Hypoxic Ischemic Encephalopathy (HIE) – Neonatal – Inpatient Guideline Summary

Target Population: Neonatal infants with suspected or diagnosed HIE

Link to Full Guideline: Hypoxic Ischemic Encephalopathy - Neonatal - Inpatient

Therapeutic Hypothermia Assessment Tool

Infant must meet the following criteria to be considered for treatment:

- Gestational age ≥ 36 and 0/7 weeks
- Birth weight ≥ 1800 grams
- ≤ 6 hours of life at time of initial evaluation
- No exclusion criteria are present

AND

I. Clinical and biochemical criteria

II. Demonstrate moderate or severe encephalopathy

Step I: Clinical and biochemical criteria

- History of acute perinatal event (e.g., uterine rupture, placental abruption, umbilical cord prolapse or avulsion, or severe fetal heart rate abnormality)
- APGAR score < 6 at 10 minutes of life
- Prolonged resuscitation, defined as positive pressure ventilation (via bag-mask or advanced airway) initiated at birth and continued for at least 10 minutes
- pH ≤ 7.0 on arterial cord blood gas or first postnatal hour blood gas
- Base deficit ≥ 12 mEq/L on arterial cord blood gas or first postnatal hour blood gas

Infant meets clinical and biochemical criteria if A or B are met:

A. pH ≤ 7.0 **or** base deficit ≥ 12 mEq/L

B. pH between 7.0 and 7.15 with history of an acute perinatal event **and** at least one of the following:

i. Apgar score < 6 at 10 minutes

ii. Prolonged resuscitation

Step II: Neurologic evaluation using neonatal encephalopathy exam

- Inborn evaluation should occur after 15 minutes of life using .HIEEXAM
- Outborn evaluation should be done with referring site under guidance of medical control, use of telemedicine (if able) is strongly encouraged

Infant meets neonatal encephalopathy criteria if A or B are met:

A. Seizures

B. Moderate or severe encephalopathy using neonatal encephalopathy exam (See Appendix A: Neonatal Encephalopathy Exam or EPIC smartphrase .HIEEXAM)

Exclusion criteria:

- Presence of major congenital anomalies
- Moribund infants for whom no additional intensive therapy will be offered, as determined by attending neonatologist

Relative contraindications:

- Infant > 6 hours old at time of initial evaluation
- Severe hemodynamic compromise
- Severe coagulopathy with active bleeding
- Confirmed venous sinus thrombosis

Additional considerations:

- Consult PICU for infants with critical congenital heart disease who require cooling
- If there is a question whether to initiate cooling, place aEEG, obtain STAT Pediatric Neurology consult, and begin passive cooling for up to 6 hours while decision is being made
- If infant is outborn, eligibility will be determined in conjunction with the referring clinician. An infant with a qualifying exam prior to transfer, will still be cooled per the guideline regardless of admission exam

Therapeutic Hypothermia Strategy: Cooling and Re-Warming

Cooling – Targeted esophageal temperature of 33.5-34.5°C

- Therapeutic hypothermia (i.e., active or passive cooling) should be initiated within 6 hours of life
- Once targeted temperature is reached (i.e., first esophageal temperature), maintain for 72 hours

Re-warming

- Re-warm after 72 hours from first esophageal temperature
- Slow re-warming of patient preferred at rate of 0.5°C per hour to core body temperature of 36.5°C
- Maintain normothermia with the cooling blanket for 24 hours s/p rewarming to avoid rebound hyperthermia

For additional information on conducting cooling on transport, passive cooling and cooling in NICU, refer to Neonatal Whole Body Cooling Procedure

Therapeutic Hypothermia – Patient Labs for Monitoring

Lab (Normal Range)	Suggested Frequency
Temperature corrected blood gas, lactate, ionized calcium (iCa) (4.5-5.3 mg/dL which equals: 1.12-1.32 mmol/L; 2.25-2.65 mEq/L)	Every 6 hours for first 24 hours then every 12-24 hours (minimum during cooling) **Note:** Temperature corrected blood gases are available on the NICU ABL 90 and the main lab. To get temperature corrected readings, do the following: • On workstation order, clearly write patient's temperature at time of draw • If processed in the NICU, notify respiratory therapy of the patient's current temperature and desire for temperature corrected blood gases. The temperature corrected values that will appear in Health Link include: • PH, TEMP CORRECTED • PCO2, TEMP CORRECTED • PO2, TEMP CORRECTED
Glucose	Every hour during initiation of cooling until temp 33.5-34.5°C is reached; thereafter, check every 6 hours during cooling. During rewarming, check at start of rewarming, every 2 hours x 2, then PRN and with lab draws
Chemistries (Ca 8.7-10.1 mg/dL) (Mg 1.8-2.3 mg/dL) (K 4.0-6.0 mEq/L)	Check Electrolytes, Ca, Mg, Phos every 12-24 hours during cooling Consider monitoring during rewarming
CBC	Check every 12-24 hours
Cultures	Obtain blood culture; consider sputum and cerebral spinal fluid culture
PT/PTT/INR	Check every 24 hours
BUN/CR	Check every 12-24 hours
AST/ALT	Check every 24 hours

Therapeutic Hypothermia – Medical Management by System

System	Considerations
Monitoring (including radiographic studies)	• Babygram STAT on admission; confirm esophageal probe placement • aEEG/cEEG on admission • Cranial ultrasound on admission with Doppler* • NIRS (i.e., cerebral and renal) • Echocardiogram if hemodynamically unstable or concern for pulmonary hypertension • Brain MRI* - If severely encephalopathic and family is considering withdrawal of support, discuss early MRI with neuroradiologist and consider obtaining at 24-48 hours of life - Routine MRI and MRS on DOL #4-5 - Consider follow-up MRI and MRS on DOL #10-14 **** When ordering, must note "HIE Protocol" in comment section to ensure appropriate study***
Fluids, Electrolytes, Nutrition (FEN)	• NPO through rewarming • Initial total fluid goal of 50-60 mL/kg/day (D10W) • Treat hypovolemia with volume (normal saline, PRBCs) • If acidosis worsens base deficit > 10 mEq/L, consider: - Normal Saline (NS) (10 mL/kg IV) - Sodium bicarbonate (1-2 mEq/kg IV over 30 mins) - Add sodium acetate to maintenance fluids
Respiratory	• Avoid hypocapnia (goal PCO_2 45-50 mmHg) • Avoid hyperoxia (goal PaO_2 80-100 mmHg, SpO_2 94-98%)

	• Persistent pulmonary hypertension (PPHN) may worsen in some cases, consider pre- and post-ductal monitoring
Cardiovascular	• Continuous BP monitoring with arterial line preferred • Monitoring with 3-lead EKG • Maintain BP in normal range (SBP 60-70 mmHg / DBP 40-50 mmHg and MAP 40-50 mmHg) • If needed, support BP: 1st choice dopamine 2-5 mcg/kg/minute • Heart Rate: Expect bradycardia < 100 bpm • For deep bradycardia (< 80 bpm): - May be tolerated if BP is stable within target range and perfusion is appropriate on physical exam - If not tolerated, raising core temp to 34°C may be adequate; if symptomatic bradycardia persists, consider dopamine
Infectious Disease (ID)	• Initiate rule out sepsis evaluation with empiric antibiotics for all infants being treated with therapeutic hypothermia • Start ampicillin 100 mg/kg/dose IV q12 hours and gentamicin 4 mg/kg/dose q24 hours - If concern for meningitis, increase ampicillin dose to 100 mg/kg IV Q8 hours - For patients with renal concerns, consider ceftazidime 50 mg/kg/dose IV q12 hrs in place of gentamicin • Consider lumbar puncture to rule out meningitis
Neurologic	• Obtain Pediatric Neurology consult • Document complete neuro exam and neonatal encephalopathy exam using .HIEEXAM Epic SmartPhrase • Maintain adequate sedation; *NPASS score goal -1 – Do not allow patients to shiver!* - Morphine is drug of choice - **Day 1:** Morphine loading dose 0.05 mg/kg IV - Start maintenance continuous infusion at 0.01 mg/kg/hr - Escalate infusion rate by 0.005 mg/kg/hr as needed - Provide bolus doses of morphine 0.02 mg/kg IV every 3-4 hours PRN - If continuous infusion not available, schedule morphine 0.05 mg/kg every 4 hours - **Day 2:** Wean continuous morphine infusion by half to avoid toxic accumulation; goal rate of 0.005 mg/kg/hr - If patient is on scheduled morphine boluses instead of continuous infusion, decrease scheduled morphine by 50% as tolerated - **2nd Line**: Consider starting dexmedetomidine 0.2 mcg/kg/hr if morphine infusion > 0.015 mg/kg/hr - Do not administer dexmedetomidine loading or bolus dose due to risk of bradycardia and hypotension - When administering dexmedetomidine, wean morphine infusion to lowest rate tolerated (may discontinue) - If on-going concerns for pain and normal liver function, consider acetaminophen 7.5-10 mg/kg IV every 6 hours PRN • Treat seizures; load with levetiracetam 50mg/kg/dose (refer to Neonatal Seizures – Neonatal – Inpatient/Emergency Department Clinical Practice Guideline for ongoing management) • Continue aEEG/EEG monitoring through re-warming process or until patient is seizure free for 24-72 hours based on Pediatric Neurology's recommendation
Skin	• Maintain pressure relieving device • Reposition every 2 hours • Monitor for fat necrosis, pressure ulcers

Patient Follow-Up

- Patients should follow up at 3 months of age after discharge with Waisman Center Newborn clinic or accessible neurodevelopment clinic
- May consider consult with Waisman Center prior to discharge for transition of care consultation
- Patients should follow up with Pediatric Neurology per service's recommendation