

Status Epilepticus and Epilepsy

Status Epilepticus

- Defined as protracted or recurrent seizures causing prolonged changes in sensorium and other neurological impairment
- Often due to missed doses of daily seizure prevention medication
 - May result from noncompliance, illness, or vomiting
 - Caregivers should always have emergency seizure medications on hand
- Convulsive status epilepticus
 - Characterized by continuous seizures lasting > 15 minutes, or a series of seizures lasting > 30 minutes without a return to baseline consciousness
 - Can occur in patients with epilepsy (4% incidence overall); more common in children < 5 years old
 - More common in “bad syndromes” (eg, Lennox-Gastaut, cerebral dysplasias, etc)
 - Also seen in acute or chronic brain disease (eg, trauma, hypoxic ischemic encephalopathy, infection, neurodegeneration, toxic or metabolic disease, neoplasm)
 - Complications
 - ▶ Pediatric mortality rate is around 5%
 - ▶ Other complications include hypoxia, oropharyngeal obstruction, aspiration, hypotension, pulmonary edema, cardiac arrhythmia, hyperkalemia, acidosis, hypoglycemia, hyponatremia, fractures, oral injuries, rhabdomyolysis, hyperthermia, primary neuronal injury, sudden unexplained death
 - Emergency management can be simplified into a series of sequential interventions using the memory aid **AAP** (Table 25-1)
 - Computed tomography (CT) scan of the head is indicated in the following cases:
 - ▶ Head trauma
 - ▶ Evidence of increased intracranial pressure (ICP)
 - ▶ Focal neurologic deficits

Table 25-1. Status Epilepticus Emergency Management

Time (min)	Mnemonic	Intervention
0–5	A	ABCs, ample Hx (allergies, medications, past medical Hx, last meal, preceding events), adjuncts (glucose, Na ⁺ , Ca ²⁺ , ABG, anticonvulsant levels)
5–10	A	Ativan * 0.1 mg/kg IV (2 mg maximum single dose in a child); can cause respiratory depression and decreased BP; consider IO if IV unavailable
10–20	P	Phosphenytoin 20 mg/kg IV (2–3 mg/kg/min; can cause respiratory depression, decreased BP, and arrhythmias)
	A	ABCs
	A	Repeat Ativan 0.1 mg/kg IV
20–30	P	Phenobarbital 20 mg/kg IV over 5–10 min (can cause respiratory depression and decreased BP)
	A	ABCs ; anticipate intubation; volume bolus may be needed
> 30	A	Repeat Ativan 0.1 mg/kg IV
40–60	P	Repeat phenobarbital 10 mg/kg aliquots × 2 (will cause respiratory depression and decrease BP)
	A	ABCs , intubate
	A	Consider arterial line for BP monitoring and central line for possible dopamine administration
	P	Take patient to PICU for pentobarbital or versed drips; consider continuous EEG, especially if neuromuscular blockade is needed (goal is burst suppression)

ABC: airway, breathing, and circulation

ABG: arterial blood gas

BP: blood pressure

EEG: electroencephalogram

Hx: history

IO: intraosseous

IV: intravenous

PICU: pediatric intensive care unit

*Ativan (lorazepam) is manufactured by Biovail Corporation (Mississauga, Ontario, Canada).

- ▶ Focal seizure activity
- Lumbar puncture is contraindicated in the following cases:
 - ▶ Suspected increased ICP
 - ▶ Focal neurologic deficits
 - ▶ Cardiopulmonary instability
 - ▶ Severe coagulopathy or thrombocytopenia
- If status epilepticus persists, consider inducing coma with electroencephalogram (EEG) monitoring
 - ▶ Titrate EEG to seizure suppression, burst suppression pattern, or flat line
 - ▶ Administer midazolam (versed) infusion
 - ▷ 0.2 mg/kg (range 0.05–0.2 mg/kg bolus), repeat every 5 minutes as needed, to total 3 mg/kg
 - ▷ 0.1 (range 0.05–1.1) mg/kg/h

OR

- ▶ Pentobarbital infusion
 - ▷ 5 (3–15) mg/kg bolus, repeat as needed
 - ▷ 1–3 mg/kg/h
- ▶ Alternatively, consider:
 - ▷ Rectal diazepam (helpful if IV is unavailable)
 - 2–5 years old: 0.5 mg/kg/dose
 - 6–11 years old: 0.3 mg/kg/dose
 - 12 years and older: 0.2 mg/kg/dose
 - ▷ Buccal diazepam
 - ▷ Thiopental: 1–3 mg/kg IV bolus, (3–5 mg/kg/h infusion)
 - ▷ Ketamine: 1–2 mg/kg (1–2 mg/kg/h)
 - ▷ Isoflurane: titrate to burst suppression on EEG

Posttraumatic Seizures

- These require treatment in the acute setting, especially in the presence of increased ICP
 - Phenobarbital is the preferred antiepileptic agent in patients < 2 years old
 - Treat older children with phenytoin sodium or fosphenytoin (see Chapter 10, Neurosurgery)
- Seizures within the first week of trauma need to be treated

acutely; however, there is a low risk of long-term epilepsy

- Patients who develop seizures after the first week following trauma are more likely to have posttraumatic epilepsy

Evaluation of First-Time, Nonfebrile Seizure in Children

- Laboratory studies
 - Based on and directed at individual clinical circumstances
 - History: record clinical findings such as vomiting, diarrhea, dehydration, and failure to return to baseline alertness
 - Chemistry: check serum glucose and calcium in infants with seizures and in older children whose histories indicate the possibility of a metabolic disturbance
 - ▶ Consider hyponatremia if history suggests fluid imbalance
 - ▶ Screen toxicology or specific drug levels if drug exposure or substance abuse is possible
- Lumbar puncture
 - Of limited value unless meningitis or encephalitis is possible
 - Consider in infants who have sustained their first seizure
- EEG (if available) does not need to be emergent, although it may provide more information if obtained within 24 hours following seizure
- Neuroimaging
 - Perform emergent imaging (CT scan) in the following cases:
 - ▶ Presence of focal deficit (eg, Todd paralysis) that does not quickly resolve
 - ▶ Patient has not returned to baseline within several hours after the seizure
 - ▶ At-risk patients with abnormal neurological examination, history of malignancy, sickle cell disease, bleeding disorder, closed head injury, or travel to an area endemic for cysticercosis
 - ▶ Focal seizures
 - Magnetic resonance imaging (MRI) is preferred, but frequently unavailable

Febrile Seizures

- Simple febrile seizure
 - Single, brief, generalized seizure that occurs with fever (sei-

- zure may occur while the fever is rising or may be present before the fever is discovered)
- Patient looks normal after the seizure (no obtundation or mental status change)
 - A third of infants with one simple febrile seizure have a second; half of these have a third
 - ▶ Half of recurrences are experienced within a year of the first
 - ▶ 90% develop within 2 years
 - ▶ There is no evidence that a second or third simple febrile seizure, even if prolonged, causes epilepsy or brain damage
 - Febrile seizures not related to infection or other definable cause
 - Occur in 4% of children; 2% of those with a first seizure associated with fever have nonfebrile seizures (epilepsy) by age 7
 - Most important predictor of epilepsy is abnormal neurological or developmental state
 - Complex febrile seizures (prolonged, focal, or multiple seizures) as well as family history of epilepsy, slightly increase the probability of epilepsy in a patient
 - Evaluation
 - Lumbar puncture
 - ▶ Perform only if concerned about nervous system infection (age < 12 mo, focal seizure, abnormal neurological examination)
 - ▶ Unnecessary after a brief, generalized seizure from which infant recovers rapidly and completely, especially if fever subsides spontaneously or is otherwise explained
 - Check complete blood count (CBC), electrolytes and/or urinary analysis (UA), depending on clinical circumstances
 - Treatment
 - Unnecessary in low-risk children who have had a single, brief, generalized seizure
 - Antipyretics given at the time of another febrile episode do not prevent recurrence
 - Prophylactic antiepileptic drugs may be considered when the patient has:

- ▶ An abnormal neurological examination or developmental delay
- ▶ A family history of epilepsy with an initial complex febrile seizure
- Consider phenobarbital or valproic acid daily for 1–2 years
 - ▶ Decreases the risk of recurrence, but has severe side effects
 - ▶ Blood levels need to be monitored
 - ▶ If there is an adverse drug reaction (ADR), change to oral or rectal diazepam 0.5 mg/kg/day at the onset of subsequent fevers

Epilepsy

- Recurrent convulsive or nonconvulsive seizures caused by partial or generalized discharges in the cerebrum
- Two or more seizures not precipitated by a known cause
- Treatment
 - Goal: eradicating seizures or decreasing them so that they no longer interfere with physical and social well being
 - Consider treatment:
 - ▶ After a first unprovoked seizure (treatment in this case is rarely warranted)
 - ▶ After a second seizure or first seizure with ancillary evidence (family history, abnormal EEG, or MRI) indicating increased recurrence risk
 - **Consult a neurologist for help managing specific epilepsy syndromes**
 - Treatment by seizure type (drugs available in the US Army Central Command formulary)
 - ▶ Partial: simple, complex, and secondary generalized
 - ▷ Carbamazepine
 - ▷ Valproate (second choice)
 - ▷ Phenobarbital
 - ▶ Partial and generalized
 - ▷ Valproate
 - ▷ Topiramate
 - ▶ Myoclonic seizures
 - ▷ Valproate
 - ▷ Topiramate
 - ▷ **Caution** carbamazepine and phenobarbital can make

myoclonic seizures worse

Drugs, Doses, and Adverse Reactions in Pediatric Patients

- Carbamazepine: 5 mg/kg/day PO divided bid
 - Increase by 5 mg/kg/day every 3–5 days up to 15–20 mg/day divided bid or qid
 - Maximum adult dose is 2,400 mg/day, which can be as high as 35 mg/kg
 - If patient is taking more than 400 mg/day, convert to extended release carbamazepine (same dose, divided bid), if available
 - Levels 4–12 µg/mL therapeutic (toxic serum level ≥ 15 µg/mL)
 - Monitor CBC, blood chemistry (sodium, blood urea nitrogen), serum iron, lipid panel, liver function tests (LFTs), UA, and thyroid function tests at 1 week, 1 month, 3 months, 6 months–1 year, then yearly
 - ADRs include hepatitis, neutropenia, aplastic anemia, diplopia, ataxia, rash, and syndrome of inappropriate antidiuretic hormone
- Clonazepam: 0.01–0.03 mg/kg/day PO divided qd–tid
 - Increase by 0.025 to 0.05 mg every 3–7 days until condition is controlled
 - Maximum: 0.1–0.2 mg/kg (adult 20 mg)
 - Levels (none)
 - Monitor LFTs
 - ADRs include rebound insomnia, anxiety, dysphoria, disinhibition, tremor, headache, confusion, dysarthria, and syncope (tolerance may develop to ADRs and drug)
- Diazepam: 0.2–0.3 mg/kg/dose IV; 0.5–0.75 mg/kg/day rectal
 - Levels (none)
 - Monitor CBC and LFTs
 - ADRs include sedation and disinhibition
- Gabapentin: 5 mg/kg/day PO
 - Not preferred for seizures; has minimal interactions with other medications
 - Increase by 5 mg/kg/day every 3 days to 15–20 mg/kg/day divided tid
 - ▶ Usual dose is 30–40 mg/kg/day divided tid

- ▶ Maximum: 45–60 mg/kg/day
- Levels: < 5
- Monitor white blood cell count
- ADRs include irritability, tremor, neuropsychosis, sedation, headaches, fatigue, weight gain, and ataxia
- Lorazepam: 0.025–0.10 mg/kg PO (usually 0.05 mg/kg due to respiratory suppression)
 - Maximum: 10 mg/dose
 - Levels: not established
 - ADRs include sedation, dizziness, and disinhibition
- Phenobarbital (luminal)
 - Used mostly in newborns and infants 2–12 months old
 - Associated with cognitive slowing in older patients
 - Interacts with several other drugs and increases the metabolism of many drugs
 - Not recommended for woman of childbearing age; decreases oral contraceptive effectiveness
 - Dosing
 - ▶ Oral load 4 mg/kg bid × 2 days
 - ▶ Maintenance 4 mg/kg/day divided qd–bid
 - ▶ Faster oral 4 mg/kg/d every 4–6 hours × 4
 - ▶ IV load 20 mg/kg/dose
 - Levels: 15–40 µg/mL (check after 2–5 days); toxic: 40 µg/mL
 - ▶ Slowness, ataxia, nystagmus 35–80 µg/mL
 - ▶ Coma with reflexes 65–117 µg/mL
 - ▶ Coma without reflexes > 100 µg/mL
 - Monitor CBC and LFTs
 - ADRs include rash, Stevens Johnson Syndrome, serum sickness, depression, and rickets
- Phenytoin
 - Oral (PO) load 6 mg/kg/dose every 8 hours × 3 doses
 - ▶ Maintenance 5 mg/kg/day divided bid or tid
 - ▶ Maximum: 10 mg/kg/day (adult 500 mg/day)
 - IV load 18–20 mg/kg once, then 10 mg/kg × 2 (check levels at 2 h)
 - ▶ Fosphenytoin preferred in children: 18 mg/kg/dose phenytoin equivalent
 - ▶ Then 5–6 mg/kg/day divided bid
 - Levels 10–20 (free 0.1–2)

- ▶ Toxic > 30; lethal > 100
- ▶ Zero order kinetics; can become toxic quickly; must monitor levels closely
- ADRs
 - ▶ IV: hypotension, bradycardia, arrhythmia, venous irritation
 - ▶ PO: gingival hypertrophy, coarsening facial features, hirsutism, rash, hepatitis, rickets, folic acid deficiency, peripheral neuropathy, lupus, vision problems, dizziness, fatigue, alterations in mood
- Topiramate: 0.5–1 mg/kg/day divided once or bid; increase 0.5–1 mg/kg every 2 weeks × 2, then weekly
 - Usual dose 5–8 mg/kg/day PO divided once or bid
 - Maximum: 15 mg/kg/day (25 mg/kg for infantile spasms)
 - Levels not established (10–35)
 - Monitor electrolytes occasionally (however, medication is often not decreased because of acidosis)
 - ADRs include renal stones, anhydrosis, low bicarbonate levels, metabolic acidosis, dehydration, anorexia, encephalopathy, somnolence, nausea, ataxia, confusion, dysarthria
 - ▶ Also decreases appetite and the effectiveness of oral contraceptives
 - ▶ Keep the patient hydrated
- Valproic acid
 - Good anticonvulsant; limited by ADRs
 - Regular release and delayed release varieties are usually divided bid or qid; extended release is usually given once a day
 - When moving to extended release, might need to increase daily dose 8%–20% for same serum concentrations
 - IV/PO doses are equivalent
 - ▶ PO: 5–10 mg/kg/day divided once or bid; increase by 5–10 mg/kg/day divided bid every 3–5 days to 15–25 mg/kg/day divided bid or tid
 - ▶ IV: load 20 mg/kg/dose (maximum < 20 mg/min)
 - ▷ Give oral dose with IV load
 - ▷ IV maintenance equals total daily dose divided every 6 hours
 - ▷ Maximum: 60–70 mg/kg/day

- Levels 40–140 $\mu\text{g}/\text{mL}$
- Monitor LFTs and CBC before starting, then at 1 week, 1 month, and 3 months, then every 6 months; if lethargy or mental status changes, check prothrombin time, partial thromboplastin time, and serum ammonia
- The following conditions increase risk for hepatotoxicity:
 - ▶ Underlying liver disorder in a child < 2 years of age
 - ▶ Taking multiple antiepileptic drugs
- Carnitine can be used for hepatoprotection
- ADRs
 - ▶ Not recommended for women of childbearing age
 - ▶ Slows metabolism of other drugs
 - ▶ Can cause hepatitis, thrombocytopenia, pancreatitis, alopecia, weight gain, nausea, polycystic ovaries, somnolence, headaches, and tremor