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

Infants with HIE must meet all of the following 3 criteria within 6 hrs of life to be considered for therapeutic hypothermia:

1. Gestational age ≥ 36 and 0/7 weeks
2. One of the following clinical scenarios:
    a. pH ≤ 7.0 or base deficit ≥ 16 (cord gas or baby gas within 1hr of life)
    b. If blood gas not available or pH is 7.01-7.15 or base deficit is 10-15.9, then patient must have:
        i. Acute perinatal event (i.e., uterine rupture, placental abruption, umbilical cord prolapse/avulsion, or severe fetal heart rate abnormality)
        AND
        ii. Either Apgar ≤ 5 at 10 min or need for prolonged resuscitation (CPR, CPAP, PPV) for ≥ 10 min
3. Evidence of moderate or severe encephalopathy on clinical exam or seizures
HealthLink dot phrases (e.g., .HIE or .HIEexam are available to be used in clinical documentation.

Exclusion criteria:

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

Relative contraindications:

- Birth weight < 1800 grams
- Infant > 6 hours old at time of initial evaluation
- Severe hemodynamic compromise
- Severe coagulopathy with active bleeding
- Confirmed venous sinus thrombosis

Additional considerations:

- Serial exams
    - If cooling criteria are not met on the initial exam (at 30-60 min of life), a second exam should be performed at 4–5 hours of life (or sooner), with at least one exam performed by or directly supervised by newborn/neonatology attending.
- If there is a question whether to initiate cooling, place aEEG and/or cEEG, 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 within the targeted therapeutic range
- 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 6-12 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 initially; reduce frequency when stable
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)	• Initial total fluid goal of 50-60 mL/kg/day (D10W) • Consider initiating minimal trophic feeds (up to 20ml/kg/day) after 24hrs in infants undergoing therapeutic hypothermia if they are hemodynamically stable and do not show signs of feeding intolerance • 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 may worsen in some cases, consider pre- and post-ductal monitoring
Cardiovascular	• Continuous BP monitoring with arterial line preferred and cardiac activity monitoring with 3-lead EKG • Maintain BP in normal range (SBP 60-70 mmHg / DBP 40-50 mmHg and MAP 40-50 mmHg) • For hypovolemia, use isotonic crystalloids judiciously (10-20 mL/kg). • For hypotension, consider use of medications based on the infant's hemodynamics assessment: - Dopamine may worsen pulmonary hypertension due to pulmonary vasoconstrictive effects and should be considered with caution in this context (suggested dosing range 5-25 mcg/kg/min) - Epinephrine (suggested dosing range 0.01-0.1 mcg/kg/min) - Norepinephrine (suggested dosing range 0.05-1.0 mcg/kg/min) - Vasopressin (suggested starting dose 0.17-10 milliUnits/kg/min) • For ventricular dysfunction, dobutamine (suggested dosing range 2-20 mcg/kg/min) is an additional option. • 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 suffice; if symptomatic bradycardia, consider dopamine
Infectious Disease (ID)	• Initiate rule out sepsis evaluation with empiric antibiotics for all infants being treated with therapeutic hypothermia • Start ampicillin 50 mg/kg/dose IV q8 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 -2 to +3 – Do not allow patients to shiver!* • Dexmedetomidine is preferred initial agent unless any exclusion criteria* are present - *Exclusion: Persistent HR ≤ 60 if associated with signs of poor perfusion or persistent hypotension, uncontrolled or refractory seizures - Initial dose: 0.3 mcg/kg/hr IV (no loading dose) - Adjustments to achieve goal N-PASS of -2 to +3 ▪ If N-PASS >3 or shivering: May increase by 0.1 mcg/kg/hr every 30-60 min (Max dose 1.3 mcg/kg/hr) • If agitation persists despite max dose, add PRN morphine 0.05 mg/kg IV Q3hr ▪ If N-PASS <-2: Decrease by 0.1 mcg/kg/hr every 30-60 min - Adjustments for bradycardia ▪ If HR 60-69 bpm for >30 min, decrease by 0.1 mcg/kg/hr and continue to monitor ▪ If HR <60 bpm • Hold dexmedetomidine for 30-60 min and re-evaluate • Use PRN morphine 0.05 mg/kg IV Q3hr to manage pain, agitation while holding • IF HR stabilizes, consider re-starting dexmedetomidine at lower rate with use of PRN morphine - If on-going pain and normal liver function, consider acetaminophen 7.5-10 mg/kg IV every 6 hours PRN • Treat seizures; load with IV levetiracetam 60mg/kg/dose or IV phenobarbital 20 mg/kg (refer to Neonatal Seizures – Neonatal – Inpatient/Emergency Department Clinical Practice Guideline for ongoing management) • Continue aEEG/EEG monitoring through re-warming process and for 6 hours of normothermia, or until patient is seizure free for 24-48 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

Moderate to Severe HIE

- Schedule follow-up visit at Waisman Center Newborn Clinic or an equivalent neurodevelopment clinic, at 3 months of age
- Additionally, infants requiring ongoing antiseizure medication should follow-up within 4-8 weeks post-discharge with Pediatric Neurology

Mild HIE

- For NICU patients with mild HIE, consider follow-up at Meriter high-risk follow-up clinic