
Neonatal Task Force Recommendations

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THERAPEUTIC HYPOTHERMIA

IDENTIFICATION OF AT-RISK NEONATES

- **Identify At-Risk Neonates:**
 - Potentially eligible neonates may be identified by the Licensed Independent Provider, based on any eligibility criteria listed in EL-I or EL-II (see below).
 - Neonatal encephalopathy examination to be completed and documented by a Licensed Independent Provider as soon as possible, following admission of any neonate meeting at least one criterion (e.g., Apgar score, sentinel event, pH, or BE) for therapeutic hypothermia or any neonate with finding of encephalopathy.
 - If the neonate is being considered for therapeutic hypothermia and a definitive decision has not yet been reached, a repeat exam, ideally, by the same Licensed Independent Provider (to maintain continuity), should be performed within the first hour to evaluate evolution of neonatal encephalopathy.

- **Screening criteria:**
 - **Neonates \geq 34 weeks gestational age**
AND
 - **Concern for encephalopathy or seizure event.**
AND
 - **Any one of the following:**
 - Sentinel event prior to delivery such as uterine rupture, profound bradycardia or cord prolapse.
 - Low Apgar scores $\rightarrow \leq 5$ at 10 minutes of life.
 - Prolonged resuscitation at birth \rightarrow chest compressions and/or intubation and/or mask ventilation at 10 minutes.
 - Acidosis \rightarrow pH < 7.1 from cord or patient blood gas within 60 minutes of birth.
 - Abnormal Base Excess $\rightarrow \leq -10$ mEq/L from cord gas or patient blood gas within 60 minutes of birth.

Any one of the following abnormal behaviors may be an indicator of encephalopathy and may suggest need for further evaluation:

- Hyperalertness
- Irritability
- Lethargy or obtundation
- Coma
- Decreased spontaneous activity
- Hypotonicity or flaccidity
- Decerebrate posturing
- Absent or weak suck
- Abnormal pupillary reflex
- Abnormal Moro reflex
- Persistent bradycardia
- Periodic breathing or apnea

ELIGIBILITY CRITERIA

Eligibility for Therapeutic Hypothermia is met through one of two criteria levels:

- Eligibility Level I (EL-I): Therapeutic Hypothermia is indicated
- Eligibility Level II (EL-II): Therapeutic Hypothermia should be considered

The criteria for determining each eligibility level is detailed below.

ELIGIBILITY I: Therapeutic Hypothermia is INDICATED:

- Must fulfill all three criteria. Additional, separate, written parental consent is NOT legally required.
 - **Neonates \geq 36 weeks gestational age and less than 6 hours of age**
 - AND**
 - **Any one of the following:**
 - Sentinel event prior to delivery such as uterine rupture, profound fetal bradycardia or cord prolapse.
 - Low Apgar scores $\rightarrow \leq 5$ at 10 minutes of life.
 - Prolonged resuscitation at birth \rightarrow chest compressions and/or intubation and/or mask ventilation at 10 minutes.
 - Severe acidosis \rightarrow pH < 7.0 from cord or neonate blood gas within 60 minutes of birth.
 - Abnormal Base Excess $\rightarrow \leq -16$ mEq/L from cord gas or neonate blood gas within 60 minutes of birth.

AND

- **Any one of the following:**
 - Clinical event concerning for seizure.
 - Neonatal encephalopathy (defined as a clinical exam consistent with abnormal neurological findings by a standardized evaluation tool.* (See sample assessment scales – attached.)

*If exam unreliable, an EEG may be a useful adjunct tool for assessing and qualifying neonatal encephalopathy.

ELIGIBILITY II: Therapeutic Hypothermia should be CONSIDERED:

- In the setting of neonatal encephalopathy or concern for seizure with the less rigid criteria listed below.* Shared medical decision-making should be documented. Additional, separate written, parental consent may be required, as guided by institutional policy.
 - **Neonates ≥ 34 weeks gestational age and up to 12 hours of age**
AND
 - **Any one of the following:**
 - Sentinel event prior to delivery such as uterine rupture, profound fetal bradycardia or cord prolapse.
 - Low Apgar scores $\rightarrow \leq 5$ at 10 minutes of life.
 - Prolonged resuscitation at birth \rightarrow chest compressions and/or intubation and/or mask ventilation at 10 minutes.
 - Acidosis \rightarrow pH < 7.1 from cord or neonate blood gas within 60 minutes of birth.
 - Abnormal Base Excess $\rightarrow \leq -10$ mEq/L from cord gas or neonate blood gas within 60 minutes of birth.
 - Post-natal collapse resulting in hypoxic-ischemic injury (i.e., near-SIDS type event).
 - AND**
 - **Any one of the following:**
 - Clinical event concerning for seizure.
 - Neonatal encephalopathy (defined as a clinical exam consistent with abnormal neurological findings by a standardized evaluation tool.** (See sample assessment scales – attached.)

*Note that there is no clinical trial evidence to support use of hypothermia in this population outside of Eligibility I criteria.

**If exam unreliable, an EEG may be a useful adjunct tool for assessing and qualifying neonatal encephalopathy.

RECOMMENDATION: Call your local Level III NICU with hypothermia capabilities. Discuss the rationale for therapeutic hypothermia. Document the discussion and rationale for decision to offer or not offer therapeutic hypothermia.

EXCLUSION CRITERIA

- **Exclusion Criteria for Therapeutic Hypothermia:**
 - **Absolute Exclusion Criteria:**
 - Gestational age < 34 wks.
 - **Relative Exclusion Criteria** (at the discretion of the accepting attending physician at the Level III facility):
 - IUGR < 1750grams.
 - Severe congenital anomalies / genetic syndromes / established metabolic disorders.
 - Major intracranial hemorrhage.
 - Overwhelming septicemia.
 - Uncorrectable, clinically relevant coagulopathy.

STABILIZATION AND MANAGEMENT

INITIAL STABILIZATION AND MANAGEMENT IN THE COMMUNITY SETTING:

- **Passive Cooling:**
 - Passive cooling should be initiated as soon as a potentially eligible neonate is identified, ideally in the Delivery Room (core temperature should be monitored).
 - Turn off Radiant Warmers or Isolette Heaters (including transport isolette).
 - Target core temperature (rectal or esophageal) for therapeutic cooling is 33.5°C +/- 1°C.
 - Do not use skin thermometers.
 - Core temperature should be monitored every 5-15 minutes.
 - Slowly titrate heat source as needed to achieve target temperature.
 - Note: If neonate has never been warmed, they are easily over-cooled, even passively.
 - Once core temperature falls to 34°C, have external heat source available set at 33.5°C.
 - Continue close monitoring to prevent rapid rewarming.
 - If core temp rises above 34°C, try opening isolette port(s) or unwrapping neonate.
 - Caution: Asphyxiated neonates have depressed metabolism, so generate less heat. Severely asphyxiated newborns can be quickly overcooled with removal of radiant heat source.
 - Cooled neonates will have a low resting heart rate, often in the 80-100 range and sometimes slightly lower.
 - Passive cooling (with core temperature monitoring) should continue on transport if thermo-regulated cooling is not available for the transport. Active cooling should be initiated immediately upon arrival to accepting center.

- **Blood Gases:**

- There should be a low threshold for obtaining cord gases or early neonate blood gases.
- If cord gases are not obtained or there is ongoing concerns, then neonatal blood gases should be sent within the first hour of birth. Repeat as appropriate.

INITIAL MANAGEMENT BY CLINICAL SYSTEMS (LEVEL II OR LEVEL III):

- **Access:**

- UVC or peripheral IV
 - Peripheral IV line should be placed (and central access, if possible) for IVF and access.
 - IV Access becomes more difficult to obtain as core temperature decreases.

- **Labs:**

- CBC with differential
- Electrolytes, Magnesium, Calcium, Glucose
- Blood cultures
- ABG (with measured lactate, if possible)
- LFT's
- Coagulation studies in Level III facilities

- **Respiratory:**

- If receiving mechanical ventilation, do not over-ventilate.
 - Target SpO₂ 94-99%.
 - Target pCO₂ 40-50mmHg.

- **Cardiovascular:**

- Support and maintain blood pressure in normal range with fluids and pressors, as indicated.
- Neonate may become bradycardic (< 100 bpm) when temperature < 34°C.

- **Infectious Disease:**

- Evaluate for Suspected Sepsis – treat appropriately. Avoid Aminoglycosides.

- **Fluid and Electrolyte:**

- Avoid administering NaHCO₃ as acidosis will slowly correct.
- NPO.

- **Neurological Care:**

- Neurological consult in Level III centers.
- Obtain full channel EEG for a minimum of 24 hours monitoring when available.
- **1st choice agent for treating seizures – Phenobarbital.**

- Consider prophylactic phenobarbital, in consultation with the accepting center, in the setting of an intubated neonate with moderate to severe encephalopathy in the community setting.
- **Avoid Over Sedation:**
 - Gentle sedation during initial stabilization and transport, if needed.

MEDICAL MANAGEMENT GUIDELINES FOR THERAPEUTIC HYPOTHERMIA AFTER ADMISSION TO ACCEPTING CENTER

- **After Admission to the NICU (Cooling Center):**
 - The target core temperature for therapeutic cooling is 33.5°C +/- 1°C.
 - Secure Vascular Access:
 - Establish venous access, as soon as possible. Scalp IV is not ideal and may need to be removed for EEG lead placement.
 - Establish UVC (double lumen), if possible.
 - Do not delay the commencement of therapeutic hypothermia to place umbilical lines.
 - Arterial line, if indicated.
 - Consult Neurology Service for review of the history, examination of the neonate, and reading of an EEG/EEG monitoring for seizures.
 - Cooling should not be delayed for the neurology service review, cranial ultrasound, or an EEG/EEG evaluation.
- **Neurology Consultation and Evaluation:**
 - Obtain HUS as soon as possible to evaluate for intracranial hemorrhage as potential contraindication to continued cooling.
 - Obtain an EEG/EEG to assess for encephalopathy and seizures.
 - Seizure control:
 - **1st choice agent for treating seizures – Phenobarbital.**
 - Confirmation with full-channel EEG is recommended as soon as possible.
 - Continue video EEG recording for 24 hours or longer if seizures detected.
 - MR imaging:
 - In consultation with neurology, determine optimal timing of MRI.
- **Laboratory Monitoring While Receiving Therapeutic Hypothermia:**
 - Blood cultures should be obtained, as indicated.
 - Other Labs should be monitored per institutional protocol.
 - Platelets:
 - Thrombocytopenia is common in hypothermia.
 - Due to the ongoing risk of cerebral hemorrhage, consider transfusing at a threshold platelet count of 50K.
 - PT/PTT/INR should be checked, as soon as possible.
 - AST and ALT.

- Serum lactate, ideally from blood gas.
- Anti-epileptic levels, if indicated.
- **Fluid and Electrolytes:**
 - Neonates should be kept NPO during hypothermia. At the attending's discretion, very small (non-nutritive priming) volumes of human breast milk may be given if the neonate is physiologically stable and no evidence of non-CNS organ dysfunction (i.e. good urine output, normal LFT's and bowel sounds present).
 - Start IV maintenance fluids, avoiding over hydration. IV fluids need to be restricted to avoid cerebral and pulmonary edema in the setting of compromised renal function. Typically, start at 60mL/kg/24 hours and adjust based on strict ins/outs.
 - Maintain glucose and electrolytes within normal limits.
 - Glucose (goal: euglycemia)
 - Sodium
 - Potassium
 - Calcium
 - Magnesium
 - **Management of Acidosis** – The use of sodium bicarbonate may be deleterious and should be avoided if fluid management and vasopressors stabilize the blood pressure and serial pH measurements show improvement in acidosis. Add acetate, as needed, to the TPN for correction of acidosis.
- **Respiratory:**
 - Provide respiratory support as needed.
 - Maintain arterial blood gas pCO₂ in range of 40-50 mmHg to optimize cerebral perfusion.
 - If on supplemental oxygen, avoid hyperoxia.
 - Target SaO₂ 94-99%.
 - Arterial PaO₂ should not exceed 100mmHg.
 - Of Note: Suspected or proven Pulmonary Hypertension is not a contraindication to cooling and is not an indication for early rewarming. Pulmonary Hypertension should be managed as per local protocol.
- **Infectious Disease:**
 - If not already done in the Community setting, evaluate for suspected sepsis and treat appropriately – avoid aminoglycosides.
 - Correct coagulopathy PRIOR to performing an LP.
 - Consider obtaining CSF sample for investigation if suspicion of meningitis or IF Blood CULTURE positive or unexplained encephalopathy.
 - Follow up on cultures and continue antibiotics.
- **Musculoskeletal:**
 - Monitor for fat necrosis and associated risk of hypercalcemia

- **Maintain Adequate Sedation:**

- Indirect evidence supports that modest sedation during hypothermia improves neonatal outcome.
- Sedation:
 - Consider low dose opiate sedation to avoid apnea.
 - Avoid Benzodiazepines.
 - Refer to individual institutional guidelines for choice of opioid and dosing regimen.
 - No standardized protocol sedation tool has been validated in this population.

- **Rewarming:**

- Begin after 72 hours of cooling.
- Rewarming should be done slowly. Increase core temperature 0.2 – 0.5 degrees Celsius per hour until core temperature reaches 36.5 °C.
- There is an increased risk of seizures during rewarming. Consider EEG monitoring.

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