Pediatric Seizures: Are you sure ?

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Outline

- Definitions of terms
- Seizure classifications
- Seizure causes
- Differential diagnosis
- To treat or not to treat?
- Medication therapy

Case of MH

- 15 year old male presenting to ER with headache at 08:55
- Mom drove Dad to work approx 07:00 and when returned home noted son still asleep
- Mom tried to wake son but he was confused, difficult to rouse (4x) and complaining of head pain
- Ambulance called and vomited twice enroute to SJRH

Case

- In ER:
  - no photophobia
  - no resp distress
  - pain 7/10
  - complains of nausea and given metoclop
  - 4 min later pt seizes (stiff, arms to side, skin gray)
  - O2 given along with lorazepam 1mg IV
  - seizure lasts approx 2 min
  - post ictal: moaning/groaning, incontinent +

Definitions

- Seizure:

  paroxysmal event of the CNS characterized by abnormal cerebral neuronal discharges ± loss of consciousness

- Epilepsy:

  two or more recurring seizures without consistent provocation

Definitions

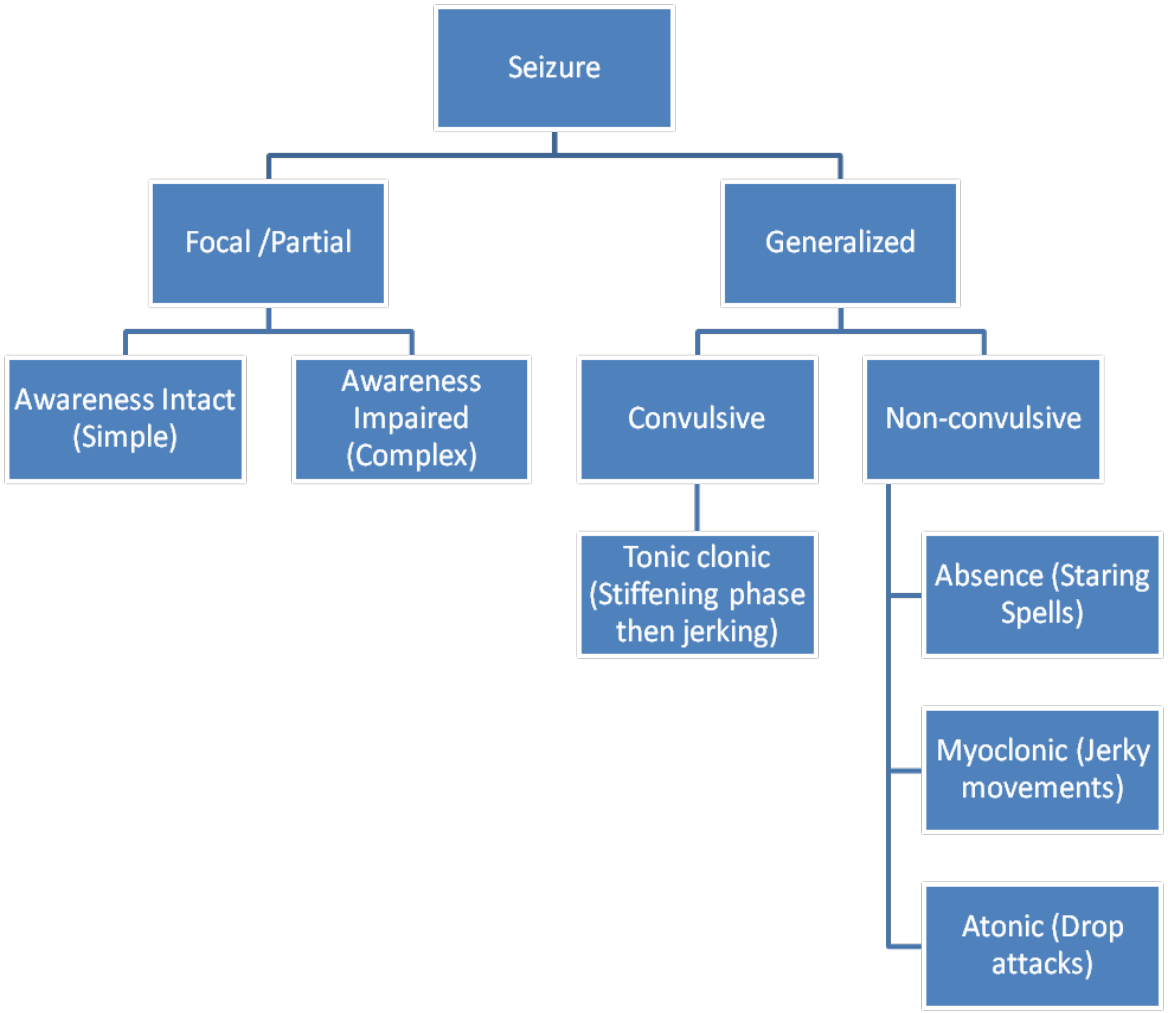
- Status Epilepticus:

  continuous seizure lasting >30 min OR >2 discreet seizures without intervening recovery of consciousness

- Ictus:

  a sudden attack, blow, stroke or seizure

Classifications

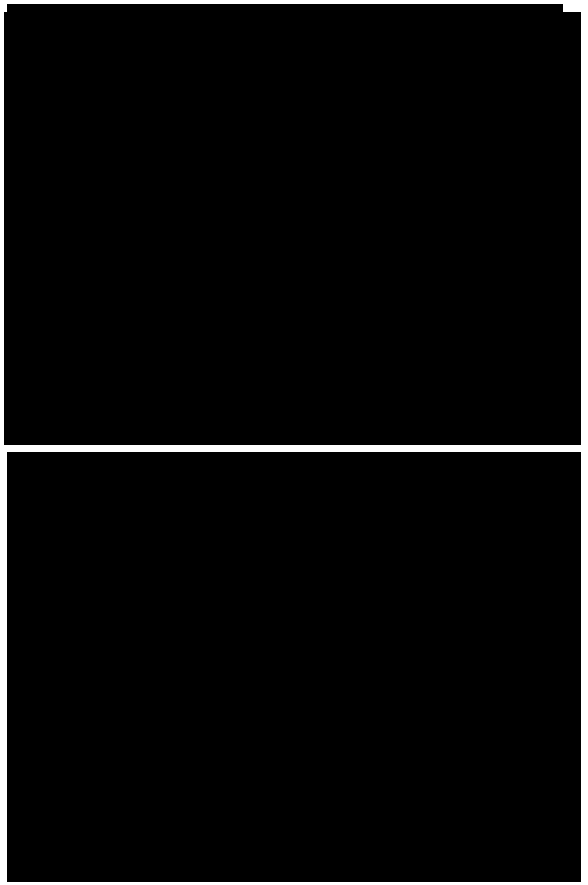


Diagnosis

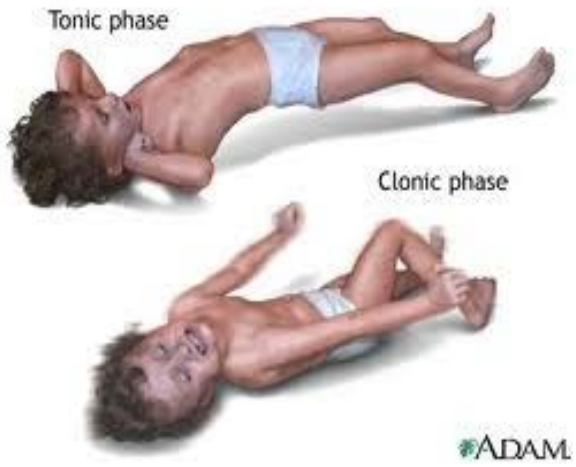
- Description of event
- Patient and family history
- Routine EEG
- Video EEG
- MRI or CT scan
- Blood work, urinalysis
- Lumbar puncture

Videos

- Complex partial
- Absence Seizure



Generalized Seizures



- Cry
- LOC
- Stiffening
- Jerks
- Bilateral
- +/- incontinence
- Some have focal start
- 90 sec
- Post ictal state

Seizure Conditions

- Neonatal seizures:

  - focal/multifocal clonic or tonic seizures
  - no neurologic abnormalities
  - occur within first few days to a week of life
  - usually brief but may reoccur until 2-3 months of age
  - spontaneous resolution
  - normal development and intellectual outcome

Seizure Conditions

- Febrile seizures:

  - occurs in otherwise healthy children 6 months to 5 years of age (2-5% of children)
  - average age is 12-18 months old
  - generalized TC seizures, brief & self limited
  - fever > 38°C
  - non CNS infection (AOM, URTI)
  - treat the cause if applicable
  - 50% can reoccur if <1 year of age (20% 1-3 years)

Seizure Conditions

- Infantile Spasms (West Syndrome)

  - children less than 12 months of age
  - peak onset is 4-6 months of age
  - presents as head dropping down, arms extended then coming in like a hug ± leg extension
  - can have poor developmental prognosis
  - 60% have some form of CNS damage
  - small number are idiopathic

V

Seizure Causes (provoked)

- Infection
- Trauma
- Brain lesions
- Metabolic problems
- Toxicity/ingestions
- Hereditary
- idiopathic

On the Differential

- Breath holding
- Syncope
- Night terrors
- Shuddering
- Migraines
- GI reflux
- Rage attacks
- Pseudo seizures

DDX

- Breath holding:

  - 2 to 4 years of age
  - 0.1 to 4% of children
  - a reflex, involuntary response to a trigger
  - stimulus → cry → pause → facial colour change → limp, unresponsive and then jerking
  - cause is unknown
  - prognosis is good

V

DDX

- Night terrors:

  - episodes of fear, flailing and screaming while asleep

  - short duration

  - usually 4-12 year olds

  - children have no recollection of event

  - causes include stress, anxiety, fatigue, unfamiliar surroundings and sleep deprivation

DDX

- Shuddering:
  - cause unknown, benign in nature
  - older infants & young children
  - short duration (5-15 seconds)
  - occur during waking hours
  - sudden flexion of neck & trunk → adduction of arms → shiver like movement of the trunk → body may stiffen
  - some have “absence like” course (V)

DDX

- GI Reflux (Sandifer's):

  - intermittent paroxysmal spells of generalized stiffening and posturing

  - pain response to acidic reflux in the esophagus

  - may also have apneas, staring and minimal jerking of the extremities

  - associated with feedings (v)

DDX

- Pseudo seizures (PNES):

  - not caused by abnormal electrical discharges

  - stress related or emotional cause

  - unusual features

  - EEG to rule out

  - potential misdiagnosis

Imitators of epilepsy: Nonepileptic paroxysmal disorders

Neonates
Apnea
Jitteriness
Benign neonatal sleep myoclonus
Hyperkplexia
Infants
Breath-holding spells
Benign myoclonus of infancy
Shuddering attacks
Sandifer syndrome
Benign torticollis in infancy
Abnormal eye movements (eg, spasmus nutans, opsoclonus-myoclonus)
Rhythmic movement disorder (head banging)
Children
Breath-holding spells
Vasovagal syncope
Migraine
Benign paroxysmal vertigo
Staring spells
Tic disorders and Stereotypies
Rhythmic movement disorder
Parasomnias
Adolescents and young adults
Vasovagal syncope
Narcolepsy
Periodic limb movements of sleep
Sleep starts
Paroxysmal dyskinesia
Tic disorders
Hemifacial spasm
Stiff person syndrome
Migraine
Psychogenic nonepileptic pseudoseizures
Hallucinations
Older adults
Cardiogenic syncope
Transient ischemic attack
Drop attacks
Transient global amnesia
Delirium or Toxic-metabolic encephalopathy
Rapid eye movement sleep disorder

To treat or not to treat?

- Prognosis:
  - neuro N
  - neuro hx N
  - no acute cause

→ 24%

Pediatrics 1990: “Risk of seizure recurrence following first unprovoked seizure in childhood: a prospective study” Shinnar S, Berg AT, Moshe SL et al.

To treat or not to treat?

- Immediately treatment:
  - reduce short term relapse rate (potential)
  - 1-2 year mark no difference
  - benefit lost at 4 years
  - no evidence that tx after initial seizure has any impact on mortality
  - high risk: EEG abn, partial vs. general ictus, SE

Neurology 1997: Treatment of first tonic clonic seizure does not improve the prognosis of epilepsy. First Seizure Trial Group. Musicco M, Beghi E, Solari A.

Lancet 2005: Immediate versus deferred AED treatment for early epilepsy and single seizures: RCT. Marson A, Jacoby A, Johnson A et al.

Neurology 2005: Mortality following a first unprovoked seizure in children, a prospective study. Shinnar S, O'Dell C, Berg AT

To treat or not to treat?

- “treatment with AED’s may be considered when the benefits of reducing the risk of a second seizure are greater than the risks of pharmacologic and psychosocial side effects”

Amer Academy of Neurology & Child Neurology Society
Quality Standards Subcommittee 2003

Treatment

- Acute (ED):
  - ABC's
  - VOICE (vitals,O2, IV, Cardiac, exposure)
  - rapid bloods (glucose, venous gas)
  - meds (1st, 2nd or 3rd line)
  - search for cause (Ca, Glu, Mg levels etc)

Emerg Management

Time	Meds		
0-5 minutes	Lorazepam 0.1mg/kg IV/SL/PR	Midazolam Nasal 0.2mg/kg Buccal 0.5mg/kg	Diazepam PR 0.5mg/kg IV 0.3 mg/kg
10 minutes	Repeat above step		
15 minutes	Fosphenytoin IM/IV 20mgPE/kg	Phenobarb IV 20mg/kg	Phenytoin IV 20mg/kg
20 minutes	Repeat above step with different 2nd line agent		
30 minutes	Refractory stage with sedation protocol – ICU admission and neurology consult		

Initial management of status epilepticus in children

Timeline*	Assessment	Supportive care	Seizure therapy
0 to 5 minutes	Obtain initial vital signs, including temperature	Open airway Suction secretions Administer 100 percent O2	**Benzodiazepine (first line):** Lorazepam 0.05 to 0.1 mg/kg IV or IO IV or IO access not achieved within 3 minutes: Rectal diazepam or Diastat® 0.5 mg/kg OR Buccal midazolam 0.2 mg/kg OR IM midazolam 0.1 mg/kg
	Identify airway obstruction and hypoxemia	Place continuous cardiorespiratory monitors and pulse oximetry	
	Identify impaired oxygenation or ventilation	Perform bag-valve-mask ventilation, as needed Prepare for RSI*	
	Obtain rapid bedside blood glucose and other studies, as indicated•	Establish IV or IO access	
	Evaluate for signs of sepsis/meningitis	Treat hypoglycemia (IV Dextrose 0.25 to 0.5 gm/kg)	
	Evaluate for signs of head trauma	Treat fever (acetaminophen 15 mg/kg rectally)	
5 to 10 minutes	Reevaluate vital signs, airway, breathing, and circulation	Maintain monitoring, ventilatory support, and vascular access	**Benzodiazepine: second dose**
	Evaluate for signs of trauma, sepsis, meningitis, or encephalitis	Give antibiotics if signs of sepsis or meningitisΔ	
10 to 15 minutes	Reevaluate vital signs, airway, breathing, and circulation	Maintain monitoring, ventilatory support, and vascular access	**Fosphenytoin (second line):** 20 mgPE/kg IV/ IO◇ OR **Phenobarbital** 20 mg/kg IV/ IO if toxin-induced seizure (expect respiratory depression with apnea)
		Place second IV	
		RSI potentially indicated*	
15 to 30 minutes	Reevaluate vital signs, airway, breathing, and circulation	Maintain monitoring, ventilatory support, and vascular access	**Phenobarbital (third line):** 20 mg/kg IV/IO (10 mg/kg if Phenobarbital given as second line) OR Valproic acid 20 to 40 mg/kg IV/ IO AND Pyridoxine 100 mg IV/IO in infants <1 year of age Pyridoxine 3 to 5 gms IV/IO if INH poisoning suspected **Obtain pediatric neurology consultation (see Refractory status epilepticus algorithm)**
	Obtain continuous EEG monitoring, if available		

IV: intravenous; IO: intraosseous; IM: intramuscular; O2: oxygen; RSI: rapid sequence endotracheal intubation; PE: phenytoin equivalents; EEG: electroencephalogram; INH: Isoniazid.
* Rapid sequence intubation should be performed if airway, ventilation, or oxygenation cannot be maintained and if the seizure becomes prolonged.
• See table "Ancillary studies in children with status epilepticus" (part of this document).
Δ Empiric antibiotic regimens vary depending on patient susceptibility and likely pathogen.
◇ Do not exceed 3 mg/kg per minute (maximum rate: 150 mg per minute). Fosphenytoin may be ineffective for toxin-induced seizures and may intensify seizures caused by cocaine and other local anesthetics, theophylline, or lindane.

NNU Management

Drug	Loading	Maint Dose	Therap Range	T½
Phenobarb	20mg/kg	3-4 mg/kg bid	20-40 mcg/L	100 hrs after 5-7d
Phenytoin	20 mg/kg	3-4 mg/kg in bid-qid	15-25 mcg/L	100 hrs (40-200)
Lorazepam	0.05 mg/kg over 2-5mn	May repeat		31-54 hrs
Diazepam	0.25 mg bolus	May repeat 1-2 times		31-54 hrs

Case

- ID: 4y9mo female term child with known hx of epilepsy
- CC: Seizure at daycare
- HPI: SC was at daycare when the staff laid her down for nap. At this point pt started having a seizure. Pt was unresponsive, so the daycare staff called 911 and Mom. Mom arrived after ambulance, came to ER with pt. Admitted to PICU at 14:45. At 16:15, pt was stable and transferred to 4AS. SC was walking around the floor in the evening.
- PMHx: Pt was dx with epilepsy by peds neurologist after a cluster of 3 seizures the pt had beginning in Sept 2010. Pt then started on clobazam. Has a cold and wet cough at this point.

Case Timeline

- Est time of incident: 12:25
- 911 call received: 12:32
- En route: 12:32
- Arrived at scene: 12:37
- Arrived at patient: 12:38
- Depart scene: 12:46
- At destination (ED): 13:03

38 minutes

Chronic Treatment

Older	Newer
Phenobarb (PB)	Lamotrigine (LTG)
Phenytoin (PHT)	Topiramate (TPM)
Carbamazepine (CBZ)	Oxcarbazepine (OXC)
Valproic acid (VPA)	Levetiracetam (LEV)
Clobazam (CLO)	Fosphenytoin (FOS)
Clonazepam (CNZ)	

Epileptic syndromes and recommended antiepileptic drugs

Syndrome	Antiepileptic drug
Localization-related (partial, focal)	1 - CBZ, PB, VPA, TPM, PHT, LTG, OXC
	2 - GBP, PRM, CRZ, LEV
Generalized epilepsies	
Absence seizures	1 - ESM, VPA, LTG
	2 - CNZ
Generalized tonic-clonic	1 - CBZ, VPA, PHT, PB, TPM
	2 - LTG
Juvenile myoclonic epilepsy	1 - VPA, LMG
	2 - PRM, CNZ, TPM
Myoclonic absence	1 - VPA, ESM
	2 - LTG, CNZ, TPM
Infantile spasms	1 - ACTH, prednisone
	2 - VPA (?), CNZ (?), TPM (?)
Lennox-Gastaut syndrome	1 - VPA, LTG, CNZ, CRZ, CBZ, TPM
	2 - ESM (drop attacks), FBM

CBZ: carbamazepine; CRZ: clorazepate; CNZ: clonazepam; ESM: ethosuximide; FBM: felbamate; GBP: gabapentin; LEV: levetiracetam; LTG: lamotrigine; OXC: oxcarbazepine; PHT: phenytoin; PB: phenobarbital; PRM: primidone; TPM: topiramate; TGB: tiagabine; VPA: valproic acid (divalproex sodium).
1: first line drugs.
2: second line drugs.
Adapted from Tharp, BR, Epilepsy in Infants and Children. In: Conn's Current Therapy, Rakel, RE (Ed), W.B. Saunders 1998; p.883.

Treatment

Syndrome	AED
Partial/focal	**1) VPA, OXC, PB, PHT, CBZ,LTG, TPM**
	2) LEV

Treatment (Generalized)

Syndrome	AED
absence	**1) VPA, LTG**
	2) CNZ
tonic-clonic	**1) VPA, OXC, CBZ, PHT, PB, TPM**
	2) LTG
myoclonic	**1) VPA, LTG**
	2) CNZ,TPM
myoclonic absence	**1) VPA**
	2) LTG, CNZ, TPM

Valproic Acid

- Mono or adjunctive therapy
- Focal and generalized coverage
- IV form available (SAP)
- Inexpensive, well studied
- Ssx: CNS, wt gain, alopecia, skin reactions, hepatic dysfunction
- Start 10-15 mg/kg/day uid-tid
- Titrate increments of 5-10 mg/kg/day qweekly
- Maintenance: 30 mg/kg/day bid-tid

Clobazam

- Mono or adjunctive therapy
- Once daily dosing
- CNS most common side effects
- Few drug interactions
- Initial 0.25-0.5 mg/kg/day uid-bid
- Dosing for <2 years of age
- Sound alike safety alert with clonazepam

Think Lamotrigine...

- For children with myoclonic or absence sz who don't want wt gain with VPA
- Children <2 on PB who want to avoid hepatic dysfunction of VPA
- Mono or combo therapy (↓ dose with VPA and ↑ dose with CBZ, PHT & PB)
- Partial & generalized seizures
- CNS effects
- Skin reactions (age, titrate, VPA)

Think Topiramate…

- For primary generalized seizures, including absence and myoclonic seizures, in children who want to avoid the adverse effects of VPA
- When avoiding hepatic metabolism desired
- Sfx: CNS, anorexia, cognitive dulling and behavioural effects
- >2 years of age dosing

Think Levetiracetam…

- For refractory partial or atypical absence seizures in children without behavioural issues
- Sfx: CNS, behavioural changes and leukopenia (3%)
- >4 years of age
- Initial 5-10 mg/kg/day uid-bid & titrate to a max of 60mg/kg/day

Think oxcarbazepine....

- Partial adjunctive therapy >2 years
- Partial monotherapy > 4 years
- Younger children (<8) have increased clearance and may require ↑ dose
- initial: 8-10 mg/kg/day bid except 2-4 years consider 16-20 mg/kg/day
- Baseline Na level, monitor q 3 months

Goals of therapy

- No seizures
- No side effects
- No stigma
- Help the child achieve his/her full potential

Questions

There is no question.....