# Seizure Update:
# Update On Seizure Disorders

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The content of my material/presentation in this CME activity will include discussion of unapproved or investigational uses of products or devices as indicated: Use of medical marijuana is investigational for seizure disorder. Evidence for its use will be discussed.

## Kate Rowland, MD, FAAFP

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Dr. Rowland is a graduate of Rush University Medical College in Chicago, Illinois. She completed her residency at Advocate Illinois Masonic Medical Center in Chicago. Dr. Rowland serves as editor-in-chief for the Family Physicians Inquiries Network's Priority Updates from the Research Literature series and is an associate medical editor for the AAFP's FP Essentials. Kate enjoys teaching about topics that aren't always easy to think about, and need research, synthesis, and empathy to understand. She also enjoys teaching about research and evidence-based medicine topics. Kate strives to make her lectures relevant to practice, thought provoking, and informative.

## Learning Objectives

1. Evaluate children presenting with febrile seizure in accordance to current AAP guidelines.
2. Develop individualized treatment plans for adult patients with an unprovoked first seizure, in accordance with current AAN/AES guidelines.
3. Establish protocols to routinely screen cognition, mood, and behavior in patients with new-onset epilepsy.
4. Evaluate the available evidence on the use of medical marijuana as a viable treatment option for seizures.

## Audience Engagement System

Step 1 Step 2 Step 3

## Seizures

- Seizure
  - *To be grabbed or taken*
  - Electrical discharges of the brain that cause alterations in behavior, consciousness, or sensation
- Epilepsy:
  - From the Latin (via the French): *To take hold of, to attack*
  - Defined as either:
    - Two unprovoked seizures, with the second occurring at least 24 hours after first
    - Or one unprovoked seizure with a >60% risk of having another within 10 years
- Early mentions in writings of Hippocrates
- Mentioned in Shakespeare

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## AES Question

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## AES Question 1

Febrile seizures:

A. Are correlated with a later risk of epilepsy
B. Are correlated with a later risk of learning disability
C. Are correlated with a family history of epilepsy
D. Will occur in up to 10% of children
E. Are common in children until age 12

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## Febrile Seizures

- Common in children 3 months-5 years
  - Can occur in older children
  - Will occur in up to 5% of children
- No known lasting neuropsych, behavioral, or intellectual sequelae
- May slightly increase the risk of epilepsy
  - Use of antipyretics to prevent is unclear
  - Use of antiepileptics does not seem to prevent
- FHx of febrile seizure increases risk of febrile seizures, but a FHx of epilepsy does not

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## Febrile Seizures

- Simple febrile seizures often require no further workup beyond a history and physical.

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## AES Question

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## AES Question 2

Which of the following are true regarding seizures?

A. Only general seizures involve loss of consciousness
B. Up to 20% of people will have at least 1 seizure during their lifetime
C. The majority of people who have one seizure will have a second seizure
D. Up to 4% of people will have a diagnosis of epilepsy
E. Epilepsy is more common in developed countries

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## Kinds of Seizures

- General
  - Involve both hemispheres of the brain
  - Characterized by loss of consciousness
  - Often manifest as "tonic-clonic"
- Partial or focal
  - Initially involve just 1 hemisphere, may spread
  - Variable presentation
  - May include behavioral, sensory, motor, or emotional changes
  - May include loss of consciousness

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## Risk Factors and Correlations

- Genetic disorders
- Neuroanatomic abnormalities or changes
  - Congenital anomalies
  - Degenerative diseases (Alzheimer disease)
- Metabolic disorders
- Demyelinating diseases
- CNS infections
- Anoxic or traumatic brain injuries
  - Birth injuries
  - Head injuries

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## Classifications

- Provoked seizures
  - Also called "situational" seizures
  - Traced to a specific, sometimes treatable cause
  - Patients with focal neurologic deficits after postictal phase are MUCH more likely to have an identifiable cause (97%) than those with return to baseline.
- Unprovoked seizures
  - Only meet definition of "epilepsy" if unprovoked

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## Provoking Factors

- Stroke
- Tumor
- Traumatic brain injury (recent or remote)
- Infection
  - Acute
  - Chronic (HIV)
  - Acute on chronic
- Surgery
- Drugs (prescribed, legal, and recreational)
  - Intoxication
  - Normal use
  - Withdrawal

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## Seizures are Common

- 10% of people will have at least 1 non-febrile seizure
  - Those with a normal EEG and no neuro sequelae:
    - 20% have a second seizure within a year
    - 5% more will have a second seizure by the second year of follow-up
    - 75% are seizure-free after two years
    - Neuro findings or EEG changes greatly increase recurrence rate
- Lifetime prevalence of epilepsy is 4%

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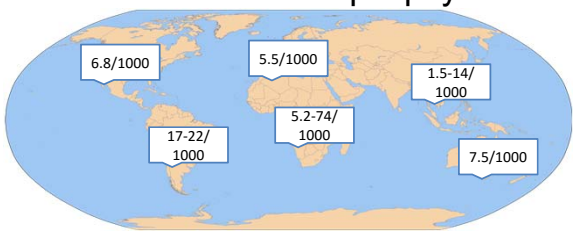
## Prevalence of Epilepsy

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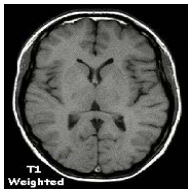
## Work-Up of Seizures in Adults

- Neuroimaging: CT or MRI
  - Usually noncontrast CT
- Labs: CBC, CMP, glucose, antiepileptic levels if appropriate, tox screen, alcohol level

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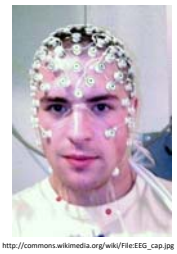
## Work-Up of Seizures in Adults

- LP if any reason to suspect CNS infection or subarachnoid bleed
- EEG
  - Within 3 days
  - Awake and asleep
  - Hyperventilation or light stimulation protocols



http://commons.wikimedia.org/wiki/File:EEG_cap.jpg

## 2015 AAN Guidelines

- Treatment of a first unprovoked seizure in adults
  - AAN recommends shared decision making after first seizure
  - After second, risk of third is 50+%, treatment is recommended

22

## Treatment of Seizures in Adults

- Strongly consider treatment:
  - Patients with EEG abnormalities
  - Patients with persistent deficits on neuro exam
  - Patients with known or discovered reason for seizure (tumor)
- These patients have the highest risk of recurrence and are most likely to benefit from treatment.

## Treatment of Seizures in Adults

- Determining which patients are likely to benefit from pharmacotherapy for seizures can be very difficult.
- Access to pharmacist comanagement can be useful if available.
- Lack of available neurology consultants can be a barrier to practice.

## Pharmacotherapy Options

- Phenobarbital
- Phenytoin (Dilantin)
- Valproic acid/divalproex (Depakote)
- Carbamazepine (Tegretol)
  - Oxcarbazepine (Trileptal)
- Gabapentin (Neurontin)
- Lamotrigine (Lamictal)
- Levetiracetam (Keppra)
- Topiramate (Topamax)
- Zonisamide (Zonegran)

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## Treatment Considerations

- Seizure type
- Side effects and toxicity
- Efficacy

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## Adherence to Medication

- For dozens of reasons, patients do not always take their medications as we ask them to.
- One study of patients with epilepsy found that 50-70% of AED doses are taken as prescribed.
- (An unrelated study of asthma patients found that about 50% met the long-term criteria of taking 70% of their doses as directed. Food for thought when we prescribe)

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## Pharmacotherapy Decisions

- Generalized seizures:
  - Levetiracetam 500 mg BID; titrate up to 1500 mg BID
  - Lamotrigine 25 mg daily; titrate up to ~125 mg BID
    - Use higher doses with concomitant carbamazepine, phenytoin or phenobarbital
    - Use lower doses with concomitant valproic acid
    - May cause Stevens-Johnson Syndrome
  - Valproate 15 mg/kg/day in 2 doses; titrate to no more than 60 mg/kg
  - Phenytoin 100 mg TID; titrate to 300-400 mg TID
    - 15 mg/kg/day in 3 doses loading then 5 mg/kg/day in 1-2 doses
    - May cause Stevens-Johnson Syndrome
  - Topiramate 50-100 mg daily; titrate to 200 mg BID
  - Zonisamide 100-200 mg daily or divided; titrate to 400-600 mg

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## Pharmacotherapy Decisions

- Partial and secondarily generalized:
  - Carbamazepine 2-3 mg/kg/day in 3 doses; titrate to 10 mg/kg
    - Multiple medication interactions
    - Risk of Stevens-Johnson syndrome
  - Lamotrigine
  - Levetiracetam
  - Gabapentin
  - Phenytoin
  - Topiramate
  - Valproate
  - Zonisamide

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## Pharmacotherapy Decisions

- Atonic or myoclonic seizures:
  - Lamotrigine
  - Levetiracetam
  - Lamotrigine
  - Topiramate
  - Zonisamide
- Absence seizures
  - Ethosuximide 20-40 mg/kg/day in 1-2 doses
  - Valproate

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## Pharmacotherapy Toxicity

- Therapeutic levels:
  - Phenobarbital: 10-40 mcg/mL
  - Phenytoin: 10-20 mcg/mL
  - Valproate: 50-100 mcg/mL
  - Ethosuxamide: 40-100 mcg/mL

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## AES Question

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## AES Question 3

Which of the following medications does not require any special considerations for women of childbearing age (regarding pregnancy or metabolism of contraception options)?

A. Carbamazepine
B. Lamotrigine
C. Phenytoin
D. Topiramate
E. Valproate

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## Special Considerations When Choosing an Antiepileptic

- Drug-drug interactions
  - Worse with older meds like valproate, phenytoin, carbamazepine
- Childbearing potential
  - Valproate: category D (neural tube defects)
  - Carbamazepine: category D (neural tube defects)
  - Topiramate: category D (palate defects)
- Contraception
  - Gabapentin, levetiracetam, lamotrigine, valproate among those with NO effect on OCPs
  - Carbamazepine, phenytoin, phenobarb, topiramate can decrease OCP effectiveness

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## AES Question

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## AES Question 4

Which of the following is true regarding the use of marijuana or cannabinoids for the treatment of epilepsy?

A. Consistent high-quality studies support its use
B. Studies support the use of cannabinoid oil only
C. Case studies support the use of cannabinoids in epilepsy
D. Moderate- and high-quality studies support the use of inhaled, oil, and edible forms of cannabinoids
E. Treatment with cannabinoids is indicated after a single seizure

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## Treatment Options for Drug-Resistant Epilepsy

- Surgery
- Ketogenic diets
- Vagal nerve stimulator
  - Partial seizures
- Evidence is unclear whether marijuana is effective
  - Lots of case studies, not a lot of high quality research

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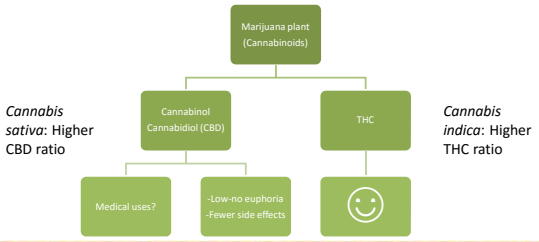
## Medical Marijuana

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## Medical Marijuana

- 2014 American Academy of Neurology systematic review
- Looked at 2 FDA-approved synthetic cannabinoids (dronabinol and nabilone)
- Also looked at "OTC" marijuana products
  - Nabiximols (Sativex) (THC/CBD spray; pharmaceutical abroad)
  - Oral cannabis extract (THC/CBD or CBD alone)
  - THC pills
  - Inhaled marijuana
- Only 2 available studies, both case series
  - No benefit seen
  - No significant AEs

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## Medical Marijuana

- RCTs underway
  - Use of CBD oil for Dravet syndrome
  - Use of CBD oil for Lennox-Gastaut syndrome
- Cohort study underway
  - Use of cannibis for pediatric epilepsy

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## More on Medical Marijuana

- 2015 study
- 75 children with refractory epilepsy received oral cannibis
- Parents were surveyed on perception of improvement
  - 1/3 reported at least 50% reduction
  - 0/8 with available data had any change in EEG

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## AES Question

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## AES Question 5

Which of the following conditions are not more common in patients with epilepsy than in the general population?

A. Benign essential tremor
B. Major depression
C. Memory impairment
D. Cognitive delay
E. Attention deficit disorder

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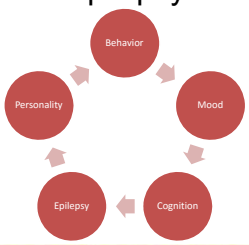
## Mood, Behavior, and Cognition in Epilepsy

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## Mood and Epilepsy

- Incidence of depression 30-60% of adults, ~25% of children with epilepsy
- >50% of patients with epilepsy and depression had mood symptoms for >1 year before any treatment was started
- 80% of neurologist report no screening for mood disorders: it's going to be us!

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## Cognition and Epilepsy

- By 9-12 months after first seizure, cognition delays are common
- Cognition delays or academic difficulty may predate epilepsy in children
  - ?neurologic insult causing both delay and seizure
- Progressive cognitive and memory impairments seen in adults

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## Behavior and Epilepsy

- Comorbid behavior diagnoses are common
  - ADHD
  - Psychotic disorders
  - Anxiety disorders
  - Aggression
  - Personality disorders
- May be due to:
  - Neurologic damage from seizures
  - Iatrogenic from seizure medicine
  - Stigma/coping of condition
  - Genetics; chance; luck

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## Primary Care of Mood, Cognition and Behavioral Problems in Epilepsy

- Neuropsych eval indicated
  - Cognitive or memory complaint
  - Academic underperformance
  - Developmental delay
- Screening for depression or mood disorders
  - Many of us already do this for adults and adolescents
- Multidisciplinary care
  - Neurology, psychology, psychiatry, interdisciplinary therapy

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## Seizure After Stroke

- Seizure as presenting sign of a stroke can be a poor prognostic feature
  - May indicate a large area of cerebral involvement
- Seizure during stroke recovery not uncommon
  - 3-23% incidence
- Generally do not begin antiepileptics for a single seizure within first 2 weeks after stroke
- Lamotrigine is preferred antiepileptic when treatment is needed
  - Recurrent seizure
  - Seizure >2 weeks after stroke

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## Special Considerations for Treatment

- Driving
  - All states have laws restricting patients with epilepsy from driving
  - Many set a seizure-free period (3-6 months is typical)
  - Some require the doctor to simply sign off (Illinois leaves it to my discretion!)

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## Nonepileptic Seizures

- "Pseudoseizure" or "psychogenic seizure"
- Seizures: electrical discharges of the brain that cause alterations in behavior, consciousness, or sensation
- Nonepileptic seizures: Involuntary alterations of behavior, consciousness, or sensation not associated with electrical discharges of the brain
- Factitious seizures: Voluntary alterations of behavior or apparent conscious to mimic a seizure

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## Nonepileptic Seizures

- Common, even among patients with epilepsy diagnosed by experts
- Dx should be considered in patients with treatment-resistant epilepsy
  - May coexist with epileptic seizures
- Considered a maladaptive coping strategy
- Treatment: affirming accurate diagnosis and psychotherapy

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## Practice Recommendations

- Simple febrile seizures often require no further workup beyond a history and physical. (SOR A)
- After first non-febrile seizure, discuss risks of recurrent seizure vs risk of treatment with the patient. After second, treatment is recommended. (SOR A)
- Many AEDs are teratogenic or reduce the efficacy of contraceptives (SOR B)
- Avoid marijuana for treatment of epilepsy until efficacy and safety can be established. (SOR *)

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## Coding

- Epilepsy: G40
  - Partial/generalized
  - Intractable/not intractable
  - Adult/childhood onset
  - Status/not status epilepticus
  - Adult-onset generalized controlled seizures not in status: G40.309
- Simple febrile seizure: R56.00
- Seizure due to alcohol: G40.5
- Psychogenic seizure: G44.5
- Post-traumatic seizure: R56.1

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# Questions

# Contact info

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# Billing & Coding

**When services performed in conjunction with:**

**Office Visit** 992xx *

*Time-based selection documentation criteria:

- Face-to-face time
- greater than 50% spent counseling/coordinating care

**Additional tests to confirm or monitor:**

**99490 Chronic Care Management-20 minutes monthly**

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