Neuroscience NICU

Therapeutic Hypothermia Guidelines

(Last Revised September 2019)

This guideline provides recommendations regarding transport, assessment, and treatment of neonatal encephalopathy. The primary management centers around therapeutic hypothermia for hypoxic-ischemic encephalopathy, although etiologies other than HIE must be considered in any infant with encephalopathy.

**Transport and initial management**

- If there is any question regarding the need for hypothermia, the transport team will take the Tecotherm Neo system and set up the system en route to the referring hospital (Appendix A: Setting up the Tecotherm)
- If neonate meets criteria both by history and by physical exam for moderate to severe encephalopathy and no contraindications exist (see eligibility section – if unclear, discuss with medical control provider) then begin whole body cooling using the Tecotherm system
- If question remains if the baby meets criteria after discussion with MCP, set the transport incubator to 28.0°C and do not exceed rectal temperature of neonate greater than 36.5°C (and no lower than 33 ºC)
- Consider performing the following, taking into account that each clinical situation is unique and these recommendations will not always be possible or appropriate given time constraints:
  - Ensure adequate vascular access (including umbilical lines or peripheral arterial line as necessary)
  - Foley catheter, NG/OG to gravity
  - Medications/infusions
    - Dextrose 10% as maintenance fluids at 50-60 ml/kg/day (may need up to 20% to maintain GIR)
    - Antibiotics if indicated: ampicillin/cefotaxime (avoid renal-excreted antibiotics if possible)
      - Cefepime (or gentamicin with close monitoring of levels) may be substituted for cefotaxime
    - Vasoactive agents as indicated (dobutamine as first line if available, otherwise epinephrine – should avoid primary vasoconstrictors such as dopamine)
    - Consider iNO if impaired oxygenation
    - Use only short-acting sedation (fentanyl) and anticonvulsant medications (lorazepam) if needed during transport
  - Labs
    - Complete EPOC panel
    - Monitor blood sugar hourly
  - Monitoring
    - Set alarm limits on monitors to low HR = 80 and high HR = 220
    - Vital signs including rectal temperature every 15 minutes.
    - Neuro checks every 30 minutes (need penlight)
  - Handling
    - Reposition every 1 hour on longer transports to avoid skin injury and for perfusion monitoring
    - Maintain head in midline position
    - Attempt minimal handling, decreased stimulation
    - Place ear protection
    - Consider using phototherapy swaddler, if available

- **Before leaving referring hospital:**
  - Leave Encephalopathy/Hypothermia brochure with family
  - Ask the referring facility to send the placenta for pathology
- The 72-hour cooling period begins when the infant’s rectal temperature reaches ≤ 34.0°C (Desired range 33.0 - 34.0°C). Record on documentation.

**Eligibility for therapeutic hypothermia**

- Gestational age ≥ 35 0/7 weeks
Cooling may be less effective in small for gestational age infants, but there appears to be no harm.

- Postnatal age <6 hours
- History: (one or more of the following)
  - Cord or blood gas in 1st hour with pH less than or equal to 7.1
  - Cord or blood gas in 1st hour with base deficit greater than or equal to 12
  - Need for ventilation support beginning at birth and continuing at 10 minutes of life, including mask or ETT ventilation
  - Apgar score less than or equal to 5 at 10 minutes of life
  - Acute period of hypoxia-ischemia (i.e. cardiac arrest, severe placental abruption)
- Physical exam (must be moderate or severe to qualify for hypothermia)
  - Should be obtained more than 10 minutes after resuscitation is completed and before being cooled
  - Must have the presence of one or more abnormal signs in 3 of the 6 following categories
  - Clinical seizures automatically qualify infant as moderate to severe encephalopathy

<table>
<thead>
<tr>
<th>Physical Exam</th>
<th>Moderate Encephalopathy</th>
<th>Severe Encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of Consciousness</td>
<td>Lethargic</td>
<td>Stupor or coma</td>
</tr>
<tr>
<td>Spontaneous Activity</td>
<td>Decreased</td>
<td>No activity</td>
</tr>
<tr>
<td>Posture*</td>
<td>Distal Flexion, complete extension-Arms are flexed and legs extended, fingers, toes and thumbs in strong flexion</td>
<td>Decerebrate- Legs and arms are extended with the wrists flexed and hands fisted</td>
</tr>
<tr>
<td>Tone</td>
<td>Hypotonia (focal or general)</td>
<td>Flaccid</td>
</tr>
<tr>
<td>Primitive Reflexes</td>
<td>Weak</td>
<td>Absent</td>
</tr>
<tr>
<td>Suck</td>
<td>Incomplete</td>
<td></td>
</tr>
<tr>
<td>Moro</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autonomic system</td>
<td>Constricted</td>
<td>Deviated, dilated or non-reactive</td>
</tr>
<tr>
<td>Pupils</td>
<td>Bradycardia</td>
<td>Variable</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>Periodic breathing</td>
<td>Apnea</td>
</tr>
<tr>
<td>Respiration</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Images adapted from Fletcher’s Physical Diagnosis of Neonatology*

- Relative contraindications
  - Life-threatening congenital anomalies, infant not expected to survive transport
  - Severe pulmonary hypertension or use of inhaled nitric oxide
  - Difficulty in controlling active bleeding, DIC, coagulopathy
  - Known intracranial hemorrhage or stroke

**Neuroimaging for neonatal encephalopathy**
- Head ultrasound should be obtained immediately upon admission to assess for non-HI causes of encephalopathy and potential contraindications to therapeutic hypothermia
- MRI should be obtained between 24 to 72 hours after rewarming (DWI, DTI, and spectroscopy may provide false-negatives >6 days after injury) on all infants with encephalopathy
  - Order should specify “HIE protocol” in the comment section
  - MR spectroscopy should be added if metabolic disease is considered as a potential etiology (requires separate order, but will be performed concurrently)
- Earlier imaging (MRI or CT) may be necessary based on clinical findings
Seizure monitoring

• Neurology should be consulted in infants with confirmed seizure activity to aid in management
• All infants undergoing therapeutic hypothermia or with suspected seizures should undergo continuous monitoring\textsuperscript{12,13,14}:
  o 24 hours of full-montage video EEG upon admission (obtain HUS prior to placing EEG leads)
    ▪ Should continue until seizure free for >12 hours
    ▪ May consider <24 hours if no seizure activity and reassuring background for first 12 hours
  o aEEG throughout the remaining hypothermia and through rewarming

Laboratory assessment

• Lab choice and frequency should be targeted to reflect the infants’ clinical status
• An example of labs to be drawn and their frequency for a typical infant with HIE is presented below:

<table>
<thead>
<tr>
<th>Admission</th>
<th>Q4H (until stable)</th>
<th>Q8H (until stable)</th>
<th>Daily in AM (until stable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chem 14</td>
<td>ABG with lactate</td>
<td>Chem 8</td>
<td>Chem 14</td>
</tr>
<tr>
<td>Mag/Phos</td>
<td>Blood glucose</td>
<td>Ionized calcium</td>
<td>Mag/Phos</td>
</tr>
<tr>
<td>CBC w/ diff</td>
<td></td>
<td>Coags (PT/PTT/INR/fib)</td>
<td>CBC w/diff</td>
</tr>
<tr>
<td>Coags (PT/PTT/INR/fib)</td>
<td></td>
<td></td>
<td>Triglyceride</td>
</tr>
<tr>
<td>Type and screen</td>
<td></td>
<td></td>
<td>*Coags (PT/PTT/INR/fib)</td>
</tr>
<tr>
<td>ABG with lactate</td>
<td></td>
<td></td>
<td>*CRP</td>
</tr>
<tr>
<td>Blood glucose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood cultures (if not done)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placental pathology (if available)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Echocardiogram</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Troponin, CK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*CRP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Microarray</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Serum amino, urine organic acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Serum ammonia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*CSF studies and/or biofire</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>*HSV cultures/PCR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Drug screens</td>
<td></td>
<td></td>
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<tr>
<td>*Phenobarbital level (if applicable)</td>
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</table>

* May consider obtaining these labs, based on clinical presentation

Feeding

• All infants undergoing therapeutic hypothermia should initially be NPO
• Very little data exists regarding the appropriate timing of initiating enteral feeds\textsuperscript{15}
• Minimal enteral feeds may be considered after the first 24 hours of cooling if:
  o Not on any vasopressors
- Not oliguric/anuric
- Abdominal exam reassuring with no emesis

- Due to a high incidence of dysphagia and aspiration in infants after HIE, all infants with HIE should be evaluated by the feeding team once initiating oral feeds.

**Sedation**

- Normal HR for term infants undergoing TH is ~100 bpm; HR>110-120 should be considered tachycardia
- Morphine drip should be standard for pain/shivering
  - Dosing: 5-10 µg/kg/hr, as >10 µg/kg/hr may lead to toxic levels

**Rewarming**

- Rewarming will begin 72 hours after first recorded rectal temperature of ≤ 34.0°C
- Rate of rewarming will not exceed 0.5°C/hour
- If seizures noted on rewarming, cool infant back to 34.5°C and restart rewarming at half the prior speed

**Documentation**

- Physicians/NNPs should be documenting in daily progress note:
  - aEEG tracing and trend
  - Sarnat staging
- Nursing will document
  - Any clinical seizure activity and all cares that create artifact on the aEEG device
  - Administration of anti-epileptic drugs in EPIC and on aEEG device
  - Rectal, skin, blanket temperatures in the Hypothermic Cooling Blanket Treatment Log in EPIC
  - Infant’s response to therapeutic hypothermia in the nurses assessment
  - Re-warming procedure and infant’s response in the nurses assessment
  - Skin appearance as needed in the skin assessment section of the NICU Assessment flowsheet in EPIC

**References**


