Therapeutic Hypothermia in Neonates

RECOMMENDATIONS OF THE NEONATAL ENCEPHALOPATHY TASK FORCE

Created: 2016

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STATEMENT

The Neonatal Encephalopathy Task Force Recommendations on Therapeutic Hypothermia were developed under the auspices of the Academic Medical Center Patient Safety Organization (AMC PSO) Neonatal Encephalopathy Task Force. These consensus recommendations are for informational purposes only and should not be construed or relied upon as a standard of care. The AMC PSO recommends institutions review these guidelines and accept, modify or reject these recommendations based on their own institutional resources and patient populations. Additionally, institutions should continue to review and modify these recommendations as the science continues to evolve.

Executive Summary

In 2014, at the behest of its membership, the Academic Medical Center Patient Safety Organization (AMC PSO) convened a Neonatal Encephalopathy Task Force to arrive at a set of consensus-based guidelines for the most effective use of therapeutic hypothermia in cases of suspected neonatal encephalopathy. With an expanding set of patients for whom this therapy may be applicable, the AMC PSO sought to build a set of literature-supported recommendations.

The Task Force began with a review of the latest scientific evidence, guidance, and opinion statements from relevant professional societies on the appropriate and effective use of therapeutic hypothermia for neonates presenting with symptoms of encephalopathy. That review was based on guidelines from the 2014 joint Task Force Report on Neonatal Encephalopathy and Neurologic Outcome by The American College of Obstetricians and Gynecologists (The College) and the American Academy of Pediatrics (AAP). Further insights were gathered from AMC PSO member subject matter experts in Neonatology, Neurology, Maternal Fetal Medicine, Obstetrics and Gynecology, and Pediatrics.

Over the course of 18 months, the Task Force generated a list of recommendations for the identification and management of suspected neonatal encephalopathy. While the core focus of these guidelines is infant screening and eligibility, the guidelines also address several other areas critical to the treatment of suspected neonatal encephalopathy, including:

- exclusion criteria
- stabilization & management
- transport

What follows is a document that reflects the aim, mission, and consensus opinion of the Neonatal Encephalopathy Task Force. It offers guidance for clinicians in their efforts to provide the safest, most effective, evidenced-based approach to care delivery.

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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 Eligibility Criteria I or Eligibility Criteria II. *(See page 3).*
- 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 base excess (BE)) for therapeutic hypothermia or any neonate with findings 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 ≥ 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 ➔ ≤ 5 at 10 minutes of life
- prolonged resuscitation at birth ➔ chest compressions, and/or intubation, and/or mask ventilation at 10 minutes
- acidosis ➔ pH < 7.1 from cord or patient blood gas within 60 minutes of birth
- abnormal base excess ➔ ≤ -10 mEq/L from cord gas or patient blood gas within 60 minutes of birth

INDICATORS

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

EXCLUSION CRITERIA FOR THERAPEUTIC HYPOTHERMIA

Absolute Exclusion Criteria

- gestational age < 34 weeks

Relative Exclusion Criteria

(at the discretion of the accepting attending physician at the Level III facility)

- IUGR < 1,750 grams
- severe congenital anomalies/genetic syndromes/ established metabolic disorders
- major intracranial hemorrhage
- overwhelming septicemia
- uncorrectable, clinically relevant coagulopathy

RECOMMENDATION

For neonates meeting the eligibility criteria level I or II for therapeutic hypothermia:

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

ELIGIBILITY CRITERIA I

Therapeutic Hypothermia *Is Indicated*

Must fulfill *all three* criteria. Additional, separate, written parental consent is *not* legally required.

1 **Neonates ≥ 36 weeks gestational age and less than 6 hours of age**

+ **and**

2 Any **one** of the following:

- **sentinel event** prior to delivery, such as uterine rupture, profound fetal bradycardia, or cord prolapse
- **low Apgar** scores ➔ ≤ 5 at 10 minutes of life
- **prolonged resuscitation** at birth ➔ chest compressions and/or intubation and/or mask ventilation at 10 minutes
- **severe acidosis** ➔ pH < 7.0 from cord or neonate blood gas within 60 minutes of birth
- **abnormal base excess** ➔ ≤ -16 mEq/L from cord gas or neonate blood gas within 60 minutes of birth

+ **and**

3 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)**

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

** To support alignment and continuity of care between referring and accepting neonatal units, the Neonatal Task Force recommends that institutions adopt a standardized, mutually agreeable assessment tool that meets the needs of the providers and the patient population served.

ELIGIBILITY CRITERIA 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.

1 **Neonates ≥ 34 weeks gestational age and up to 12 hours of age**

+ **and**

2 Any **one** of the following:

- **sentinel event** prior to delivery, such as uterine rupture, profound fetal bradycardia, or cord prolapse
- **low Apgar** scores ➔ ≤ 5 at 10 minutes of life
- **prolonged resuscitation** at birth ➔ chest compressions and/or intubation and/or mask ventilation at 10 minutes
- **acidosis** ➔ pH < 7.1 from cord or neonate blood gas within 60 minutes of birth
- **abnormal base excess** ➔ ≤ -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**

3 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)***

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

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

*** To support alignment and continuity of care between referring and accepting neonatal units, the Neonatal Task Force recommends that institutions adopt a standardized, mutually agreeable assessment tool that meets the needs of the providers and the patient population served.

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 temperature 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 over-cooled 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 thermoregulated 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 are ongoing concerns, neonatal blood gases should be sent within the first hour of birth. Repeat as appropriate.

STABILIZATION AND MANAGEMENT

Initial Management by Clinical Systems (Level II or Level III Center)

Access

- Umbilical vein catheter (UVC) or peripheral intravenous (IV) lines:
  - Peripheral IV line should be placed (and central access, if possible) for intravenous fluids (IVF) and access.
  - IV access becomes more difficult to obtain as core temperature decreases.

Labs

- Complete blood count (CBC) with differential.
- Electrolytes, magnesium, calcium, glucose.
- Blood cultures.
- Arterial blood gas (ABG) (with measured lactate, if possible).
- Liver function tests (LFTs).
- Coagulation studies in Level III facilities.

Respiratory

- If receiving mechanical ventilation, do not over-ventilate.
  - Target SpO_2 94–99%.
  - Target pCO_2 40–50 mm Hg.

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 Electrolytes

- Avoid administering sodium bicarbonate ($NaHCO_3$), as acidosis will slowly correct.
- Nothing by mouth (NPO).

Neurological Care

- Neurological consult in Level III centers.
- Obtain full channel EEG for a minimum of 24 hours monitoring, when available.
- ***First 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.

STABILIZATION AND MANAGEMENT

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 umbilical venous access (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/aEEG monitoring for seizures.
  - Cooling should not be delayed for the neurology service review, cranial ultrasound, or an EEG/aEEG evaluation.

Neurology Consultation and Evaluation

- Obtain head ultrasound (HUS) as soon as possible to evaluate for intracranial hemorrhage as a potential contraindication to continued cooling.
- Obtain an EEG/aEEG to assess for encephalopathy and seizures.
- Seizure control:
  - ***First 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 are 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 LFTs and bowel sounds present).
- Start IV maintenance fluids, avoiding over-hydration. IV fluids should be restricted to avoid cerebral and pulmonary edema in the setting of compromised renal function. Typically, start at 60 mL/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 ($NaHCO_3$) 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 pCO_2 in range of 40–50 mmHg to optimize cerebral perfusion.
  - If on supplemental oxygen, avoid hyperoxia.
    - Target SaO_2 94–99%.
    - Arterial PaO_2 should not exceed 100 mmHg.
- *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 a lumbar puncture (LP).
- Consider obtaining CSF sample for investigation if suspicion of meningitis, or blood culture positive, or unexplained encephalopathy.
- Follow up on cultures and continue antibiotics.

Medical Management Guidelines for Therapeutic Hypothermia After Admission to Accepting Center (continued)

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 °C 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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About the AMC PSO

In 2009, the Patient Safety and Quality Improvement Act (PSQIA) was enacted to create a culture of safety by providing federal privilege and confidentiality protections for information that is assembled and reported to a PSO, or developed by a PSO, for the conduct of patient safety activities.

The act promotes the sharing of best practices and knowledge to continuously improve the quality of patient care. Before the PSQIA, legal protections for quality activities were limited in scope and existed only at the state level.

The PSQIA encourages voluntary reporting. Identification of common, systemic errors can be achieved more effectively through the aggregation of information reported from providers across the health care delivery system.

In 2010, the Risk Management Foundation of the Harvard Medical Institutions, Inc. formed a component entity, the Academic Medical Center Patient Safety Organization (AMC PSO) to function as a national convener of clinicians and health care organizations to collect, aggregate, and analyze data in a secure environment in an effort to identify and reduce the risks and hazards associated with patient care.

Our objectives:

- Create a bridge between themes driving malpractice activity and factors seen in real-time data with a particular focus on high severity/high significant events seen in root cause analysis (RCA)
- Convene member organizations in response to real-time events and bring context to patient safety issues by providing a secure venue for discussion
- Translate learnings gleaned from our convening sessions and data analyses into focused clinical interventions that can improve quality, reduce costs, and decrease liability
- Reach beyond data reporting and generate actionable responses that can inform the development of best practice recommendations
- Inform institutional patient safety efforts by pinpointing the areas of highest risk and vulnerability to help guide organizational patient safety initiatives

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