

http://www.mindcreators.com/neuronbasics.htm

Brain Physiology

Inducing Conditions

- Neurological disorder
- Sleep deprivation
- Alcohol intoxication
- Drug withdrawal
- Menstruation
- Infection
- Fever
- Hyponatremia
- Hypoglycemia
- Cerebral hemorrhage
- Tumor

Drugs that can lower the Seizure threshold

- Antipsychotics
  - clozapine,phenothiazines, butyrophenones
- Antivirals
  - amantadine, rimantadine, foscarnet, ganciclovir, acyclovir IV
- Bupropion
- Carbapenems
  - Poor renal function
  - Especially Imipenem
- Cephalosporins
- Fluoroquinolones
- Lindane
- Lithium and theophylline
  - in toxicity
- Meperidine
  - poor renal function
- Metoclopramide
- Penicillins
Age

- Highest frequency of newly diagnosed cases
  - children <5
  - adults >65:
    - represent 25% of new seizures diagnosed
- The incidence of seizures is highest during the first decade of life, especially within the first year
- The developing brain is most susceptible to changes altering the excitatory-inhibitory balance
  - Unequal brain development
    - Excitatory>inhibitory
    - Depolarization>repolarization
    - GABA has excitatory effect vs inhibitory
- Elderly: degenerative CNS diseases, brain tumors, cerebrovascular disease

SEIZURES WITHOUT IMMEDIATE UNDERLYING CAUSE

- Focal
- Tonic-Clonic (grand mal)
- Absence (petite mal)
- Myoclonic
- Tonic
- Atonic
Classifications

- Status Epilepticus
  - Seizures lasting longer than 5 minutes or 2 or more seizures where a patient does not regain consciousness
  - Multiples subtypes
- Partial (Focal)
  - Stem from a certain location in the brain with symptoms that reflect that area
- Generalized
  - Simultaneous abnormal electrical activity from both hemispheres of the brain
  - Consciousness is impaired

Focal Seizures

- Initial onset from localized area of the brain
- Often due to localized injury, but majority are idiopathic
  - ie tumor, stroke, trauma
- Can be subtle, often mistaken for daydreaming
  - Usually lasting less than a minute
- No longer distinction between different types
  - ie complex partial and simple partial
- Preferred Descriptors:
  - Without impairment of consciousness (simple partial)
  - With impairment of consciousness (complex partial)
  - Evolving to bilateral, convulsive seizure (secondarily generalized seizure)
Tonic-clonic Seizures (grand mal)

- Often begin with a sudden “epileptic cry”
- Loss of consciousness with tonic (stiff) contraction of muscles throughout the body
  - Contractions become clonic (jerk like) and can persist for several minutes
- The individual may drool or lose control of their bladder (~35%)
- Duration: 2-5 minutes
- Post-ictal period with confusion, flat affect, and lethargy
  - Headaches and muscle soreness common

Absence Seizures (petite mal)

- Almost always begin during childhood
- Characterized by staring, loss of facial expression, unresponsiveness, cessation of activity, eye blinking or upward eye movement
- Duration: Start and stop abruptly, lasting <1 minute
- Mental function immediately returns, but with no memory of the event
- Brief post-ictal period

Myoclonic

- Brief but significant muscle jerk that typically involve the upper body
  - Can involve the lower body as well
- No loss of consciousness
- Often occur after awakening
- Duration: 1-2 seconds
- Also occur in health individuals as they fall asleep

Clonic

- Series of sudden rhythmic muscle contractions and relaxations (myoclonus) that occur repeatedly
Tonic

- Brief stiffening of the muscles throughout the body
- More common during sleep, or immediately after awaking
- No loss of consciousness
- Duration: < 20 seconds
- Recovery is quick

Atonic

- Onset often between 2-5 years old
- Sudden and total loss of muscle tone and posture control
  - Eyelids drop, sudden fall to the ground
- Often falling head first
  - Facial/head injuries common
- No loss of consciousness
- Duration: < 1 minute
Pseudoseizures

- Seizures occurring on a psychogenic basis
- Many patients will have both pseudoseizures and epilepsy
- Extremely difficult to differentiate
- Signs:
  - Repeatedly normal EEG
  - Lack of response from medications
  - Personal or family history of psychiatric disease

Electroencephalography (EEG)

- Measures electrical activity within the brain
- Role:
  - Confirmation of the presence of abnormal electrical activity
  - Information on the type of seizure
  - Location of the seizure focus
- EEG findings alone do not diagnosis epilepsy
- 5% of individuals without epilepsy will have abnormal EEGs
- 50% of those with epilepsy will have normal findings on their first EEG
Repeated Seizures

- The consequences of seizures increase with their duration and frequency
- Seizures actually promote further seizure activity via neuronal damage and depleted ATP
- Kindling effect
  - Process where a normal brain gradually becomes epileptic as a result of repeated seizures

Starting Treatment

- Rule out an acute reversible medical problems or precipitating factors
- Refer to neurologist
- Therapy typically delayed until patient experiences a second unprovoked seizure
- Type of seizures
  - Therapy not indicated for certain types
  - Type of seizure guides treatment
- Start low and go slow
General Goals of Drug Therapy

- Complete suppression of seizure in the absence of disabling side effects
  - Roughly half of newly diagnosed patients will achieve this goal after institution of monotherapy
- When we are unsuccessful, the goal is to achieve the best balance between seizure control and minimizing side effects
- Monotherapy is preferred for most

Treatment Failure

- The first medication should be titrated up to maximum tolerated dose
- Second agents can be added
  - Titrate up second agent, then titrating down first agent
- Monotherapy should be tried until 2-3 individual drugs have failed before advancing to combination therapy
- Roughly 80% can become seizure free with AED treatment
AED Timeline

Monitoring

- Presence of seizures
- Changes in frequency, seizure free intervals, changes in presentation, pattern, or duration?
- Adverse medication effects?
- Laboratory tests
  - Baseline and periodically during treatment
- Drug levels

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<th>AED</th>
<th>&quot;Usual&quot; Daily Dose</th>
<th>Reference Range</th>
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<tr>
<td>carbamazepine</td>
<td>400-1800 mg</td>
<td>4-12 ug/ml</td>
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<td>ethosuximide</td>
<td>500-1600 mg</td>
<td>40-100 ug/ml</td>
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<td>felbamate</td>
<td>1200-4500 mg</td>
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<tr>
<td>levetiracetam</td>
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<td>oxcarbazepine</td>
<td>600-2700+ mg</td>
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<td>200-400+ mg</td>
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<tr>
<td>zonisamide</td>
<td>100-500+ mg</td>
<td>1.5-40 ug/ml</td>
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</table>

Common Concerns with Anti-Epileptic Therapy

- Pregnancy Category
- CNS S/E’s
- Suicide Risk
- Rash
- Drug Interactions
- Fracture Risk
- Abrupt Discontinuation

Pregnancy Categories

- D:
  - Carbamazepine
  - Clonazepam
  - Phenobarbital/Primidone
  - Phenytoin/Fosphenytoin
  - Topiramate
  - Valproate
- All others are category C
CNS Side Effects

• Drugs must penetrate the CNS to be effective
  → CNS side effects:
    Dizziness
    Somnolence
    Cognitive dysfunction

• FDA warning:
  • Valproate exposure in utero associated with decreased IQ score

Suicide Risk

• Medguide required:
  • “Like other antiepileptic drugs, this medication may cause suicidal thoughts or actions in a very small number of people, about 1 in 500”

• FDA placebo controlled studies in 2008
  • Increased risk seen from within one week to completion of study at 24 weeks
  • Risk seen in all of the 11 AEDs included

• Overall risk is low
  • Does not outweigh benefits of AED treatment
Rash

- Many AEDs will cause a rash within the first few weeks of therapy
- Severe idiosyncratic reactions involving fever and mucocutaneous lesions:
  - Stevens-Johnson syndrome (SJS)
  - Toxic epidermal necrolysis (TEN)
  - Drug rash with eosinophilia and systemic symptoms (DRESS)
- Associated with numerous AEDs
- Risk is highest within first two months of use
- HLA-B*1502 screening prior to carbamezepine, oxcarbazepine, and phenytoin
  - Asian ancestry

Drug interactions

- Many AEDs are metabolized by the liver
  - Inducers: Phenytoin, phenobarbital, carbamazepine, primidone
  - Inhibitor: Valproic acid
- Other drugs can alter concentrations of anti-epileptic medications
- Drug interactions should always be screen when starting AED therapy or adding a medication for a patient already on it
  - warfarin, oral contraceptives, antibiotics, antidepressants, statins
Fracture Risk

- Mechanism not fully understood
- AED induction reduces vitamin D and calcium levels
- Bone loss can begin within two years of beginning therapy
- All patients on AED therapy should also be taking vitamin D and calcium supplementation

Discontinuation

- Often considered after 2-4 years being seizure free
- Should always be tapered slowly
  - One drug at a time if taking multiple AEDs
  - No universal guidelines
  - Benzodiazepines and barbiturates should be discontinued gradually to avoid withdrawal seizures
Test Your Knowledge

• Which of the following are known to lower the seizure threshold?

A. Demerol (meperidine)
B. Primaxin (imipenem/cilastatin)
C. Infection
D. Reglan (metoclopramide)
E. All of the above

Test Your Knowledge

• Which of the following are common concerns to consider with anti-epileptic medications?

A. Pregnancy Category
B. Drug Interactions
C. Abrupt Discontinuation
D. Suicide Risk
E. All of the above
How to handle seizures

- Prevent injury: clear the area and person of any hard or sharp objects
- Ease the person to the floor and place something soft beneath their head
- Turn the person gently to their side to protect their airway
- Remove eyeglasses, loosen ties, etc
- DO NOT hold people down or try to stop their movements
- It is not possible to swallow one’s tongue during a seizure
- Do not give the person food or water until they are fully alert
- Reassure the individual

1ST GENERATION DRUGS

- Carbamazepine
- Ethosuximide
- Phenobarbital
- Phenytoin
- Valproic Acid
General Characteristics

- Broad familiarity
- Well-documented efficacy
- Lower cost
- More adverse effects as a group
- Complex pharmacokinetics
- Significant effects on liver enzymes
- Many drug-drug interactions

Carbamazepine (Tegretol)

- Blocks fast sodium channels
- First line therapy:
  - Generalized tonic-clonic
  - Focal
- Adjunctive therapy:
  - Myoclonic
- NOT used for:
  - Absence seizures
- Also used for:
  - Bipolar disorder
  - Neuropathic pain
  - Restless legs syndrome

Photo via: http://middlesexhospital.org/our-services/hospital-services/the-comprehensive-sleep-center/services/restless-leg-syndrome-rls
Accessed [09-01-2014].
Adverse Reactions

- Hyponatremia
- Bone marrow suppression (black box warning)
- Rash
  - Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis
    - Asian heritage
    - HLA-B*1502
- Hepatotoxicity
- Osteomalacia
- Drug-Drug Interactions:
  - Auto-inducer
  - ↓ birth control effectiveness
  - ↓ valproic acid levels
  - ↑ levels with concomitant lamotrigine or valproic acid

Stevens-Johnson Syndrome

Clinical Pearls

- Need to titrate dose
  - Nausea, vomiting, sedation, diplopia
- Typical dosage range
  - 400-2400 mg/day divided BID-QID
- Requires therapeutic monitoring
  - 5-12 mcg/mL
- Linear kinetics
- Transient cognitive effects

Therapeutic Equivalents

<table>
<thead>
<tr>
<th>Extended-Release Capsule</th>
<th>Carbamazepine ER capsule</th>
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<tbody>
<tr>
<td>Carbatrol 100mg, 200mg, 300mg</td>
<td>Carbamazepine ER capsule</td>
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<td>Equetro 100mg, 200mg, 300mg</td>
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<th>Extended-release tablet</th>
<th>Carbamazepine ER tablet</th>
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<table>
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<tr>
<th>Tablet</th>
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<td>Tegretol 200 mg</td>
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<table>
<thead>
<tr>
<th>Chewable tablet</th>
<th>Carbamazepine tablet</th>
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<td>Tegretol chewable tablet 100mg</td>
<td>Epitol</td>
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<table>
<thead>
<tr>
<th>Oral suspension</th>
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<tbody>
<tr>
<td>Tegretol</td>
<td>Carbamazepine</td>
</tr>
</tbody>
</table>
Test Your Knowledge

• Which of the following is a therapeutic equivalent to Tegretol XR

A. Carbamazepine XR capsule
B. Carbamazepine XR tablet
C. Carbamazepine oral solution
D. Carbamazepine chewable tablet
E. A and B

Ethosuximide (Zarontin)

• Blocks T-type calcium channels
• FDA approved for absence seizures – DOC
• Maintenance dose: 1500 mg/day divided BID
• Therapeutic range: 40-80 mcg/mL
• Available as capsules and solution
• Adverse reactions:
  • Common
    • Nausea and vomiting (40%)
    • CNS
  • Rare
    • SJS
    • Lupus-like syndrome
    • Blood dyscrasias
Phenobarbital (Luminal)

- GABA receptor agonist, modulates Na, Ca, and K conductance
- FDA Indications:
  - Generalized tonic-clonic seizures
  - Partial seizures
  - Status epilepticus
  - Non-epileptic use:
    - Anxiety (sedative hypnotic)

Adverse Reactions

- One of most sedating antiepileptics
- Hyperactivity
- Cognitive impairment
- Physical dependence
- Withdrawal symptoms
- Tissue damage with extravasation or intra-articular injection
- Drug-drug interactions
  - birth control effectiveness
Dispensing

- CIV
- Typical maintenance dose
- Oral: 50-100 mg/day divided BID-TID (400 mg max)
- IV: 100-320 mg/day (600 mg max)
- Therapeutic level: 15-40 mcg/mL
- Dosage forms
  - Tablet
  - Oral solution
  - Injection
  - Primidone (Mysoline) tablets = prodrug

Phenobarbital injection

- 65 mg/mL or 130 mg/mL
- Can give IM (max 5 mL) or IV
- Avoid SC or intra-arterial
- Stable in NS, 1/2NS, D5W, LR
- Incompatible with pantoprazole and hydromorphone in both Y-site and syringe
Phenytoin (Dilantin)

- Blocks fast sodium channels
- FDA approved for:
  - Partial seizures (simple or complex)
  - Generalized tonic-clonic (not first line)
- NOT used for absence seizures
- Dosing
  - 300-600 mg/day
  - 7-10 days to reach steady state
  - 90% protein bound
  - Therapeutic: 0.5-3mcg/mL (free) 10-20 mcg/mL (total)
  - Nonlinear kinetics
  - Suspension, tablet, chewable tablet, injection

Adverse Reactions

- Dose limiting
  - Nystagmus
  - Ataxia
  - Sedation
- Long term
  - Gingival hyperplasia
  - Vitamin D/folic acid deficiency
  - Peripheral neuropathy
  - Hirsutism
  - Acne
  - Coarsening of facial features
- Rare
  - SJS
  - Lupus-like syndrome
  - Bone marrow suppression

Therapeutic Equivalents

<table>
<thead>
<tr>
<th></th>
<th>Extended-Release Capsule</th>
<th>Chewable tablet</th>
<th>Oral Suspension</th>
<th>Capsule</th>
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<tr>
<td>Phenotype 200 mg, 300 mg</td>
<td>Phenytoin sodium extended capsule</td>
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<tr>
<td>Dilantin 100 mg capsule</td>
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<tr>
<td>Dilantin 50 mg chewable tablet</td>
<td>Phenytoin</td>
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<tr>
<td>Dilantin-125 suspension</td>
<td>Phenytoin</td>
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<tr>
<td>Dilantin 30 mg Capsule</td>
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Fosphenytoin (Cerebyx)

- Water-soluble prodrug of phenytoin
  - 1 mg phenytoin = 1.5 mg fosphenytoin = 1 mg PE
- Adverse effects: nystagmus, ataxia, sedation
- Formulation: solution for injection
  - Preferred over phenytoin for IV administration
    - Phenytoin dilution = crystallization
  - Dilute with D5W or NS to concentration of 1.5 to 25 mg PE
  - Max infusion rate: 150 mg PE/min
    - Max phenytoin infusion rate: 50 mg/min
  - Refrigerate after preparation
  - Expires after 48 hours at room temperature
Test Your Knowledge

Which of the following are true regarding phenytoin and fosphenytoin?

A. Phenytoin can be infused at a faster rate than fosphenytoin
B. Phenytoin can be administered by IM injection
C. Common side effects of fosphenytoin and phenytoin include nystagmus, ataxia, and sedation
D. Fosphenytoin comes as an oral suspension
E. Fosphenytoin is a generic equivalent of phenytoin

Valproic Acid (Depakene)

- Increase GABA levels in CNS
  - Some effect on Na and Ca channels
- FDA approved for:
  - Absence seizures
  - Partial seizures (simple or partial)
  - Tonic-clonic seizures
- Dosing
  - Formulations: solution, DR capsule, injection, tablet, sprinkle capsule, ER tablet
  - 15-60 mg/kg/day divided BID
  - Highly protein bound
  - Therapeutic range: 50-100 mcg/mL (4-15 mcg/mL free fraction)
  - IV:PO = 1:1
Adverse Reactions

• Common:
  • Hair loss
  • GI (20%)  
    • Solution tastes bad – high association with nausea
  • Weight gain or anorexia
  • CNS
  • Tremor (more at increased doses)

• Rare:
  • Hepatotoxicity
  • Thrombocytopenia

• Pregnancy category X/D
  • Most teratogenic of all antiepileptics
    • Fetal malformations
    • Effects on IQ

Therapeutic Equivalents

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<th>Valproic Acid</th>
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<td>Depakene Capsule 250 mg</td>
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<td>Depakene Syrup 250mg/5mL</td>
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<td>Stavzor Delayed-release capsule 125 mg, 250 mg, 500 mg</td>
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<td>None</td>
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<tr>
<td>Valproate Sodium Injection</td>
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<td>Depacon 100 mg/mL</td>
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<tr>
<td>Divalproex - all available as generic</td>
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<tr>
<td>Depakote Delayed-release, EC 125 mg, 250 mg, 500 mg</td>
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<tr>
<td>Depakote extended-release tablets 250 mg, 500 mg</td>
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<td>Depakote Srinkles 125 mg</td>
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</table>
IV Preparation

- Dilute with 50-100 mL D5W, NS, or LR
- Infuse over 60 min or max rate of 20 mg/min
- BID if dose >250 mg/day
- Incompatible (Y-site) with vancomycin
- Do NOT refrigerate
- Expires 24 hours after preparation

2ND GENERATION DRUGS

- Gabapentin
- Pregabalin
- Lacosamide
- Oxcarbazepine
- Topiramate
- Zonisamide
- Felbamate
- Lamotrigine
- Levetiracetam
- Vigabatrin
Gabapentin (Neurontin®)

- FDA-Labeled Indications:
  - Partial seizures (adjunct)
  - Postherpetic neuralgia

- Dosing (Partial Seizure):
  - Initial: 300 mg three times a day
  - May increase up to 1800 mg/day (in 3 doses)
  - 2400 mg/day has been tolerated as well

- ADRs: sedation, ataxia, and dizziness common during initiation. Weight gain or peripheral edema

Gabapentin (Neurontin®)

- Requires dose adjustment for renal impairment
- Can also be used for: peripheral neuropathy, restless leg syndrome, fibromyalgia, hot flashes
- Available as Capsules, Tablets, and oral suspension
- Tablets (under trade name Gralise®)
  - Do not split, chew, or crush tablets
  - Swallow tablet whole with evening meal
- Tablets (Neurontin®)
  - Can be split, discard unused half-tabs in several days
  - Take with or without food
Pregabalin (Lyrica®)

- FDA-Labeled Indications:
  - Partial Seizures (adjunct)
  - Diabetic peripheral neuropathy, neuropathic pain
  - Fibromyalgia
  - Postherpetic neuralgia

- Dosing (Partial Seizure):
  - Initial: 75 mg orally twice daily, or 50 mg three times daily
  - Titrate based on response and tolerability. Maximum 600 mg/day

Pregabalin (Lyrica®)

- ADRs:
  - Dizziness, sedation, dry mouth, edema, blurred vision, weight gain, cognitive impairment
  - Serious: PR prolongation, angioedema, myopathy, decreased platelet count

- Requires dose adjustment for renal impairment
- Can also be used for: social phobia, restless leg syndrome, anxiety
- Available as capsule and oral suspension
- Schedule V Controlled Substance, Brand Only
Lacosamide (Vimpat®)

- Slow sodium channel blocker
- FDA-labeled indications:
  - Partial Seizures (monotherapy and adjunct)
- Dosing (both PO and IV):
  - Monotherapy: initial 100 mg twice daily, increase weekly by 50 mg twice daily up to 150 to 200 mg twice daily
  - Adjunct: initial 50 mg twice daily, increase weekly by 100 mg/day in 2 divided doses up to 200 to 400 mg/day
- ADRs: nausea, dizziness, headache, double vision
- Requires dose adjustments for renal and hepatic impairment
- Schedule V Controlled Substance, Brand Only
- Available as IV solution, Oral solution, and oral tablet

IV Preparation

- Can be administered without dilution
- If diluted can use NS, D5W, or LR
  - Diluted solution must be stored at room temperature
  - Use within 4 hours

Administration

- Infuse over 30-60 minutes

DO NOT REFRIGERATE
Test Your Knowledge!

Which of the following medications are FDA-indicated for partial seizures as well as neuropathic pain?

   I. Gabapentin
   II. Lacosamide
   III. Pregabalin
   IV. Topiramate

a) I only  
b) III only  
c) I & III  
d) I, II, & III  
e) IV only

Oxcarbazepine (Trileptal®)

- Blocks voltage gated sodium channels
- FDA-labeled indications
  - Partial Seizure (monotherapy and adjunct)
- Dosing:
  - Monotherapy:
    - Initial 300 mg twice daily,
    - Increase dose 300 mg/day every third day to 1200 mg/day target
    - 2400 mg/day target if converting from other antiepileptic medication
  - Adjunct:
    - Initial 300 mg twice daily (IR) or 600 mg once daily (ER)
    - Increase by 600mg/day at weekly intervals to 1200 – 2400 mg/day
- ADRs: abdominal pain, nausea, vomiting, involuntary muscle movements, dizziness, headache, somnolence
- Requires dose adjustments in renal and hepatic impairment
- Available as: ER tab, IR tab, IR oral suspension
Oxcarbazepine (Trileptal®)

**Administration**

- **ER tablets**
  - Empty stomach, 1 hr before or 2 hrs after a meal
  - Swallow whole, no crushing or chewing
- **IR tablets**
  - Can be taken with or without food
- **IR Suspension**
  - Shake well
  - Can be given directly from oral syringe or mixed in small glass of water just prior to administration

Topiramate (Topamax®)

- Blocks voltage gated sodium channels, augments GABA activity
- FDA-labeled indications:
  - Partial seizure (monotherapy and adjunct)
  - Tonic-clonic seizure (monotherapy and adjunct)
  - Migraine prophylaxis
- Dosing:
  - 25 mg twice daily (IR) or 50 mg once daily (ER)
  - Titrated up weekly to MAX dose of 200 mg twice daily (IR) or 400 mg daily (ER)
- ADRs: loss of appetite, weight loss, confusion/impaired cognition, dizziness, impaired psychomotor performance, memory impairment, reduced concentration, somnolence, tingling
- Dose adjustments for renal impairment and geriatrics
- Other Uses: alcoholism, eating disorders, essential tremor, obesity
- Available as: sprinkle capsule, tablet, and ER capsule, generic
Topiramate (Topamax®)

Administration
• May be taken without regard to meals
• IR tablets:
  • Do not break, has bitter taste
• IR capsules:
  • Can be swallowed whole or contents can be sprinkled on a teaspoon of soft food. Swallow immediately, do not chew
• ER capsules:
  • Do not chew, crush, or sprinkle
  • Avoid alcohol 6 hrs before and after

Quick Phone Call…

A nurse calls down to the pharmacy and asks if she can crush oxcarbazepine ER tablets and put them in apple sauce for a patient that has a feeding tube.
• Can she crush the medication?
• If not, what can you recommend?
**Zonisamide (Zonegran®)**

- Blocks sodium channels
- FDA-labeled indications
  - Partial Seizure (adjunct)
- Dosing:
  - Initial: 100 mg/day
  - Increase by 100 mg/day every 2 weeks to the usual effective dose range or 100-600 mg/day in 1-2 divided doses
- ADRs: Loss of appetite, somnolence, dizziness, agitation, inability to concentrate, speech disturbance, depression
- May require slower titration and more frequent monitoring in renal and liver impairment
- Other uses: partial seizure monotherapy, migraine prophylaxis, Parkinson’s disease
- Available as: capsules, generic

**Administration**

- May take with or without food
- Swallow whole, do not bite or break
- Use caution with alcohol
- Keep hydrated

DO NOT CHEW OR CRUSH. SWALLOW WHOLE.

http://www.vetrxdirect.com/images/6175-1.jpg
### Felbamate (Felbatol®)

- NMDA receptor antagonist, blocks excitatory amino acids, suppressing seizure activity
- FDA-labeled indications:
  - Partial Seizure (adjunct)
- Dosing:
  - 1200 mg/day in 3-4 divided doses
  - Reduce other antiepileptic drugs by 20%
  - Increase in 1200 mg/day increments at weekly intervals to 3600 mg/day
- Dose adjustments for renal impairment. Contraindicated in hepatic impairment
- ADRs: Photosensitivity, weight loss, abdominal pain, constipation, indigestion
- Available as: Oral Suspension, Oral Tablet, generic

### Lamotrigine (Lamictal®)

- Fast sodium channel blocker, thus inhibiting glutamate the excitatory neurotransmitter
- FDA-labeled indications:
  - Partial seizure (adjunct or monotherapy)
  - Tonic-clonic seizure (adjunct)
  - Bipolar I disorder
- Dosing: (may differ when added to other anti-epileptics)
  - Initial 50 mg/day for 2 weeks, then 50 mg twice daily for 2 weeks
  - Increase dose by 100 mg/day every 1-2 weeks
  - Maintenance dose: 300-500 mg/day in 2 divided doses
- Consider dose adjustments in renal and liver impairment
- Never abruptly discontinue
- ADRs: Nausea, vomiting, blurred vision, diplopia, dizziness, rash (SJS, titrate slowly), toxic epidermal necrolysis
- Other uses: resistant depression, migraine, obesity, OCD, convulsions in newborns, trigeminal neuralgia
Lamotrigine (Lamictal®)

- Tablet
- Chewable Tablet:
  - May be swallowed whole, chewed, or dispersed in water or diluted juice
  - Use entire tablets only, round down to nearest whole tablet
  - Use 1 teaspoon, or just enough to cover the medication
- Oral Disintegrating Tablet (Brand):
  - Place onto tongue and move around in the mouth
  - May be swallowed with or without water and may be taken with or without food
- ER Tablet:
  - Swallow whole with or without food
  - Must not be chewed, crushed or divided

Levetiracetam (Keppra®)

- FDA-labeled indications:
  - Partial seizure (adjunct)
  - Myoclonic seizure (adjunct)
  - Tonic-clonic seizure (adjunct)
- Dosing:
  - Initial 500 mg daily for 2 weeks, then increase to 500 mg twice daily, titrate over two weeks as necessary
  - MAX dose 3000 mg/day
- Dose adjusted for renal and hepatic impairment
- ADRs: loss of appetite, vomiting, decreased bone mineral density, infection, headache, irritability, fatigue
- Other uses: Manic bipolar I disorder, migraine prophylaxis, partial seizure monotherapy
Levetiracetam (Keppra®)

- **IV Solution**
  - Dilute in 100 mL of a compatible diluent (NS, LR, D5W)
  - Diluted solutions stable for 24 hrs in polyvinyl bags at room temperature (15-30°C)
  - Infuse over 15 minutes
- **Oral Solution**
  - Children or patients 20 kg or less should be dosed with oral solution
  - Use calibrated measuring device
- **Tablet, ER Tablet**
  - Swallow whole, do not chew, break, or crush

Tech Check

An order for levetiracetam IV calls for a dose of 750 mg

- How many mL's of levetiracetam solution for injection do you need for the prescription?
  
  \[
  \frac{100 \text{ mg}}{1 \text{ mL}} = \frac{750 \text{ mg}}{X} \\
  X = 7.5 \text{ mL}
  \]

- How many vials of levetiracetam do you need?
  
  \[
  \frac{5 \text{ mL}}{1 \text{ vial}} = \frac{7.5 \text{ mL}}{X} \\
  X = 2 \text{ vials}
  \]

- What diluent can you use, and what volume is needed?
  - NS, LR, or D5W
  - 100 mL must be used
Test Your Knowledge

Which of the following is true of IV levetiracetam?

a) It is stable once diluted for 24 hours if refrigerated
b) It is stable once diluted for 24 hours at room temperature

Vigabatrin (Sabril®)

- Inhibits GABA transaminase, to increase GABA levels
- FDA-labeled indications
  - Complex partial epileptic seizure, refractory (adjunct)
  - West syndrome (epileptic disorder in infants)
- Dosing:
  - Initial 500 mg twice daily
  - Increase total daily dose in 500 mg increments at weekly intervals, depending on response, up to 1500 mg twice daily
- ADRs: weight gain, somnolence, tremor, blurred vision, nystagmus, respiratory infection, ear infection, liver failure, suicidal thoughts
- Only available through special restricted distribution program: SHARE (1-888-45-SHARE)
- Available as: oral tablet and oral powder for solution, Brand only
Summary

- Seizures are caused by either decreased inhibitory signals or increased excitatory signals in the CNS
- Medications work by either decreasing excitatory transmission or increasing inhibitory transmission
  - Largely accomplished through alteration of various voltage gated ion channels (sodium, potassium, calcium, etc.)
- Anti-seizure medications vary in formulations, potential adverse reactions, dosing, and administration
- Technicians can play a large role in preventing medication errors and promoting patient safety by staying up to date with anti-seizure medications

Sources

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Sources