FIRST & SECOND SEIZURES: What to Know & What to Do

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I will discuss unapproved/investigative uses of a commercial product/device in my presentation.
As a result of attending this AZ AAP session, I encourage you to incorporate these changes in your practice:

- Distinguish when an event is a seizure
- Perform an initial work-up for a seizure
- Initiate at least two antiepileptic drugs for epilepsy
YOU NEED A SYSTEMATIC APPROACH TO ANSWER THE 5 FOLLOWING QUESTIONS IN A POSSIBLE FIRST OR SECOND SEIZURE

1. Was it a seizure?
2. What, if any, investigations to do?
3. When to treat?
4. Does status epilepticus change things?
5. What precautions are necessary?
1. WAS IT A SEIZURE?

Paroxysmal Events: Not Everything that Shakes is a Seizure!

- Neonatal apnea
- Breath-holding spells
- Syncope
- Dizziness and vertigo
- Migraine
- Acute confusional state/transient global amnesia
- Nightmares (REM)
- Night terrors (nREM)
- Somnambulism (nREM)
- Narcolepsy/cataplexy
- Sandifer syndrome (reflux)
- Tic
- Masturbation

- Dystonia
- Myoclonus
- Shuddering attacks
- Hyperekplexia
- Spasmus nutans
- Hyperventilation
- Arrhythmia
- Myocardial infarction
- Transient ischemic attack
- Daydreaming/attentional disorder
- Depression/fugue state
- Paroxysmal behavior outburst
- Psychogenic seizure (pseudoseizure)
1. WAS IT A SEIZURE?

**Definitions I**

- **Seizure** - an abnormal, paroxysmal, excessive synchronous neuronal discharge resulting in alteration of function or behavior.
- **Epilepsy** - recurrent seizures, without an acute precipitant. Thus, febrile seizures do not represent epilepsy.
1. WAS IT A SEIZURE?
Definitions II

- **Generalized seizure** - an abnormal, symmetrical neuronal discharge of both hemispheres, likely without focal onset, but perhaps originates inferiorly from thalamus. Always associated with loss of consciousness.
- **Focal (partial) seizure** - an abnormal focal cortical discharge in one hemisphere. Consciousness impaired when complex.
1. WHAT IS A SEIZURE?

Seizure Classification

Generalized
- Tonic-clonic (grand mal)
- Tonic
- Clonic
- Absence (petit mal)
  - Typical
  - Atypical
- Myoclonic
- Atonic (astatic, drop attack)

Focal (partial)
- Simple (motor, somatosensory, autonomic, or psychic)
- Complex
- Secondarily generalized

Unclassified epileptic seizures
Absence Seizures

- Staring spells, lasting 5-20 seconds
- Onset 5-6 years
- No aura, no postictal state
- Multiple episodes per day
- Mistaken for daydreaming or attention deficit disorder
- EEG with 3 per second generalized spike and wave
- Provoked by hyperventilation and photic stimulation
- Rarely associated with automatic behaviors or myoclonic movements of face or body (atypical absence)
- May resolve after several years
3 cycle-per-second spike and wave discharges in absence epilepsy
### SEIZURES
*Differentiating Atypical Absence and Complex Partial Seizures*

<table>
<thead>
<tr>
<th>Atypical absence</th>
<th>Complex partial</th>
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</thead>
<tbody>
<tr>
<td>• No aura</td>
<td>• May have aura</td>
</tr>
<tr>
<td>• Automatisms possible</td>
<td>• Automatisms likely</td>
</tr>
<tr>
<td>• &lt; 30 seconds</td>
<td>• &gt; 30 seconds</td>
</tr>
<tr>
<td>• Multiple events per day</td>
<td>• Rarely more than 1-2/day</td>
</tr>
<tr>
<td>• No postictal state</td>
<td>• May have postictal state</td>
</tr>
<tr>
<td>• Precipitated by hyperventilation</td>
<td>• Usually not precipitated by hyperventilation</td>
</tr>
<tr>
<td>• EEG: generalized 3 Hz spike and wave</td>
<td>• EEG: focal spikes, often temporal</td>
</tr>
</tbody>
</table>
1. WAS IT A SEIZURE?

Definitions III

- **Clonus** - unidirectional, rhythmic involuntary muscular contractions and relaxations
- **Myoclonus** - sudden, involuntary shock-like contractions of a group of muscles, often irregular in rhythm and amplitude, and sometime asymmetric in distribution
- **Aura** - an event that precedes ictal unconsciousness (e.g., déjà vu)
- **Prodrome** - a preictal physiological state change (e.g., vague uneasiness) hours or days before the onset of a seizure
- **Automatism** - a highly integrated, complex behavioral act that occurs during the seizures for which the patient has no recall afterwards (e.g., disrobing, clapping, walking in circles)
1. WAS IT A SEIZURE?

*Pearls*

- For episodes that occur frequently, home video is an excellent, cost-effective, first step.
- Eyes are open, not closed, during a seizure. Consider instead a psychogenic (i.e., non-electrical or behavioral) seizure.
- Patients with new-onset, daily seizures rarely have completely normal interictal EEGs.
- Seizures rarely produce “negative phenomena,” such as pallor, cold, apnea, and bradycardia. Consider instead syncope, breath holding spells, or prematurity.
- Directed acts of violence are not a feature of epilepsy. Consider instead rage attacks or other behavioral disorders.
- Conversion disorder and malingering, which can manifest as psychogenic seizures, are uncommon in the first decade.
2. WHAT, IF ANY, INVESTIGATIONS TO DO?

Is the patient a child with fever? Febrile Seizures

- Partial or generalized seizures with fever
- Occur ages 6 months to 5 years
- Complex febrile seizure = focal, ≥15 min, or twice in 24 hours
- Positive family history in 8-22%
- Relatively benign events
- Consider strongly lumbar puncture if <12 months
- Other tests should be ordered only to address the child’s underlying fever or illness
- Emergent head CT not warranted for complex febrile seizure, unless toxic, meningismus, or persistent post-ictal deficit/mental status change *Pediatrics* 2006;117:528
- Routine EEG is not warranted
2. WHAT, IF ANY, INVESTIGATIONS TO DO?

*Febrile Seizures*  
*Pediatrics* 2011;127:387

- A lumbar puncture should be performed in any child who presents with a seizure and a fever, and has meningeal signs and symptoms, e.g., neck stiffness, Kernig and/or Brudzinski signs, or in any child whose history or examination suggests the presence of intracranial infection.
- While clinical signs and symptoms of meningitis may be subtle in a child between 6 and 18 months of age, a lumbar puncture should not be performed routinely in a well-appearing child over 6 months of age.
- Since antibiotic treatment can mask the signs and symptoms of meningitis, a lumbar puncture is an option that should be considered in the child pretreated with antibiotics.
- A lumbar puncture should be considered in an infant younger than 18 months of age who presents with a seizure and fever and is considered to be deficient in immunizations, because of an increased risk of bacterial meningitis.
- No grop-a-gram (serum electrolytes, calcium, phosphorus, magnesium, CBC, or blood glucose)
- No neuroimaging
- No EEG
2. WHAT, IF ANY, INVESTIGATIONS, TO DO?


- CT emergently if persistent focal deficit or clouded mental status not resolving over 1-2 hours; otherwise non-urgent MRI after second or third seizure
- Routine EEG (but there is controversy! *Pediatrics* 2003;111:194 and *Neurology* 2000;54:635)
- Blood count or electrolytes should be ordered acutely only in circumstances such as vomiting, diarrhea, dehydration, or failure to return to baseline
- Lumbar puncture only if concern about meningitis or encephalitis
- Consider toxicology screen
3. WHEN TO TREAT?

Febrile Seizures

• Almost never!
• After first febrile seizure, 33% risk for more; after second, 50% risk for more
• 3% chance developing epilepsy by 7 years
• Risk factors for epilepsy: family history epilepsy; pre-existing neurologic deficit; complex febrile seizure
• Reserve treatment (phenobarbital or valproic acid), if possible, because no evidence establishes that reduction of recurrences prevents long-term sequelae, such as epilepsy, and the side-effects are significant

Pediatrics 2008;121:1281-6
3. WHEN TO TREAT?
Nonfebrile Seizures  Neurology 2003;60:166

- Only 1/3 of child with a first unprovoked seizure will have a second, and among those, slightly less than 1/3 will not experience a third seizure
- Antiepileptic drugs do not eliminate seizure recurrence and do not influence long-term elimination of epilepsy
- Start therapy after a second, third, or fourth spell, once benefits of therapy exceed the risks of medication side-effects
3. WHEN TO TREAT?

Which drug?

Generalized convulsive

- Valproic acid, topiramate, levetiracetam, and lamotrigine, perhaps clobazam, rufinamide, felbamate, or vigabatrin

Generalized nonconvulsive

- Absence: ethosuximide, valproic acid, maybe lamotrigine or zonisamide

Partial (focal)

- Oxcarbazepine, levetiracetam, carbamazepine, valproic acid, and topiramate, maybe lacosamide
Physicians should be comfortable starting at least a few of the antiepileptic drugs…

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Starting dosage</th>
<th>Maintenance dosage</th>
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</table>
| Carbamazepine (Tegretol, Epitol, Atretol) | Suspension 100 mg/5 ml  
Chewables 100 mg  
Tablets 200 mg  
Extended release tablets (Tegretol XR) 100, 200, 400 mg  
Extended release capsules (Carbatrol) 100, 200, 300 mg | 5-10 mg/kg divided BID to TID | 20-30 mg/kg/day |
| Ethosuximide (Zarontin)       | Syrup 250 mg/5ml  
Gel capsules 250 mg | 10-15 mg/kg divided BID | 15-50 mg/kg/day |
| Lamotrigine (Lamictal)        | Chewables 2, 5, 25 mg  
Tablets 25, 100, 150, 200 mg | 0.6 mg/kg divided BID (if not on valproic acid) | 5-20 mg/kg/day |
| Levetiracetam (Keppra)        | Syrup 100 mg/ml  
Tablets 250, 500, 750, 100 mg  
Intravenous 500 mg/5 ml | 10-20 mg/kg divided BID | 20-60 mg/kg/day |
| Oxcarbazepine (Trileptal)     | Suspension 300 mg/5ml  
Tablets 150, 300, 600 mg | 8-10 mg/kg divided BID | 30-45 mg/kg/day |
| Topiramate (Topamax)          | Sprinkles 15, 25 mg  
Tablets 25, 100, 200 mg | 1-3 mg/kg divided BID | 5-15 mg/kg/day |
| Valproic acid (Depakote, Depakene) | Syrup 250 mg/5 ml  
Sprinkles 125 mg  
Capsules 250 mg  
Tablets 125, 250, 500 mg  
Extended release tablets (Depakote ER) 250, 500 mg  
Intravenous (Depacon) 100 mg/ml | 10-15 mg/kg divided BID to TID | 30-60 mg/kg/day |

and be familiar with side effects…
3. WHEN TO TREAT?

“Newer” Drugs I

- **Fosphenytoin (Cerebyx)**
  - Water soluble, faster infusion rate, less infusion site reactions, same dosing as DPH
- **Valproic acid IV (Depacon)**
  - Approved for maintenance substitution, not status epilepticus
- **Diazepam rectal gel (Diastat)**
- **Oxcarbazepine (Trileptal)**
  - No hepatic auto-induction
  - Dosing 10-30 mg/kg day divided bid
  - Side-effects: hyponatremia, rash
- **Topiramate (Topamax)**
  - Blocks voltage-dependent Na⁺ channels
  - Dosing 3 to >10 mg/kg/day
  - Side-effects: nephrolithiasis, cognitive dulling, anorexia, hypohidrosis
- **Lamotrigine (Lamictal)**
  - Slow titration
  - Side-effects: rash, including Steven-Johnson syndrome, tics, insomnia
Also as 600 and 800 mg tablets
Now available as liquid preparation 250 mg/5ml

**Trileptal®**
(oxcarbazepine)

**Neurontin®**
(gabapentin capsules)

**Topamax®**
(topiramate tablets)

**Topamax® Sprinkle**
(topiramate capsules)

**Lamictal®**
(lamotrigine)

**Lamictal® Chewable Dispersible Tablets**
(lamotrigine)
3. WHEN TO TREAT?

“Newer” Drugs II

- Levetiracetam (Keppra)
  - Minimal drug interactions
  - Possible behavioral side-effects
- Zonisamide (Zonegran)
  - 2-20 mg/kg/day
- Vigabatrin (Sabril)
  - Pending approval in United States, available in Mexico and Canada
  - Associated with progressive constriction of visual fields
  - Efficacious in infantile spasms, particularly with tuberous sclerosis
- Lacosamide (Vimpat)
- Rufinamide (Banzel)
- Clobazam (Onfi)
4. DOES STATUS EPILEPTICUS CHANGE THINGS?

- Not that much!
- Continuous seizure activity or serial seizures without return of consciousness, \( > \) 15-30 minutes
- May be convulsive or nonconvulsive, generalized or partial
- **Causes:** rule of fourths--febrile, prior symptomatic/noncompliance, new symptomatic, and idiopathic
- Routine imaging not warranted in children *Neurology 2006;67:1542*
4. DOES STATUS EPILEPTICUS CHANGE THINGS?

- **Management** needs to follow a well-conceptualized protocol for support and drug therapy.
- **Drug therapy** for generalized convulsive status epilepticus usually starts with lorazepam 0.1 mg/kg > diazepam 0.1-0.3 mg/kg IV/PR, followed by fosphenytoin IV/IM > phenobarbital IV, both 18-20 mg/kg.
- **Prognosis:** <5% mortality, predominantly in symptomatic cases; morbidity rather low in the absence of a progressive neurologic insult or metabolic disorder.
- Do *not* treat a child chronically with an antiepileptic drug after febrile status epilepticus.
- What about levetiracetam? IV? Now or on the way home?
5. WHAT PRECAUTIONS ARE NECESSARY?  

- Most patients lead normal lives
- Restriction is unnecessary for most activity
- Patients do not need to wear helmets or other protective devices
- No bathing or swimming unattended
- Driving laws vary, i.e., 3-12 months seizure-free before operating a motor vehicle
- Family should understand seizure first aid

*J Pediatr* 2007;151:172
5. WHAT PRECAUTIONS ARE NECESSARY?

- Epilepsy has a significant impact on self-image/esteem, particularly in adolescence and young adulthood.
- Careful monitoring of development and academic performance needed, secondary to effects of symptomatic illness, antiepileptic drugs, or accompanying learning disabilities.
- Antiepileptic drugs can all have significant effects on fetal development, so intensive counseling is needed for the sexually active patient.

- Postpubertal girls requiring carbamazepine, oxcarbazepine, or valproic acid should be started on oral folate 0.4 mg daily (*Neurology* 2009;73:142)

www.epilepsyfoundation.org
www.epilepsy.com
www.ilae.epilepsy.org
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