

Seizure Clinical Pathway: NICU Management

Diagnosis and Workup

August 2025



A newborn has a high-risk for seizure (eg. encephalopathy) or clinical concern for seizure. ^{1, 2}

If not already completed, order stat EEG with consideration for cranial ultrasound (US) if able to be obtained quickly prior to starting EEG.

Consider empiric rescue **lorazepam** (0.1 mg/kg) for clinical seizure without EEG confirmation and delay in access to EEG.

Confirmed electrographic seizures?

NO

Stop EEG if no seizures are detected after 24 hours of monitoring, or in cases of HIE, when rewarming is completed, whichever occurs later.

No further workup needed.

As soon as possible:

- Start seizure management per **Medication Escalation Pathway** on page 2.
- Consider empiric rescue **lorazepam** (0.1 mg/kg) **ONLY** if Phenobarbital not immediately available
- **Consult Children's Neurology.**³
- Consider empiric antibiotics/antivirals.

Suspicious for HIE?

YES

Follow the **Neonatal HIE Pathway**
Revisit alternate etiologies if seizures are persistent or clinical course indicates.

NO

Work-Up for Underlying Etiology

Work-up for underlying etiology which includes acute symptomatic seizures, congenital malformations, & underlying genetic or metabolic conditions:

Procedures

- **Lumbar Puncture**
 - When stable
 - Order CSF culture, CSF protein, CSF glucose, CSF cell count
 - Consider holding extra CSF for additional labs.

Imaging

- **Brain MRI when clinically stable**
 - If MRI is delayed, consider cranial US until MRI can be performed.
- Cranial US should NOT replace MRI.**

Labs

- **Basic**
 - CBC, CMP, cultures (blood, urine, and CSF), HSV & viral studies, CSF studies
- **Metabolic**
 - Ammonia, lactate, pyruvate, plasma amino acid, urine organic acid, urine alpha-AASA, acylcarnitine, total and free carnitine, pipecolic acid, CSF lactate, CSF pyruvate, CSF amino acid
 - Additional as indicated
- **Genetic**
 - Consider whole exome sequencing, epilepsy gene panel and/or microarray in consultation with **pediatric neurology** and/or **genetics**.

¹Inclusion Criteria

Newborns with concerns for clinical seizure or confirmed electrographic seizure.

²Considerations for Pre-term Infants

Treatments and interventions described in this document may not be appropriate for some pre-term infants. Consultation between Neonatology and Neurology to determine appropriate interventions for pre-term infants should be handled on a case-by-case basis.

³Children's Contact Information

To consult *Children's Neurology* or reach the *Transfer Center* call **404-785-7778**.

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Neonatal Seizure Medication Escalation Pathway

August 2025



Neonatal Seizure Medication Escalation Pathway

Start Phenobarbital (PHB)

Loading Dose: 20 mg/kg IV
If still seizing, give 2nd Loading Dose: 20 mg/kg IV
Maintenance Dose⁴: 5mg/kg/day IV divided q12h
Labs: PHB level (goal 40-60)
 Check PHB level 1-2 hours after 1st loading dose for baseline if seizures subside.
 Check PHB level 1-2 hours after 2nd loading dose if seizures did not subside after 1st dose.

Consider Phenobarbital bolus 10-20 mg/kg IV

Is PHB level between 40-60?

Is patient hemodynamically stable with regular heart rhythm?

Start Fosphenytoin

Loading Dose: 20mg/kg IV
Maintenance Dose⁴: 5 mg/kg/day IV divided q12h
Labs: Free phenytoin level (goal 1-2 mcg/mL) **OR** total phenytoin level with albumin (goal 10-20 ug/mL).
 Check levels 1-2 hours after dose.

Start Levetiracetam

Loading Dose: 60 mg/kg IV
Maintenance Dose⁴: 60 mg/kg/day IV divided q12h

TRANSFER TO CHILDREN'S³

Do not delay Midazolam drip. If awaiting transfer, skip Pyridoxine Challenge⁵ and start Midazolam. Return to Pyridoxine Challenge⁵ after transfer complete.

Consider Pyridoxine Challenge⁵

Loading Dose: 100mg IV slow push, repeat q5min x3-5 doses, along with Leucovorin 5mg IV slow push
Maintenance Dose⁴: 30mg/kg/day divided q12, and Folic acid 5mg BID

Start Midazolam

Loading Dose: 0.2 mg/kg IV
Continuous Drip: 0.1 mg/kg/hr IV
Escalate with bolus: current drip rate + 0.1mg/kg IV
Escalate drip rate: 0.1mg/kg/hr q30-60min until seizure free or max rate of 0.5mg/kg/hr.
Goal: Seizure freedom or significant reduction (≤ 2 seizures/hour, <30 sec each).

Discuss next steps with neurology consult team.
 Consider epilepsy work-up & trial of other medications.

Escalate steps in pathway for persistent electrographic seizures

Continue consultation with *Children's Neurology*.³

⁴Maintenance Dose Consideration

Consult neurology³ to discuss starting maintenance of an anticonvulsant if loading dose(s) achieved seizure cessation and respective blood level is in the goal range (if indicated).

Start maintenance within X hours of last loading dose:

- Phenobarbital: 24 hours
- Fosphenytoin: 12 hours
- Levetiracetam: 12 hours

⁵Pyridoxine Challenge

Consider challenge, **only once transferred to Children's**, for either:

- persistent status epilepticus of unclear etiology **or**
- suspicion for a genetic metabolic disorder with myoclonic jerks, spasms, or tonic seizures.

Rarely, **bradycardia** and **respiratory suppression** can occur. Perform with close cardiopulmonary monitoring.

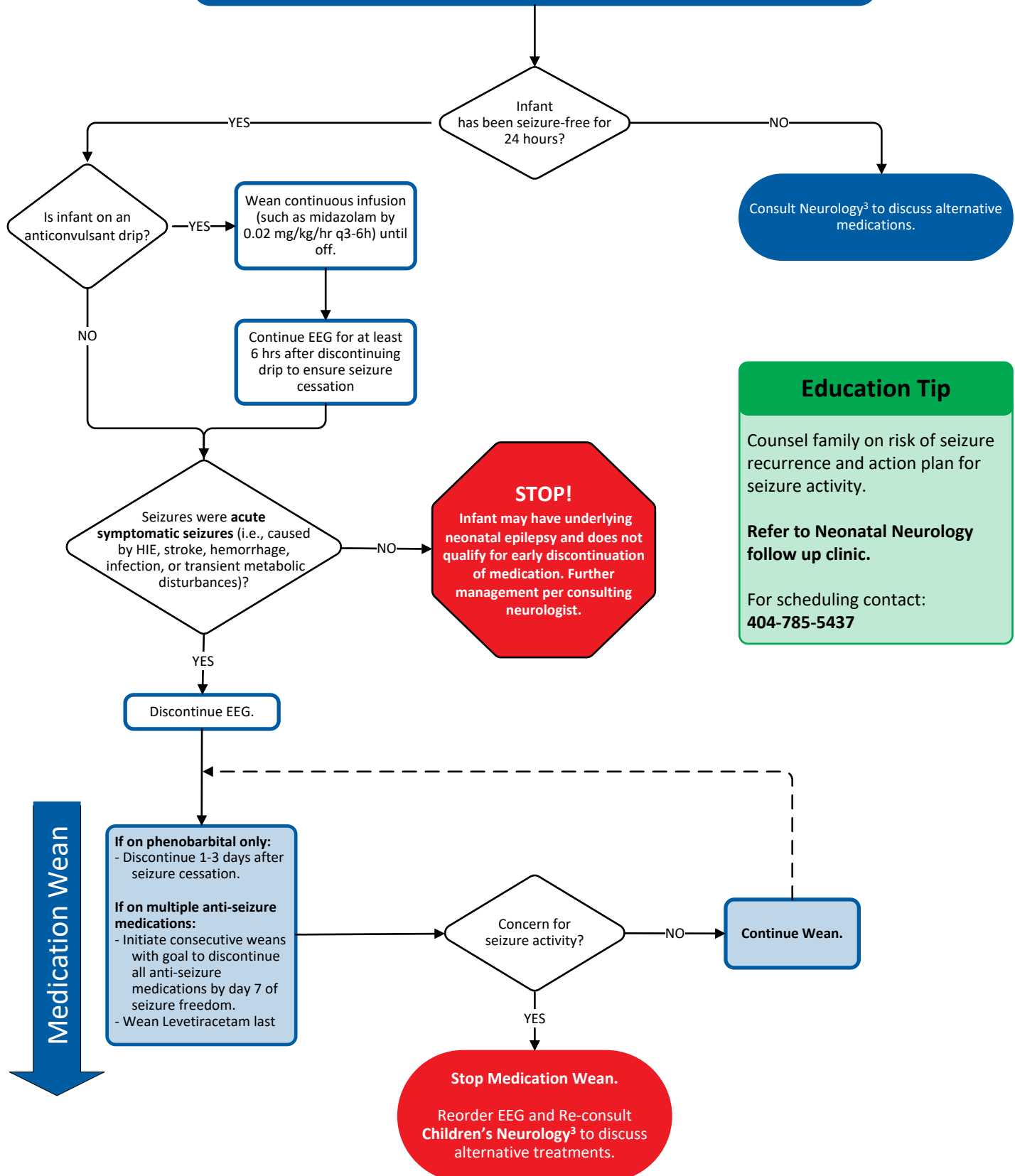
Seizure Clinical Pathway: NICU Management

Neonatal Seizure Medication Weaning Pathway

August 2025



Neonatal Seizure Medication Weaning Pathway



Education Tip

Counsel family on risk of seizure recurrence and action plan for seizure activity.

Refer to Neonatal Neurology follow up clinic.

For scheduling contact:
404-785-5437

References

- Bittigau P, Sifringer M, Felderhoff-Mueser U, Ikonomidou C. Apoptotic neurodegeneration in the context of traumatic injury to the developing brain. *Experimental and Toxicologic Pathology*. 2004 Oct 26;56(1-2):83-9.
- Boylan GB, Kharoshankaya L, Wusthoff CJ. Seizures and hypothermia: importance of electroencephalographic monitoring and considerations for treatment. In *Seminars in Fetal and Neonatal Medicine* 2015 Apr 1 (Vol. 20, No. 2, pp. 103-108). WB Saunders.
- El-Dib M, Soul JS. The use of phenobarbital and other anti-seizure drugs in newborns. *Semin Fetal Neonatal Med*. 2017;22(5):321-327.
- Farwell JR, Lee YJ, Hirtz DG, Sulzbacher SI, Ellenberg JH, Nelson KB. Phenobarbital for febrile seizures—effects on intelligence and on seizure recurrence. *New England Journal of Medicine*. 1990 Feb 8;322(6):364-9.
- Forcelli PA, Kozlowski R, Snyder C, Kondratyev A, Gale K. Effects of neonatal antiepileptic drug exposure on cognitive, emotional, and motor function in adult rats. *Journal of Pharmacology and Experimental Therapeutics*. 2012 Mar 1;340(3):558-66.
- Glass HC, Numis AL, Gano D, Bali V, Rogers EE. Outcomes after acute symptomatic seizures in children admitted to a neonatal neurocritical care service. *Pediatric Neurology*. 2018 Jul 1;84:39-45.
- Glass HC, Soul JS, Chang T, Wusthoff CJ, Chu CJ, Massey SL, Abend NS, Lemmon M, Thomas C, Numis AL, Guillet R. Safety of early discontinuation of antiseizure medication after acute symptomatic neonatal seizures. *JAMA neurology*. 2021 Jul 1;78(7):817-25.
- Glass HC, Shellhaas RA, Wusthoff CJ, Chang T, Abend NS, Chu CJ, Cilio MR, Glidden DV, Bonifacio SL, Massey S, Tsuchida TN. Contemporary profile of seizures in neonates: a prospective cohort study. *The Journal of pediatrics*. 2016 Jul 1;174:98-103.
- Keene JC, Morgan LA, Abend NS, et al. Treatment of neonatal seizures: comparison of treatment pathways from 11 neonatal intensive care units. *Pediatric neurology*. 2022;128:67-74.
- Krishnan V, Ujjanappa V, Vegda H, et al. Sequential levetiracetam and phenytoin in electroencephalographic neonatal seizures unresponsive to phenobarbital: a multicenter prospective observational study in India. *The Lancet Regional Health-Southeast Asia*. 2024.
- Maitre NL, Smolinsky C, Slaughter JC, Stark AR. Adverse neurodevelopmental outcomes after exposure to phenobarbital and levetiracetam for the treatment of neonatal seizures. *Journal of Perinatology*. 2013 Nov;33(11):841-6.
- Painter MJ, Scher MS, Stein AD, et al. Phenobarbital compared with phenytoin for the treatment of neonatal seizures. *New England Journal of Medicine*. 1999;341(7):485-489.
- Pavel AM, Rennie JM, de Vries LS, et al. Neonatal Seizure Management: Is the Timing of Treatment Critical? *J Pediatr*. 2022;243:61-68.e62.
- Pressler RM, Abend NS, Auvin S, et al. Treatment of seizures in the neonate: Guidelines and consensus-based recommendations—Special report from the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2023;64(10):2550-2570.
- Pressler RM, Cilio MR, Mizrahi EM, et al. The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2021;62(3):615-628.
- Sewell EK, Hamrick SEG, Patel RM, Bennett M, Tolia VN, Ahmad KA. Association between anti-seizure medication and outcomes in infants. *J Perinatol*. 2021.
- Sharpe C, Reiner GE, Davis SL, et al. Levetiracetam Versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial. *Pediatrics*. 2020;145(6).
- Shellhaas RA, Chang T, Tsuchida T, et al. The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates. *J Clin Neurophysiol*. 2011;28(6):611-617.
- Shellhaas RA, Wusthoff CJ, Numis AL, Chu CJ, Massey SL, Abend NS, Soul JS, Chang T, Lemmon ME, Thomas C, McNamara NA. Early-life epilepsy after acute symptomatic neonatal seizures: A prospective multicenter study. *Epilepsia*. 2021 Aug;62(8):1871-82.
- Spagnoli C, Seri S, Pavlidis E, Mazzotta S, Pelosi A, Pisani F. Phenobarbital for neonatal seizures: response rate and predictors of refractoriness. *Neuropediatrics*. 2016 Jul 26;318-26.
- Sulzbacher S, Farwell JR, Temkin N, Lu AS, Hirtz DG. Late cognitive effects of early treatment with phenobarbital. *Clinical pediatrics*. 1999 Jul;38(7):387-94.
- Tsuchida TN, Wusthoff CJ, Shellhaas RA, et al. American clinical neurophysiology society standardized EEG terminology and categorization for the description of continuous EEG monitoring in neonates: report of the American Clinical Neurophysiology Society critical care monitoring committee. *J Clin Neurophysiol*. 2013;30(2):161-173.
- Wisnowski JL, Wintermark P, Bonifacio SL, et al. Neuroimaging in the term newborn with neonatal encephalopathy. Paper presented at: *Seminars in Fetal and Neonatal Medicine* 2021.