Status Epilepticus

Definition:

For the purpose of these guidelines, **Status Epilepticus (SE)** is defined as (i) 5 minutes or more of continuous clinical seizure activity, (ii) 10 minutes or more of electrographic seizure activity, or (iii) recurrent seizure activity without recovery (returning to baseline mental status) between seizures. It is the most common neurologic emergency in children; it is associated with significant morbidity and mortality. SE is considered a medical emergency because it can lead to severe health complications and, in some cases, be life-threatening if not promptly treated.

Most seizures will self-resolve (terminate without intervention) within 90 seconds of seizure onset; however, as seizure activity continues, early intervention is important, in order to prevent the progression to status epilepticus. DCMC will aim to treat seizures prior to meeting the criteria for status epilepticus.[10]

Etiology:

Overall, the etiology of status epilepticus in pediatric patients is diverse, often requiring a systematic approach to diagnosis and management tailored to the individual patient's clinical presentation and underlying risk factors. SE may also be an acute symptom of a medical or neurologic disease.

Etiologies to consider in patients experiencing seizures:

- Epilepsy (focal, generalized, combined focal and generalized, or unknown)
- acute brain injuries (e.g. traumatic brain injury, hypoxic injury, or hemorrhagic/ischemic stroke)
- metabolic disturbances (e.g. hypoglycemia, hypocalcemia or hyponatremia)
- autoimmune disorders (e.g. NMDAR encephalitis, SLE, ADEM, FIRES)
- febrile seizures in children (between ages 3 months and 6 years)
- CNS infections (e.g. encephalitis, meningitis)
- structural brain lesions (e.g. tumor, malformation of cortical development)
- drug withdrawal (e.g. benzodiazepines, barbiturates, alcohol)
- toxic ingestions
- Nonconvulsive status epilepticus, which may not present with overt convulsions but can still have abnormal brain electrical activity
- Unknown factors

Prompt identification and addressing of the underlying cause are crucial for effective management.

Prevalence is highest in pediatric patients from zero to four years of age.[1] Each year, 20 per 100,000 children are affected by SE with an overall mortality of 3%.[2] Population-based studies show that the one common underlying etiology for pediatric status epilepticus is non-CNS infection-related fever, commonly febrile SE.[2]

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[1] Ng YT, Maganti R. Status epilepticus in childhood. Epilepsy in Children and Adolescents. John Wiley and Sons; 2013.

[2] Swarnalingam, E., Woodward, K., Esser, M. et al. Management and prognosis of pediatric status epilepticus. Z. Epileptol. 35, 332–344 (2022). https://doi.org/10.1007/s10309-022-00538-0

[10] Theodore WH, Porter RJ, Albert P, Kelley K, Bromfield E, Devinsky O, Sato S. The secondarily generalized tonic-clonic seizure: a videotape analysis. Neurology. 1994 Aug;44(8):1403-7. doi: 10.1212/wnl.44.8.1403. PMID: 8058138.

Differential Diagnosis:

- Movement Disorder (e.g. status dystonicus, motor tics)
- Cardiac arrhythmia
- Breath-holding spell
- Syncope
- Toxic encephalopathy
- Hemiplegic migraine or migraine with aura
- Alternating hemiplegia of childhood
- Psychogenic nonepileptic events (PNEE)

Guideline Inclusion Criteria:

- Age ≥ 3 months, with:
  - clinical findings of convulsive seizure activity with impaired awareness lasting ≥ 3 minutes, OR
  - Nonconvulsive seizures or convulsive seizures without impaired awareness, at the discretion of an Epileptologist or Neurologist
  - Recurrent seizures w/o return to baseline mental status (typically ≥ 3 in 30 mins)

Guideline Exclusion Criteria:

- Age < 3 months
- Patients with an established individualized seizure plan (e.g. EMU patients, patients in the PICU)
- Patients admitted to the Epilepsy Monitoring Unit (EMU) under the Epilepsy team - please refer to the EMU Guideline

Status Epilepticus (SE) Classification

STATUS EPILEPTICUS CLASSIFICATIONS BY SEIZURE CHARACTERISTICS		
Type		**Characteristics**
Convulsive SE	***WITH* Impaired Awareness**	• Focal or generalized (bilateral) movements (rhythmic jerking or sustained stiffening of extremities) • Mental status impairment (altered awareness, confusion, behavioral changes, loss of consciousness, lethargy, coma) • Increased risk of complications such as respiratory compromise or injury
	***WITHOUT* Impaired Awareness**	• Rhythmic jerking or sustained stiffening of extremities • May have motor or sensory symptoms in one body part • Patient maintains awareness of surroundings
Non-convulsive SE (NCSE)		• Electrographic seizure activity without clinical symptoms or w/ subtle clinical features • Prolonged or repetitive episodes of impaired consciousness or staring spells (may be mistaken for daydreaming or inattention) **Includes:** ○ 'wandering confused' w/ relatively good prognosis or chronic epileptic syndromes ○ acutely ill patients with impaired mental status
Refractory SE (RSE)		• Standard treatments for SE have been ineffective • Patient continues to experience either clinical or electrographic seizure activity DESPITE the administration of ≥ 2 appropriately selected and dosed parenteral medications
Super Refractory SE (SRSE)		≥ 24 hours of seizure activity despite anesthetic treatment, OR recurring on attempted weaning of anesthetics.
Prolonged Super Refractory SE		≥ 7 days of seizure activity with ongoing need for anesthetics.

These distinctions help categorize and address the different presentations and challenges posed by SE in clinical practice.

Diagnostic Evaluation:

History:

Assess for:

- Seizure onset and semiology (e.g. which parts of the body are involved, the patient's actions prior to seizure onset, body/facial movements)
- Context of seizure onset (e.g. out of sleep or wakefulness, any identified triggers)
- Known epilepsy
- Birth history (e.g. pregnancy, delivery, NICU stay)
- Ingestion
- Fever or other signs of infection or illness
- Medications
  - Received prior to presentation (type, dose, dosage, route)
  - Current anticonvulsant medications
  - Use of psychopharmacologic medications
  - Toxic/subtherapeutic anticonvulsant levels
  - Nonadherence and/or recent change in dosing
- Presence of a Vagus Nerve Stimulation (VNS) or other neuromodulatory device
- Metabolic abnormalities
- Trauma
- Dietary therapies (e.g. ketogenic diet)
- Prior neurosurgical intervention

Physical Examination:

- Ensure patient's ABC's (Airway, Breathing, and Circulation) are intact and address any needs, if present.
  - Obtain vital signs, including pulse oximeter
  - Provide respiratory support, as appropriate (suction secretions, secure the airway, administer O_2)
  - Assess perfusion (cap refill, lip color, etc.)
  - Obtain intravenous access
  - Cardiac monitor, if indicated
- Neurologic Exam
  - Mental status (GCS)
  - Any ongoing seizure activity (assess pupils, eye movement)
  - Motor, reflex, and gait assessment for focal motor deficit and/or ataxia
  - Assess for meningeal signs
- Careful examination for the source of fever (particularly ear, throat, and lung exam)
- Examine for specific rashes or ticks

Critical Points of Evidence

Evidence Supports

- Parenteral benzodiazepines remain the first-line treatment of choice in status epilepticus[1]
- Use of lumbar puncture for febrile children with signs and symptoms of meningitis or encephalitis
- A stabilization phase as initial management at the onset of seizure activity.[8]

Evidence Lacking/Inconclusive

- Although levetiracetam appears to have fewer serious side effects compared to phenytoin, there is insufficient evidence to establish its superiority in efficacy.[3] Randomized, double blind trials of the use of levetiracetam, fosphenytoin, and valproate showed equal treatment success in about half of pediatric and adult patients without superiority of one agent (ESETT - Established Status Epilepticus Treatment Trial).[9]
- Low level evidence suggests lacosamide can be an effective treatment for pediatric status epilepticus, but studies directly comparing lacosamide to standard of care medications like phenytoin, valproic acid or levetiracetam are lacking.
- The Emergency treatment with Levetiracetam or Phenytoin in Status Epilepticus in children (EcLiPSE) trial, which compared levetiracetam with phenytoin, did not demonstrate any statistically significant or meaningful difference between the two medications.[2]
- Use of lumbar puncture for febrile children 6 to 12 months of age with deficient or unknown immunization history
- Use of lumbar puncture for febrile children pretreated with antibiotics

Evidence Against

- Use of propofol in children due to higher risk of Propofol Related Infusion Syndrome (PRIS).[7]

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[3] Appleton, R. E., Rainford, N. E., Gamble, C., Messahel, S., Humphreys, A., Hickey, H., Woolfall, K., Roper, L., Noblet, J., Lee, E., Potter, S., Tate, P., Al Najjar, N., Iyer, A., Evans, V., & Lyttle, M. D. (2020). Levetiracetam as an alternative to phenytoin for second-line emergency treatment of children with convulsive status epilepticus: the EcLiPSE RCT. *Health technology assessment (Winchester, England)*, *24*(58), 1–96. https://doi.org/10.3310/hta24580

[7] Hemphill, S., McMenamin, L., Bellamy, M. C., & Hopkins, P. M. (2019). Propofol infusion syndrome: a structured literature review and analysis of published case reports. *British journal of anaesthesia*, *122*(4), 448–459. https://doi.org/10.1016/j.bja.2018.12.025

[8] AES 2024! (n.d.). Default. Retrieved October 29, 2024, from https://aesnet.org/default

[9] Chamberlain, J. M., Kapur, J., Shinnar, S., Elm, J.,Efficacy of levetiracetam, fosphenytoin, and valproate for established status epilepticus by age group (ESETT): a double-blind, responsive-adaptive, randomised controlled trial. *Lancet (London, England)*,

Practice Recommendations & Clinical Management

(for full recommendations see attached pathway and addendums)

Treatment of SE

The primary objective of treatment of SE is to halt both clinical and electrographic seizure activity promptly. The initial approach involves assessing and addressing airway, breathing, and circulation simultaneously (such as obtaining intravenous access, administering oxygen, and securing the airway if necessary), providing seizure-stopping medications (1st line therapy, 2nd line therapy, etc. as appropriate), screening for the root cause of SE, and promptly managing any life-threatening conditions associated with SE (such as meningitis, severe metabolic derangement, or intracranial lesions with potential for herniation).[4]

Although the treatment is given in stages, treatment is a continuum. Urgent cessation of seizure activity is the goal in each stage.

The treatment of SE should occur rapidly and continue sequentially until clinical seizures are halted.[4] ***(Strong recommendation; High-quality evidence.)***

Critical care treatment and monitoring should be started simultaneously with emergent initial therapy and continued until further therapy is considered successful or futile.[4] ***(Strong recommendation; Moderate quality evidence.)***

Laboratory Testing

Initial Evaluation	Additional Evaluation to Consider
● Fingerstick glucose ● Comprehensive Metabolic Panel (CMP) ● CBC ● Serum drug levels (if established on anti-seizure medications) ● Urine toxicology screen ● Beta Hydroxybutyrate (if on a ketogenic diet) ● VBG/CBG ● If patient receives a loading dose of an antiseizure medication, consider obtaining post-load medication levels (e.g. fosphenytoin, phenobarbital, valproic acid)	● Lumbar puncture should be considered in the following circumstances: ○ Clinical signs or symptoms concerning for meningitis[5] ***(Strong recommendation; High-quality evidence.)*** ○ Infant (6-12 months) presenting with seizure, fever, and/or ill appearing,with deficient or unknown immunization history[5] ○ Presents with seizure and a fever and is pre treated with antibiotics[5] ● Specific toxicology testing (if history or physical exam suggests a specific toxin) ● Comprehensive toxicology screen (if no clear etiology for SE)

[4] Brophy, G. M., Bell, R., Claassen, J., Alldredge, B., Bleck, T. P., Glauser, T., Laroche, S. M., Riviello, J. J., Jr, Shutter, L., Sperling, M. R., Treiman, D. M., Vespa, P. M., & Neurocritical Care Society Status Epilepticus Guideline Writing Committee (2012). Guidelines for the evaluation and management of status epilepticus. Neurocritical care, 17(1), 3–23. https://doi.org/10.1007/s12028-012-9695-z

[5] Neurodiagnostics evaluation of the child with a simple febrile seizure. American Academy of Pediatrics, Subcommittee on Febrile Seizures. Pediatrics [IBD]. 2011;127(2):389-394.

Imaging

- In children presenting with status epilepticus of unknown etiology, neuroimaging is recommended.
- In the appropriate clinical context, such as persistent focal deficits or refractory status epilepticus, urgent imaging with CT or MRI should be considered.

Diagnosis

- Continuous EEG monitoring is indicated for all patients treated for refractory status epilepticus
- In patients without refractory status epilepticus, continuous EEG should be strongly considered if there is no clear return to baseline mental status

Consults/Referrals:

- Neurology
- Critical Care

Patient Disposition

Admission Criteria (Admit for any of the following)

- New onset recurrent seizures
- Persistent encephalopathy
- Focal deficit
- Parental anxiety
- Other medical indications

Consideration For **ICU Admission**:

- Refractory Status Epilepticus or need for continuous medication infusions
- Need for advanced respiratory support (beyond supplemental O_2)
- Persistent severe encephalopathy
- Hemodynamic instability

Minimum Discharge Criteria

- Cessation of status epilepticus
- Appropriate mental status; return to baseline mental status
- Appropriate support system (e.g. primary care physician, caregiver/family)

Follow-Up Care

- Children should follow up with a Neurologist
- Additional follow-up care, as indicated (e.g. therapies, neurosurgery, PM&R)

Addendums

1. DCMC Status Epilepticus ED/Inpatient Pathway
2. DCMC Status Epilepticus Critical Care Pathway

Outcome Measures

1. Re-presentation rate to the Emergency Department (w/n 30 days)
2. Readmission rate to DCMC (w/n 30 days)
3. Inpatient average length of stay
4. Time to outpatient Neurology clinic follow-up
5. Utilization of Computed Tomography
6. Utilization of Magnetic Resonance Imaging
7. Utilization of Electroencephalogram
8. Time to administration of first anti-seizure medication.
9. Time to administration of second anti-seizure medication.
10. Time to seizure termination.
11. Recurrence of status epilepticus (within 1 day; within the same hospital stay)
12. Time to Neurology notification (by EEG tech)
13. Balancing measure: wasted rescue meds

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6. Gaínza-Lein M, Sánchez Fernández I, Jackson M, Abend NS, Arya R, Brenton JN, Carpenter JL, Chapman KE, Gaillard WD, Glauser TA, Goldstein JL, Goodkin HP, Kapur K, Mikati MA, Peariso K, Tasker RC, Tchapyjnikov D, Topjian AA, Wainwright MS, Wilfong A, Williams K, Loddenkemper T; Pediatric Status Epilepticus Research Group. Association of Time to Treatment With Short-term Outcomes for Pediatric Patients With Refractory Convulsive Status Epilepticus. JAMA Neurol. 2018 Apr 1;75(4):410-418. doi: 10.1001/jamaneurol.2017.4382. PMID: 29356811; PMCID: PMC5885266.
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DELL CHILDREN'S MEDICAL CENTER
EVIDENCE-BASED OUTCOMES CENTER

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May 2020	Seizure Diagnostic Evaluation table added.
July 2020	Status Epilepticus Critical Care Pathway added. Seizure Clusters Pathway removed.
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