



Neuroscience NICU
Neonatal Stroke Guidelines
(Last Revised October 2019)



This guideline provides recommendations regarding assessment and treatment of neonatal stroke. Neonatal stroke includes two primary pathologies – cerebral venous sinus thrombosis (CSVT) and perinatal arterial ischemic stroke (PAIS), and as such, these guidelines will differentiate between the two when necessary. Ultimately, the final decision for care of the infant will be determined by the primary medical team.

When to Suspect Neonatal Stroke

- Apnea (especially in term infants)
- Seizures – most common presentation (60-70%) of CSVT and (69-90%) of PAIS
 - Usually focal and within the first day in PAIS
 - General and focal both common and commonly seen later in the first week or beyond in CSVT
- Asymmetric movement of limbs (especially with PAIS)
- Encephalopathy
- Unexplained thrombocytopenia

Initial Imaging Evaluation

- Head US within the first 24 hours to evaluate for hemorrhage (may be normal in 1/3 of neonatal stroke¹)
- MRI, MRA, MRV of head as soon as clinically stable (ideally within the first 1-2 days)
 - If not stable enough for MRI, may consider CT/CTA/CTV

Further Evaluation Once Diagnosed

- Obtain maternal history, focusing on:
 - Maternal or family history of bleeding/hemophilia
 - History of thrombotic events or multiple (2 or more) miscarriages
 - If positive history, recommend to OB that mother is tested for antiphospholipid antibodies (PT/PTT, hexagonal phospholipid neutralization test, diluted Russell's venom viper test, anticardiolipin IgA, IgG and IgM (by ELISA), beta-2-glycoprotein antibodies)
 - Family history of hypercoagulability, e.g.
 - Does any first-degree relative have a history of early heart attack or stroke (before 50)?
 - Does any first-degree relative have a history of deep vein thrombosis or pulmonary embolism?
 - Possible drug use
 - Newborn tox screens if concern for maternal drug use
- Request placental pathology, if possible
- Consider EEG monitoring
- Echocardiogram only if cardiac signs or symptoms

If suspected CSVT:

- Repeat MRI 5-7 days after initial MRI

Hematologic Evaluation

- Consider prothrombotic screening in neonates with:
 - Evidence of systemic hypercoagulable state (e.g. more than one site of thrombosis)
 - Family history of hypercoagulability (see first two bullet points under maternal history above)
- If screening deemed appropriate, should include the following (requires minimum of ~8.5 mL of blood):
 - Antiphospholipid antibodies
 - Lupus anticoagulant
 - Anti-B2 glycoprotein 1 antibodies, IgG and IgM
 - Anti-cardiolipin antibodies, IgG, IgA, and IgM
 - Protein C functional assay
 - Protein S
 - Plasminogen
 - Serum lipoprotein (a)
 - Fibrinogen
 - Factor VIIIc

- Factor V Leiden gene mutation
- Prothrombin gene mutation
- ATIII levels

Management

- Control seizures, if present (see neonatal seizure guideline)
- Avoid dehydration – may require vascular access and intravenous fluids
- Attempt to maintain stable cerebral perfusion – normal serum glucose, blood pressure, temperature (avoid hyperthermia), ventilation (P_{CO2} 45-50 mmHg, and oxygenation)
- PT/OT consult when clinically stable

Anticoagulation

- Anticoagulation is not indicated in most cases
- May be considered in select infants **with ischemic infarction and²:**
 - Clinical or radiological evidence of propagating CSVT despite supportive therapy³ (occurs in 25-30%⁴)
 - Intracardiac or intravascular thrombus considered at risk for embolization
 - Recurrent AIS
 - Severe thrombophilic disorders
- Relative contraindications for anticoagulation:
 - Hemorrhagic transformation of the infarct
 - MCA infarct greater than 50% of the MCA territory
 - Large cerebellar infarct
- If considering anticoagulation:
 - Consult hematology
 - UFH or LMWH for 6-12 weeks, with longer duration in children with incomplete recanalization or ongoing symptoms³

Follow-up

- Hematology
 - 1 week after discharge if receiving Lovenox
 - ~6 months of life if no Lovenox
- Neurology – 2-3 months after discharge (consider sooner if abnormal neurological exam or receiving multiple anti-epileptic drugs at time of discharge)
- PT/OT – will be determined based on initial assessment during hospital stay
- TIPS 2/3

References

1. Cowan F, Mercuri E, Groenendaal F, Bassi L, Ricci D, Rutherford M, et al. Does cranial ultrasound imaging identify arterial cerebral infarction in term neonates? *Archives of disease in childhood Fetal and neonatal edition*. 2005;90(3):F252-F256.
2. Roach ES, Golomb MR, Adams R, Biller J, Daniels S, Deveber G, et al. Management of stroke in infants and children: a scientific statement from a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young. *Stroke*. 2008;39(9):2644-2691.
3. Monagle P, Chan AKC, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Gottl U, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e737S-e801S.
4. Moharir MD, Shroff M, Stephens D, Pontigon AM, Chan... pediatric cerebral sinovenous thrombosis: a safety and ou...

When seizures cease:

1. Initiate 2nd line investigation, including CUS or MRI, metabolic/ congenital infection/ genetic screening.
2. Continue EEG or aEEG for ≥8 hours of seizure freedom.
3. If on maintenance phenobarbital, continue to monitor blood levels.
4. Attempt to wean seizure medications prior to discharge if:
 - a. There are single or rare seizures