THE PEDIATRICS FOR EMERGENCY PHYSICIANS NETWORK

Pediatric Seizures and Status Epilepticus

I. Febrile Seizures

Febrile seizures are the most common type of pediatric seizure encountered in the emergency department (ED). They are defined as seizures occurring with fever ≥100.4° F in children 6 months to 5 years old, and fall into two categories: **simple** or **complex.**

What's the difference between simple and complex?

A simple febrile seizure is a very benign event and carries an excellent prognosis. For patients who return completely to their baseline mental status and behavior there is usually no significant risk of meningitis (ie-no need for LP) and the prevalence of other serious bacterial infection is identical to febrile children without a simple febrile seizure. Therefore workups targeted towards identifying a fever source (such as blood or urine testing, CXR, etc) should be considered using the same rationale you use for other febrile children presenting to the ED. (See Module 3: "Fever In Infants")

Definition of a simple febrile seizure: (4 criteria):
1. Type: Generalized seizure
2. Age: 6 months – 5 years old
3. Duration: lasting *<15 minutes*
4. Number:: Only o*nce in 24 hours*.

Simple Febrile Seizure Pearls

1. Keep it simple. No extra bloodwork or neuroimaging is needed.

2. Know the indications for lumbar puncture (LP). Patients with simple febrile seizure almost never need an LP. However, it should be considered in a small but important subset of patients:

*Children who were recently given antibiotics—this can mask meningitis, and is referred to in the literature as "Partially-Treated Meningitis"). Therefore recent antibiotic treatment should always be elicited as part of your history.

* Children who have not **fully** returned to their normal/baseline behavior. Even if the behavior appears normal to you, always solicit parents' input as well, and rely on **THEIR** opinion. Lack of complete return to baseline may indicate on-going (non-convulsive) seizure activity, or need for LP to rule out meningitis.

Answers To Common Questions From Parents After A Febrile Seizure:

(1) Febrile seizures will not have any future impact on a child's academic progress, intellect, or behavior. **(2)** Febrile seizures commonly recur, especially in children <15 months old, those with family history of seizure, and those who seized at lower temperatures. **(3)** Parents may be reassured of " practically no increased risk of developing epilepsy"-ie- A 2-3%, risk in febrile seizure patients vs. 1-1.5% risk of normal children without a history of febrile seizure.

Complex Febrile Seizures (CFS)

A febrile seizure is termed **complex** when it fails to meet criteria for simple seizure because of focality, prolonged duration (>15 minutes), or recurrence within 24 hours The term "complex" most aptly refers to prognosis, not workup! While these patients are more likely to develop epilepsy down the line, their workup should not be extensive. Recent data show that neuroimaging and LP are very low yield in this population.

How low yield? In one study, only 3 of 360 children (0.9%) undergoing LP for complex febrile seizure had bacterial meningitis. In another study, 0 of 71 children with complex febrile seizure had a space-occupying intracranial condition that required intervention. Therefore, your workup should be guided by your history, physical exam, and overall assessment of the patient.

Risk of meningitis?

Febrile seizures that are termed "complex" because they are either *prolonged* or *focal* do carry a higher risk of bacterial meningitis than "simple" febrile seizures. Nevertheless, even with complex febrile seizure, previously healthy children that return **COMPLETELY** to both their baseline mental status and activity are very unlikely to have meningitis and the decision of whether or not to LP these patients can be made in conjunction with pediatric neurology consultation. CAVEATS: **Always consider meningitis** (for BOTH simple and complex febrile seizures) in children with meningeal signs and those that fail to return to baseline, as well as in children who are incompletely immunized, or already treated with oral antibiotics (because this "partial treatment" may mask meningeal signs and symptoms), immunocompromised (sickle cell, HIV), or otherwise at risk (travel to areas endemic for cysticercosis, past h/o herpes encephalitis).

II. Afebrile Seizures

Children with a first episode of unprovoked, afebrile seizure are approached very differently from their adult counterparts. This is because this type of seizure, when it occurs in children, is most commonly idiopathic and non-recurrent. In contrast, tumors and vascular events are a key cause of first afebrile seizure in the adult population (22-26%, vs. 1% in children). Here are the ways in which your workup should differ :

Workup	**Children**	**Adults**
Bloodwork	Guided by clinical suspicion	Guided by clinical suspicion
Lumbar puncture	No, unless meningeal signs or symptoms-- Also consider if the patient is <6 months old, or does not return to baseline	Guided by clinical suspicion
Emergent neuroimaging (MRI preferred)	No, unless the patient is high risk*, has a persistent postictal neurologic deficit, or does not return to baseline. --Also consider if the patient is <3 years old and had a focal seizure	Yes
Emergent EEG	No	Yes

* High risk= sickle cell, bleeding disorder, malignancy, HIV infection, or known CNS abnormality

III. Status Epilepticus

Status epilepticus is, essentially, a prolonged seizure. Two definitions are used: the **classical definition**, which relates to seizure pathophysiology, and the NEW **operational definition**, which helps to promote earlier, aggressive & rapid therapy**:**

OLD : Classical definition: Seizure **> 30** minutes, or 2+ seizures without recovery of consciousness. This definition is useful for epidemiologic and research purposes, and for quantifying seizure morbidity. It reminds the practitioner that compensatory mechanisms begin to fail at 30-60 minutes, resulting in hypotension, hypoxia, hypercapnia, arrhythmia, rhabdomyolysis, and cerebral edema

NEW : Operational definition: Seizure **> 5** minutes, or 2 or more seizures without recovery of consciousness. This is a more clinical definition. It encourages the practitioner to treat the seizure aggressively early-on, and is based upon the recognition that, as a seizure persists beyond 5 minutes , standard antiepileptic drugs Unare less likely to be effective.

GENERAL PHILOSOPHY & APPROACH:

The general philosophy regarding status epilepticus is to "dump as many anticonvulsants into the patient's brain as needed to get the brain to sleep" in order to terminate the seizure as quickly as possible and prevent permanent neurologic sequelae. Multiple anticonvulsants may synergistically increase the risk of respiratory depression & need for intubation, but as seizure duration approaches 30 minutes, this should be considered less important than the urgency of terminating the seizure (EXCEPTION: potentially difficult airway, such as Pierre-Roban, etc)..

Pediatric Pearls to Keep In Mind :

1. Always Watch Out For Apnea! : Even prior to ED treatment with antiepileptic medications, seizing children may often experience sudden apnea. On top of this, respiratory depression is a common response to normal doses of antiepileptics and breathing can be difficult to evaluate in a seizing child. Always have airway equipment at hand (especially ambu-bag) and when in doubt, begin assisted ventilation by BVM.

2. Make Sure The Seizure Has Stopped! : Not uncommonly, a child who stops convulsive movements and appears at first glance to be postictal, is actually still seizing and is in **Nonconvulsive Status Epilepticus** (NCE). You must make certain the seizure has stopped by attention to the following details: Normalization of vital signs, normal tone of extremities, midline eyes, and gradual but steady improvement in mental status. Seizure and status epilepticus should always be on the differential for any child with a persistently altered mental status even the absence of convulsive movements. EEG may be needed to rule out NCE.

3. Pediatric Dosing of Antiepileptics: Pediatric dosing can be hard to remember. One trick of the trade is that most second line (i.e., non-benzodiazepine) antiepileptic drugs can be given in doses of **20 mg/kg**, and repeated at half the dose. Also, if there is a standard adult dose, then use that dose as a cutoff for the maximum amount to give a child.

4. The Problem of IV Access: Obtaining venous access on a small, seizing patient can be challenging. However, several medications can be given via the **intramuscular, buccal, or intranasal route.** (More on this below) Sometimes more than one IV is necessary for fluids and medications. Do not hesitate to place IO's as needed for 1st or 2nd lines.

ANTIEPILEPTIC DRUGS

Antiepileptic therapy should be initiated within the first five minutes of seizure. This is because, as a seizure persists, standard antiepileptic drugs become less effective. First-line therapy is with benzodiazepines. After two doses, further benzodiazepine doses are unlikely to work, and second -line drugs (ie- Fosphenytoin/phenytoin and Phenobarbital) are given. If there is no response to standard first and second line drugs, the patient is in **Refractory Status Epilepticus (RSE**), and therapy should be escalated.

First line: Benzodiazepines (up to 2 doses--→ then proceed to second line)

	Ativan (lorazepam)	Valium (diazepam)	Versed (midazolam)
IV Dose	0.05-0.1 mg/kg	0.2-0.4 mg/kg	0.1 mg/kg
Alternate route?		Rectal:-0.5 mg/kg (min 5, max 20)	IM: 0.2 mg/kg (max 10) Buccal: 0.5 mg/kg (max 10) Intranasal: 0.5 mg/kg

Pediatric Treatment Pearls:

1. **No access? Which drug is best?**
   Buccal and intranasal midazolam are both more effective than rectal diazepam, without any increase in the risk of respiratory depression.

2. **Dose ranges for benzodiazipines: Which dose should I use?**
   EXAMPLE: The dose range for ativan is 0.05-0.1mg/kg. ANSWER: Benzodiazipines are your first-line drug, and dosing is usually determined by the duration of the seizure (ie- weighing the urgency of terminating the seizure vs desire to avoid potential respiratory depression and airway compromise). For instance, if the patient has only been seizing for several minutes a lower 0.05 mg/kg dose is reasonable and more likely to terminate the seizure while avoiding respiratory depression. On the other hand, for patients presenting in status epilepticus, or as seizure time becomes prolonged, especially if approaching 30 minutes, higher dosing (to terminate the seizure as quickly as possible) is advisable, so long as airway personnel and equipment are at hand by the bedside

Second line: Dilantin derivatives and Phenobarbital

	Phenytoin (dilantin)	Fosphenytoin (cerebyx)	Phenobarbital
First Dose	20mg/kg @1 mg/kg/min	20 mg PE/kg @ 3 mg/kg/min	20 mg/kg @ 1 mg/kg/min

*Each of these medications can be repeated at half the dose for a total of 30mg/kg..

*Levetiracetam, 20mg/kg,may also be considered as 2nd line agent, if immediately available.

Refractory status epilepticus: Third line agents

After three first/second line agents have been administered, the patient who continues to seize is in refractory status epilepticus, regardless of time elapsed. At this point, patient should be intubated (for airway protection +impending apnea from your next treatment), and start either midazolam or phenobarbital drip as follows:

Midazolam drip: Load with 0.2 mg/kg IV (max 10 mg), then 1 mcg/kg/min

Pentobarbital drip: Load with 2-10 mg/kg IV (max 20 mg), then 0.5-5 mg/kg/hr

Do not delay , but while preparing drip, you may also consider:

Valproate 20 mg/kg IV @ 5 mg/kg/hr

Levetiracetam 20 mg/kg IV @ 5 mg/kg/min (max 3 g), may repeat once to total of 40mg/kg

REMEMBER! Always consider treatable diagnoses:

Diagnosis	Therapy	Dose
Hypoglycemia	Dextrose	2 cc/kg of 25% dextrose IV (child) 5 cc/kg of 10% dextrose IV (infant)
Opioid overdose	Naloxone	0.1 mg/kg IV q2-3 min PRN
Vit B6 deficiency, INH toxicity	Pyridoxine	70 mg/kg IV, max 5 g 100 mg IV in neonate
Sepsis/meningitis	Ceftriaxone	100 mg/kg IV
HSV encephalitis	Acyclovir	3 m – 12 yrs: 20 mg/kg IV over 1 hr <3 m or >12 yrs: 10 mg/kg IV over 1 hr
Hyponatremia	3% NS	5 cc/kg IV over 1 hr
Hypocalcemia	10% Calcium gluconate	0.5 cc/kg IV over 2 min

The search for a source:

Outside of febrile seizure, the most common cause of status epilepticus is **acute CNS insult** such as bacterial meningitis, viral meningitis/encephalitis, metabolic derangement, intoxication, trauma, hypoxia, or cerebrovascular incident. The next most common cause of SE is **remote CNS insult**, such as perinatal hypoxia, cerebral dysgenesis, and progressive neurodegenerative disorders.

Because status epilepticus is so often caused by a real CNS insult (and not idiopathic), the workup must be more extensive than that of a single, self limited childhood seizure:.

- **Antiepileptic drug levels**
- **Electrolyte panel** (Don't forget d-stick!)
- **Neuroimaging** when patient is stabilized
- **Blood culture:** 2.5% of those obtained for status epilepticus are positive.
- **Lumbar puncture:** 12.8% of those performed for status epilepticus are positive. The highest yield is in febrile patients. (Initially administer ceftriaxone to cover for meningitis and defer LP until patient is stabilized)
- **EEG** after admission (**NOTE:** if unclear seizure has ceased, bedside EEG in ED is indicated)
- **Toxicology screening:** Treatment and screening for specific substances based on suspicion (ie- tricyclics, INH, etc) is preferable to urine drug screening.

Summary : Pediatric Status Epilepticus: Management Algorithm

* Minutes	Phase
0-5	**Impending SE vs. single seizure** - ABC's, supplemental O2, BVM ready, check dextrose, - Benzodiazepine #1
5-30	**Early SE** Benzodiazepine #2 ↓ Fosphenytoin (or phenytoin) ↓ Phenobarbital* * Consider Levetiracetam load prior to Phenobarbital (avoids respiratory depression) * Consider pyridoxine if <2 years old * Be fully prepared for intubation (additive respiratory depression from barbiturate +benzos) * Diagnostic studies (labs, cultures, antibiotics, CT/LP when stable)
>30	**Refractory SE** : after 2-3 medications, regardless of time elapsed,: : Midazolam OR Pentobarbital drip* *(If delay, consider Levitiracetam or Valproate)

References

Abend N, Huh J, Helfaer M, et. al. Anticonvulsant medications in the pediatric emergency department room and intensive care unit. Pediatric Emergency Care 2008, 24 (10): 705-21.

American Academy of Pediatrics. Febrile seizures: guideline for the neurodiagnostic evaluation of the child with a simple febrile seizure. Pediatrics 2011, 127 (2): 389-4.

Fisgin T, Gurer Y, Tezic T. Effects of intranasal midazolam and rectal diazepam on acute convulsions in children: prospective randomized study. J Child Neurol 2002; 17: 123-6.

Hirtz D, Ashwal S, Berg A, et. al. Practice parameter: evaluating a first nonfebrile seizure in children. Neurology 2000, 55 (5): 616-23.

Kimia A, Pearl Ben-Joseph E, Rudloe T, et. al. Yield of lumbar puncture among children who present with their first complex febrile seizure. Pediatrics 2010, 126 (1): 62-9

Krumholz A, Wieve S, Gronseth G, et. al. Practice parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review). Neurology 2007; 69: 1996-2007.

McIntyre J, Robertson S, Norris E, et. al. Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomized controlled trial. Lancet 2005. 366: 205-10.

Riviello JJ, Ashwal S, Hirtz D, et. al. Practice parameter: diagnostic assessment of the child with status epilepticus (an evidence-based review). Neurology 2006, 67: 1542-1550.

Sharma S, Riviello J, Harper M, et. al. The role of emergent neuroimaging in children with new-onset afebrile seizures. Pediatrics 2003, 111 (1): 1-5.

Singh R and Gaillard W. Status epilepticus in children. Current neurology and neuroscience reports 2009, 9: 137-44.

Teng D, Dayan P, Tyler S, et. al. Risk of intracranial pathologic conditions requiring emergency intervention after a first complex febrile seizure episode among children. Pediatrics 2006, 117(2):304-8

Verity C, Greenwood R, and Golding J. Long-term intellectual and behavioral outcomes of children with febrile convulsions. NEJM1998, 338 (24): 1723-28.