PEDIATRIC NEWBORN MEDICINE CLINICAL PRACTICE GUIDELINES

Therapeutic Hypothermia

Implementation Date: August 1, 2021

Clinical Practice Guideline: Therapeutic Hypothermia Guidelines

Points of emphasis/Primary changes in practice:

1. More detailed guidelines are provided for hematological management during TH
2. Infants transferred by Boston Medflight will be either actively cooled (for definitely eligible cases) or kept euthermic (for very borderline cases). For those actively cooled during transport, the plan would be to continue TH for the full 72 hours unless infant fulfills early exit criteria after 24 hours of age.
3. Minor changes:
    - Clarifying the CPG text for score 2 for sucking as weak/incoordinated to match the appendix
    - Updating admission labs to include electrolytes and LFTs to assess baseline and possibly assess timing of insult
    - Updating IV access to reflect guidelines on venous access decision tree

Rationale for change:

1. Although there are not enough studies to support transfusion practices during TH, a standardized approach based on best available evidence is needed to provide best care and possibly reduce need for non-necessary transfusions.
2. Active cooling during transport allows for reaching stable target temperature earlier than passive cooling and has the potential to provide better neuroprotection.
3. Management of infants during TH is an evolving field that needs continuous improvements and updates.

Questions? Please contact: Director of Neonatal Neurocritical Care Program- Department of Pediatric Newborn Medicine

Clinical Guideline Name	Therapeutic Hypothermia
Effective Date	3/24/2015
Revised Date	5/07/2019, 6/29/2020, 7/13/2021
Team Leader(s)	Neonatal Neurocritical Care Program- Department of Pediatric Newborn Medicine
Approved By	Department of Pediatric Newborn Medicine Clinical Practice Council 3/12/15, 12/8/15, 7/30/20 CWN SPP 3/11/15, 01/13/2016 BWH SPP Steering 3/18/15 Nurse Executive Board/CNO 3/25/15
Keywords	Therapeutic Hypothermia, Encephalopathy, Newborn Seizures, Passive Cooling, Passive Re-warming, Infant Cooling

This is a clinical practice guideline. While the guideline is useful in approaching therapeutic hypothermia, clinical judgment and / or new evidence may favor an alternative plan of care, the rationale for which should be documented in the medical record.

I. Purpose

To provide therapeutic hypothermia (TH) guidelines for NICU infants ≥34 weeks Gestational Age with evidence of neonatal encephalopathy

II. All CPGs will rely on the NICU Nursing Standards of Care. All relevant nursing PPGs are listed below.

NICU H.3 Therapeutic Hypothermia (TH) for Hypoxic Ischemic Encephalopathy (HIE)
https://hospitalpolicies.ellucid.com/documents/view/3209?product=policy

WNH M.1 Administration of Medications to Infants
http://www.bwhpikenotes.org/policies/Nursing/CWN_Clinical_Practice_Manual/WNH/WNH_M.1.pdf

III. Scope

These guidelines establish an approach for evaluation, monitoring and management of neonates presenting with neonatal encephalopathy who might be eligible for therapeutic hypothermia in the Newborn Intensive Care Unit.

IV. GUIDELINES

1. **Infant Eligibility:**

A. ≥ 34 weeks gestation

AND

B. Any <u>one</u> of the following:

1) **Sentinel event** prior to delivery such as uterine rupture, profound bradycardia or cord prolapse
2) **Low Apgar** scores → ≤ 5 at 10 minutes of life
3) **Prolonged resuscitation** at birth → chest compressions and/or intubation and/or mask ventilation at 10 minutes
4) **Severe acidosis** → pH ≤ 7.1 from cord or patient blood gas within 60 minutes of birth
5) **Abnormal Base Excess** → ≤ - 10 mEq/L from cord or patient blood gas within 60 minutes of birth

AND

C. Any <u>one</u> of the following:

1) **Seizure** or any clinical event concerning for seizure
2) **Neonatal encephalopathy** (defined as the presence of abnormal neurological behavior on the Neonatal Encephalopathy Scale of ≥4)

Notes about eligibility:

- Therapeutic hypothermia is to be initiated **<u>as soon as possible after patient meets entry criteria</u>** and should be commenced **in the first 6 hours of life**. If the patient is >6 hours and =< 12 hours, then hypothermia may be commenced at attending discretion since current evidence supports marginal benefit.
- Other infants may benefit from therapeutic hypothermia, such as sudden infant collapse on the postnatal ward, should be considered on a patient by patient basis.
- Although aEEG is not a requirement to start therapeutic hypothermia, it has a significant value especially in neonates with non-conclusive examination or those on sedatives and paralytic agents. The presence of Discontinuous, Low voltage, Burst suppression, or Flat aEEG would fulfill criteria for encephalopathy and might warrant starting therapeutic hypothermia

2. **Identification of Infants:**

A. Eligible patients may be identified at the time of resuscitation or based on cord blood gases and/or initial newborn blood gases. Discuss indication for therapeutic hypothermia as **soon as possible after birth. Request cord gas** if there is concern for sentinel event or/and abnormal clinical exam.

B. Evaluation for therapeutic hypothermia could be completed in triage or after direct NICU admission depending on significance of presentation. (**See Algorithm for Evaluation for TH)**

- A complete evaluation should be completed by Neonatology attending and/or fellow as soon as possible following admission on any patient ≥34 weeks with any eligibility criteria. **A complete assessment should include (see Algorithm):**
  - **i. A post-natal blood gas as soon as possible within 1 hour of birth.**
  - **ii. Serial neurological exams using the Neonatal Encephalopathy score (NES)**
  - **iii. aEEG monitoring for minimal of 90 minutes (when indicated)**

- Although it is important to document the neurological examination following resuscitation in the DR, the formal NES to qualify for cooling will be initiated on further assessment in triage or NICU (within 1st hour of life).

- Infants who require complete assessment but do not readily meet criteria for hypothermia, should have a minimum of 2-6 hours evaluation in Triage or minimum 12 hours if admitted to NICU. (18-24 hours if outborn)

- The decision to either commence or not commence therapeutic hypothermia should be documented in the medical chart. This documentation should include;
  a. The findings and timing at which performed, of the individual components of the evaluation (lab results, encephalopathy score, aEEG findings).
  b. Clear documentation that decision was communicated with both the family of the infant, and the obstetrician of record.

3. Exclusion Criteria for Therapeutic Hypothermia:

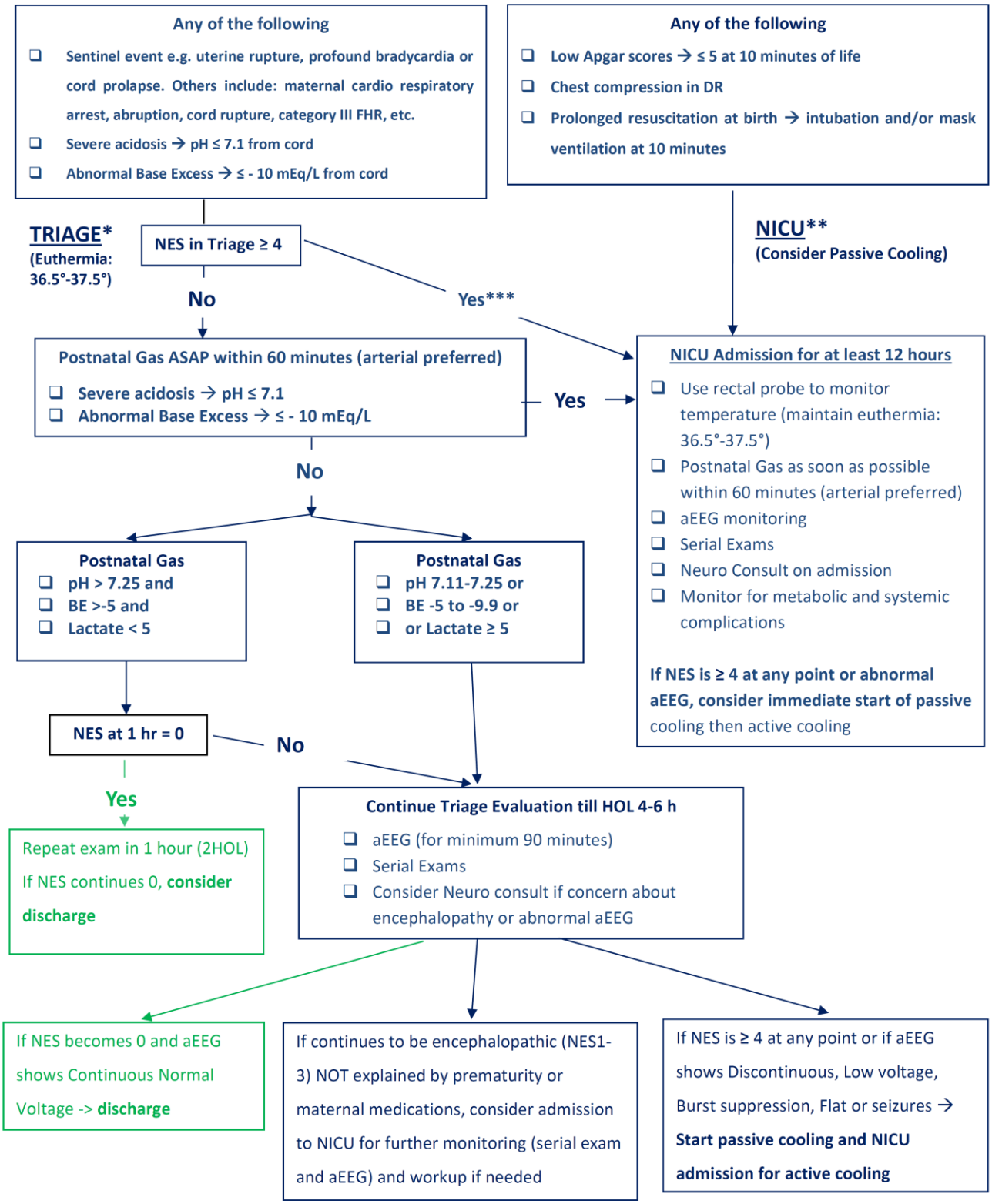
A. Absolute Exclusion Criteria:

- Gestational age less than 34 weeks

B. Relative Exclusion Criteria (at discretion of attending physician)**:**

- Severe IUGR <1750grams
- Severe congenital anomalies / genetic syndromes / known metabolic disorders
- Major intracranial hemorrhage
- Overwhelming sepsis
- Uncorrectable, clinically relevant coagulopathy

Algorithm for Evaluation for TH



*Any baby with signs of encephalopathy requires further evaluation/consultation in triage/NICU
** Any baby with clinical instability requires direct NICU admission
*** Babies who fulfill cooling criteria (see CPG text) should be considered for immediate start of passive then active cooling as soon as they are eligible

NEONATAL ENCEPHALOPATHY SCALE*

Stage	Normal (0 points each)	Mild Stage 1 (1 point each)	Moderate/Stage 2 (2 points each)	Severe/Stage 3 (3 points each)
1. Level of Consciousness	Normal **0**	Hyper-alert/Irritable **1**	Lethargic/Obtunded **2**	Stupor/Coma **3**
2. Spontaneous Activity	Normal **0**	Normal **0**	Decreased **2**	Absent **3**
3. Muscle Tone	Normal **0**	Normal **0**	Mild Hypotonia **2**	Flaccid **3**
4. Posture	Normal **0**	Mild Distal Flexion **1**	Strong Distal Flexion **2**	Decerebrate **3**
5. Primitive Reflexes				
Suck	Normal **0**	Weak **1**	Weak/Incoordinated **2**	Absent **3**
Moro	Normal **0**	Strong/Low Threshold **1**	Weak/Incomplete/ High Threshold **2**	Absent **3**
6. Autonomic Function				
Pupils	Normal **0**	Mydriasis **1**	Miosis **2**	Unequal/Fixed/ Dilated/Poor Reflex **3**
Heart Rate	Normal **0**	Tachycardia **1**	Bradycardia **2**	Variable **3**
Respirations	Normal **0**	Normal **0**	Periodic Breathing **2**	Apnea **3**
Total Score	_____	_____	_____	_____

*Please note and document the state of the baby during serial examinations

V. Management of In-born Infants Eligible for Therapeutic Hypothermia

1. Initial evaluation should be comprehensive of multisystem assessment, including cardiovascular, respiratory and metabolic monitoring and inclusive of differential diagnosis.

2. If baby meets criteria, Therapeutic Hypothermia should be initiated as soon as possible.

3. Although, parental consent is not required, decision should be communicated with parents

as soon as possible and documented in the medical record.

4. Passive cooling:

A. Initiate as soon as infant **meets therapeutic hypothermia criteria** which can occur in Labor & Delivery, **following resuscitation according to NRP guidelines**, i.e. turn off radiant warmers and/or transport isolette heater.
B. Keep baby draped with light bed sheet whenever possible.
C. **Target core (rectal) temp for passive cooling is 33.5˚C .** Use continuous rectal temperature monitoring.
D. **Caution**: Cooled babies have depressed metabolism, so generate less heat. If baby has never been warmed they are easily over-cooled, even passively.
E. Once rectal temp falls to 34˚C, have external heat sources available.
   1 If core temp falls < 33.5˚C, turn on heat source to lowest settings.
   2 If core temperature < 33˚C, use a warmed blanket over baby's chest/abdomen until core temperature reaches 33˚C and then remove the blanket.
F. Slowly adjust heat sources as needed to achieve target temperature.
G. Re-warming a **passively cooled** infant who has never been actively cooled occurs as per guidelines 0.5° C every 30 min. **(See Appendix 4)**
H. If passively cooled infant is not ultimately treated with active therapeutic hypothermia, document that passive cooling was initiated and the reason why active therapeutic hypothermia was not done.

5. Procedure to be followed after admission to the NICU:

A. Place infant on the therapeutic hypothermia system and follow guidelines for connecting and starting the device (refer to Therapeutic Hypothermia Manual with specific therapeutic hypothermia unit and Nursing Policy)
https://hospitalpolicies.ellucid.com/documents/view/3209?product=policy

Scenarios for setting target temperature:

a. The target rectal temperature during active cooling is 33.5°C.
b. If infant has core temperature of 31-37˚C, set target temperature to 33.5˚C.
c. If core temperature is <31˚C, set target temperature at 1˚C above actual core temperature. Target temperature should be reached in ~30 min. Keep increasing target temperature in increments of ~1˚C every 30 minutes until core temperature is >32˚C and then set target temperature to 33.5˚C.

Please note: The blanket remains warm to touch and this is normal as it tries to maintain the infant's temperature when the infant may have a low body temperature.

B. Workflow: The "Golden Hours"

Proceed according to workflow to achieve comprehensive and accurate monitoring within 3 hours from commencement of active cooling.

- **Decide to Cool-->** start **NIRS** and **aEEG** if not already placed.
- Neuro resident will place cEEG order and notify cEEG tech to contact bedside nurse/NNCCN to plan time for cEEG placement (Goal is to be started within 2-3 hours of active cooling)
- Initiate placement of central line (UVC).
- When Babygram is ordered for line placement a STAT HUS will be ordered
- Bedside nurse/NNCCN to page Ultrasound (US) tech on pager # 14462 and type "STAT baby head on [name] just requested for cooling. The goal for the head US is to done between 1 to 2 h after starting active cooling.
- **Head Ultrasound Performed** (anterior fontanelle views ONLY-rule out major bleeds).
- **Bedside nurse, if not already contacted by cEEG tech, will call lab** cEEG lab (617-355-6585) with new time.
- **cEEG placed**

C. Communication

Communicate with parents and obstetrical providers upon initiation of therapeutic hypothermia. Document in Epic note. Provide parents with therapeutic hypothermia information sheet.

6. Neurological Management During Therapeutic Hypothermia

A. **Neurology Consultation**

B. **Sedation:**

- Maintain adequate sedation Keep patients adequately sedated to avoid cold stress. Most trials did not use ANY sedation alongside hypothermia therapy. Indirect evidence supports that modest sedation alongside hypothermia improves outcome.
- NPASS as sedation evaluation has not been validated in this population. Use clinical judgment along with medical/nursing team to keep infant comfortable.
- Infant can be touched and when possible held by family to assist in soothing infant.
- Morphine Intravenous is drug of choice - this guideline can only be deviated from with attending approval.
- Loading dose 0.05 mg/kg IV (repeat PRN x 1 for shivering, severe irritability tachycardia HR > 120).
- Start continuous infusion: 0.01 mg/kg/hr IV drip. DO NOT INCREASE THE INFUSION RATE.

- Reduce rate to 0.005 mg/kg/hr after 12 hours.
- Note that tachycardia may also be secondary to poor cardiac function, intravascular depletion, sepsis, or other etiologies so additional sedation for tachycardia should be taken into context
- AVOID over dosage of morphine which will produce respiratory depression which can necessitate intubation.
- Avoid Benzodiazepines for distress.

C. **Neuromonitoring:**

- Start aEEG on admission. aEEG will continue from the time of admission, through the period of cooling until 6 hours after complete rewarming.
- Obtain cEEG upon initiation of active cooling (to be ordered stat by neurology resident)
- Continue video cEEG recording for 24 hours or longer if seizures detected. If no seizures and EEG recording considered low risk, may switch from cEEG to only aEEG after 24 hours (refer to aEEG CPG for details) EEG Neuro-monitoring in the NICU .
- Start NIRS monitoring on admission. Infants receiving TH will be monitored with NIRS through the period of cooling and rewarming. In neonates with encephalopathy an increased CrSO2 is associated with adverse outcome (refer to NIRS CPG for details) Clinical NIRS in the NICU .

D. **Seizure control**

- **1st choice agent for treating seizures is** Phenobarbital – if clinical events noted then consult with neurology based on review of simultaneous EEG
  - Load: 20 mg/kg IV
  - If seizures persist (>30-120 sec/hr EEG) >20-30 minutes after load complete: additional doses of phenobarbital 5-20 mg/kg IV (to total of 40 mg/kg, including load)
  - Level 2-12 hours post-load may be useful; typical therapeutic range 10-40 mcg/mL
  - Additional phenobarbital if level subtherapeutic
- If seizure activity continues (>30-120 sec/hr EEG) >20-30 minutes after previous dose complete, consider:
  - Fosphenytoin 20 mg/kg IV x 1
  - Total phenytoin level 1 hour post-load may be useful; goal 15-20 mcg/mL
  - May consider additional boluses of 5 mg/kg if level <15 mcg/mL
- Midazolam 0.15 mg/kg IV x 1, then: Midazolam infusion 0.05 mg/kg/hr,
- Levetiracetam 40 mg/kg IV x 1

May consider additional boluses of 20 mg/kg to a total of 80 mg/kg

(Refer to Neonatal Seizures Clinical Practice Guideline)

E. **Cranial ultrasound** should be ordered STAT. However, it is not required prior to the initiation of hypothermia, and therapy should not be delayed pending an ultrasound.

F. Re-warming

- Re-warming the **actively cooled** infant begins after 72 hours of therapeutic hypothermia and is accomplished over a 15 hours period.
- Increase core temperature setting by 0.2°C every hour until infant's core temperature reaches 36.5° C.
- Monitor neurological status closely (every 2-4 hours) during re-warming
- Turn therapeutic hypothermia machine off once core temperature reaches 36.5 ° C.
- The rectal temperature probe may be removed.
- EEG or aEEG monitoring should be continued **until 6 hours after rewarming**

G. MR imaging

NICU MRI Guidelines

- Routine MRI – HIE protocol on DOL #4 (after re-warming)
- Follow-up MRI on/after DOL #10- #21.
  1. Babies who are still admitted will have MRI as inpatient.
  2. Babies who are discharged will have second MRI at BCH. The neurology ICU consulting service nurse practitioner will assist in this process.
  3. The Outpatient MRI team at Boston Children's will call families to schedule MRI
  4. Once the MRI is performed, the BCH Neurology nurse practitioner will update the family and the neurologist scheduled to conduct the 3-4 month follow up with the results. This information will be available at the NICU Follow Up clinic scheduled 2-4 weeks after discharge.

7. Laboratory/blood work

Lab schedule should be determined based on assessment of the infant's condition and evaluated daily and as needed.

Recommended blood work:

- On admission: CBC, PT, PTT, INR, Fibrinogen, BMP, Mg, P, ALT, AST, glucose, Blood gas with lactate, Blood culture
- 12 hours of life: BMP, Mg, P, ALT, AST, glucose
- 24 h of life: CBC, PT, PTT, INR, Fibrinogen, BMP, Mg, P, ALT, AST, glucose
- Daily BMP
- **Placenta pathology:** The admitting resident or NP/PA will page L&D Charge Nurse to assure that placenta is sent to pathology. If placenta is transferred from referring hospital, please follow workflow indicated in Transport of Placentas from NWH to BWH guideline. **Email the mother's name and MRN to: HIEPlacenta@partnershealthcare.onmicrosoft.com indicating that baby is receiving TH.**
- Glucose: – on admission and hourly until stable X3, then Q12h X2 and prn with any concerns or fluid changes.

- Phenobarbital or Phenytoin level as clinically indicated
- Urine and meconium toxicology as clinically indicated.
- Consider LP if high risk for meningitis as clinically indicated.

Notes about specific laboratory changes possible with TH:

- Potassium levels may rise or fall with therapeutic hypothermia
- Sodium: low sodium may result if patient has ATN/renal injury and poor urine output
- Calcium levels may fall with therapeutic hypothermia, or rise in the presence of Subcutaneous Fat Necrosis: Treatment of severe hypercalcemia includes hyperhydration and intravenous furosemide. High-dose corticosteroids may also be part of the medical management of an infant with hypercalcemia
- Magnesium levels may fall with therapeutic hypothermia. Caution: High magnesium levels may cause hypotension
- Low platelet count is not uncommon with TH
- If coagulation studies (e.g. PT/PTT/INR) are drawn from the UVC and the PTT comes back prolonged (as expected due to heparin), a hepabsorb PTT does **not need to be sent** as a matter of routine practice, unless specifically requested by the attending. This test is not available 24/7 and also requires 2.7 ml of blood. All the other clinical information available along with the other laboratories (e.g. CBC/PT/INR/Fibrinogen) can be used to make a determination about factor replacement rather than sending the hepasorb test. If there is a specific clinical concerns about the coagulation cascade that requires accurate determination of the PTT, then hepasorb PTT or, preferably, a blood sample drawn peripherally that is not contaminated with heparin can be sent.

8. Multisystem Management during Therapeutic Hypothermia

A. Secure vascular access

- Establish peripheral IV access immediately (avoid scalp IVs due to need for EEG monitoring).
  NICU I.2 Intravenous Angiocatheter Insertion
- Insert UVC (double lumen) if possible.
- If unable to insert central UVC, keep low lying UVC until stable access is achieved i.e. EPIV, according to the department Venous Access Decision Tree.
- Do not delay the commencement of therapeutic hypothermia for placement of umbilical lines.
- Arterial line (e.g., UAC or radial arterial line) – for continuous monitoring and sampling if required is to be discussed with NICU attending based on the severity of the illness in the infant.

NICU C.4 Use and Care of Central Venous Catheters (CVC) and Peripherally Inserted Central Catheters (PICC)
NICU C.5 Assisting with Umbilical Vessel (Arterial and/or Venous) Catheterization and/or Peripheral Arterial Line Placement and Removal

B. Cardiovascular

1) Blood pressure management – continuous arterial line monitoring preferred prior to any inotropic support being initiated
    - Maintain blood pressure in normal range, despite bradycardia
    - Treat hypovolemia with volume administration as needed
    - **Echocardiography** is highly recommended for babies with hemodynamic instability during TH.
    - Hemodynamic support could be tailored based on presence of PPHN, LV dysfunction or RV dysfunction.
    - Medications used to treat systemic hypotension include
        - Although dopamine is commonly used, it is predominantly a vasopressor and in neonatal animal studies has been shown to increase PVR and SVR, which has the potential to increase afterload, decrease left-to-right shunting, and compromise systemic oxygen delivery.
        - Epinephrine: may be an appropriate inotrope due to its' action on α1, α2, β1, and β2 receptors and its' favorable impact on pulmonary vascular resistance (PVR)/systemic vascular resistance (SVR) ratio
        - The action of dobutamine via α and β receptors decreasing SVR may have advantages as an inotrope in the context of persistent pulmonary hypertension of the newborn (PPHN) and myocardial dysfunction
        - Milrinone has altered pharmacokinetics during TH affecting its clearance and caution needs to be used
2) Heart rate
    - Expect bradycardia (< 100 bpm) when temperature < 34 ^{o}C
    - Deep bradycardia (< 80 bpm)
        - May be tolerated, if blood pressure is maintained adequately
        - Raising rectal temperature to 34 ^{o}C alone may be adequate
    - Monitor for arrhythmias and consider an EKG and electrolytes, calcium and magnesium. Infants may have prolonged QTc and this should be monitored if severe bradycardia is present.

C. Fluid and Electrolytes

- NPO is the standard during evaluation of and active therapeutic hypothermia. However, if there is no evidence of end organ compromise, at the attending discretion and after the 1st 24 hours of therapeutic hypothermia, minimal enteral nutrition may be

provided at up to **10 mL/kg/day with no advance until fully rewarmed**. Only mother's milk may be used (i.e. no formula or donor milk) until infant is re-warmed.

- Initiate Standard TPN at 50 mL/kg/day until custom TPN is available and D10W at 10 ml/kg/day. Discontinue Standard TPN and increase concentration of dextrose if patient requires total fluids < 60 mL/kg/day before custom TPN available or is hypoglycemic. Maintain GIR no less than 4-5 mg/kg/min at all times. Adjust GIR as needed with custom TPN.
- Monitor and maintain glucose homeostasis. Evidence suggests that hypo and hyperglycemia can contribute to worsened neurodevelopment outcome in setting of HIE, especially when occurring in the first 6 hours form birth. Maintain blood sugar ≧ 60.
- Management of Acidosis –**Avoid base replacement therapy** if circulation is re-established and patient can self correct over time. Treat hypovolemia with volume administration as needed

- Normal Saline – 10 mL/kg IV
- Packed Red Blood Cells (+/- plasma) – if blood loss is etiology

D- Respiratory

1) Provide any respiratory support as needed
2) Blood gas monitoring/ TCOM.

-**Hypocarbia** in neonates treated with TH has been associated with brain injury and worsened neurodevelopmental outcome. In order to avoid iatrogenic hypocarbia, closely monitor pCO2 in babies on respiratory support with blood gas minimum every 8-12 hours or TCOM. Although accuracy of TCOM could be affected by hypothermia, it can be used as method of continuous monitoring for trends.

- Avoid hypocarbia
  - Therapeutic hypothermia can ↓ pCO2.
  - Maintain blood gas pCO2 goal: 45-50 mmHg
- Avoid hyperoxia
  - Maintain Oxygen saturations according to CPG Target O2 Saturations for Infants in the Neonatal Intensive Care Unit
  - PaO2 should be < 100mmHg
  - *Caveat: Hypothermia could be associated with pulmonary hypertension. Manage accordingly CPG for* Diagnosis and Management of the Infant with Suspected or Known Pulmonary Hypertension of the Newborn

3) Maintain air humidifier in normothermic range (37ºC).

4) **Stridor** has been reported in neonates during and after TH whether or not had received endotracheal intubation. The etiology is unclear. Consult ORL for bedside laryngoscopy prior to pharmacological intervention, as clinically indicated.

5) Late Oxygen requirement at time of rewarming has been reported and is usually self-resolving. Investigations in the form of CXR and echocardiography might be indicated. Provide respiratory support as need,

E. Infectious Disease

- Evaluation for Suspected Sepsis – start antibiotics after cultures obtained
- Use antibiotics in the form of Ampicillin AND Cefepime
- Discontinue antibiotics after 48 h if cultures are negative according to NICU guidelines. Consider obtaining CSF sample as clinically indicated.

F. Hematology: Management of thrombocytopenia, coagulopathy and anemia during therapeutic hypothermia

Hypothermia can cause thrombocytopenia and impaired coagulation cascade.
Very few studies have addressed management of thrombocytopenia, coagulopathy and anemia during TH.
Although management of symptomatic infants is highly indicated, a more conservative approach for asymptomatic infants is reasonable **Please review Appendix 5 for details.**

G. Skin: Subcutaneous fat necrosis

- Monitor for erythema, purple color, painful nodules (especially on the back and buttocks) both during TH and following rewarming that may indicate subcutaneous fat necrosis (incidence 2-4/1,000). These lesions usually appear during the first weeks of life and resolve in weeks or months
- Infant may be uncomfortable over affected skin region. If noted requires:
  - Separation of affected skin from cooling pod by gauze or cloth;
  - Adequate analgesia including local treatments such as heated blanket; (after rewarming)
  - Monitor for hypercalcemia at initial concern and then at least each week for 6 weeks. Following this, if an infant shows poor feeding or lethargy a further calcium should be checked as hypercalcemia can be noted up to 3 - 6 months following fat necrosis.

9. Documentation:

- Document parents discussion using .NICUHYPOTHERMIADISCUSSION
- Complete Neonatal Encephalopathy Exam score on admission then daily, until rewarming and discharge. .NICUENCEPHALOPATHYEXAMWITHSCORE
- Complete aEEG report on admission and then daily. .NICUAEEGREPORT

10. Discharge and Follow up

A. The attending neonatologist should review results of placenta pathology with OB and recommend parents to discuss findings at first outpatient postpartum visit with OB provider.

B. All babies who receive TH will need follow up both at BWH NICU follow up program and BCH Neurology.

- BWH NICU Follow Up Program: enter order in Epic (Discharge>Orders>Additional Outpatient Orders>Ambulatory Referral to BWH Center for Child Development) for developmental evaluation at 4 months of life **(need to enter on admission).**
- BCH Neurology: the Neurology Nurse Practitioner will contact the family and will schedule a follow up at 3-4 month

11. Special Circumstances:

A. Early Exit Criteria

- If the infant had mild encephalopathy or minimal concerns by the clinical team then the infant can be considered at 24 hours of age for exit criteria. These criteria include:
    1) Mild encephalopathy at admission
    2) Absence of significant abnormalities on the full channel EEG at 24 hours of age with no previous EEG seizures and normal cyclicity
    3) Normal neurological examination (morphine considered)
    4) Negative MRI scan at 24-48 hours of life with no restriction on diffusion weighted imaging.
- If the above criteria are fulfilled, then the infant can begin re-warming. Follow same protocol for re-warming the actively cooled infant.

B. Management of severe encephalopathy

- TH should be offered to neonates presenting with severe encephalopathy unless there is an absolute contraindication for cooling.
- TH should not be discontinued unless part of redirection of care or if TH becomes relatively contraindicated.
- Redirection of care should not be attempted prior to 24-48 h age unless the patient is critically ill requiring ongoing resuscitation.
- Decision for redirection of care will involve a team comprised of at least: parents/guardians, two attending neonatologist (the second neonatologist is not required to participate in team meetings; discussion with primary neonatologist is sufficient), attending neurologist. Notify NICU Medical Director when considering redirection of care. The primary attending neonatologist will document discussion with the consultants and the family and indicate agreement.
- Suggested criteria for considering redirection of care:

- **Serial neurological exams** showing **persistent severe encephalopathy after the first 24-48 hours,** in agreement between NICU and Neurology Team.
- Continuous **cEEG recording after the first 24-48 hours showing persistent severe encephalopathy.**
- **MRI after 24-48 h must be obtained to document severity of brain injury**. MRI findings suggestive of severe brain injury are: diffuse brain injury, Basal ganglia thalami (BGT), posterior limb internal capsule (PLIC) and brainstem injury.
- Exclude other potential causes such as inborn errors of metabolism, cardiorespiratory compromise, severe acidosis, electrolyte imbalances, hypoglycemia, severe hepatic or renal dysfunction, drug intoxication (opioids, anticonvulsants)

VI. Management of Out-born Infants Eligible for Therapeutic Hypothermia

NICU T.4 Transfer to BWH from an Outside Hospital

1. Screening criteria to be used when taking a transport call for out-born infants:

A. Infants ≥ 34 weeks gestational age

AND

B. Any one of the following:

a. Sentinel event prior to delivery such as uterine rupture, profound bradycardia or cord prolapse
b. Low Apgar scores → ≤ 5 at 10 minutes of life
c. Prolonged resuscitation at birth → chest compressions and/or intubation and/or mask ventilation at 10 minutes
d. Severe acidosis → pH ≤ 7.1 from cord or patient blood gas within 60 minutes of birth
e. Abnormal Base Excess → ≤ - 10 mEq/L from cord or patient blood gas within 60 minutes of birth

AND

C. Any one of the following:

a. Seizure or any clinical event concerning for seizure
b. Encephalopathy (any one of the following when an examination cannot be undertaken on the prescribed sheet):

1) Hyper alert
2) Irritable
3) Lethargy or obtunded
4) Stupor or coma
5) Decreased spontaneous activity

6) Hypotonia or flaccid
7) Decerebrate posturing
8) Absent or weak suck
9) Abnormal pupillary reflex
10) Abnormal Moro reflex
11) Persistent bradycardia/heart rate variability
12) Periodic breathing or apnea

2. **Eligible infants** should receive **passive cooling only with rectal temperature monitoring** documented every 5-15 minutes. While continuous rectal monitoring is preferred, intermittent rectal temperature is an alternative. (Eligible infants should NOT be actively cooled at outside hospital.)

   A complete evaluation to assess neonatal encephalopathy should be completed and documented (result and timing) by Neonatology or Pediatric attending as soon as possible, following admission on any patient meeting at least one objective criterion (*e.g.*, Apgar score, sentinel event, cord pH, or cord BE) for therapeutic hypothermia and at least one finding consistent with encephalopathy.

   A complete assessment should include:

   1. **Cord gas analysis**
   2. **A post-natal blood gas within 1 hour of birth.**
   3. **Scored using the Neonatal Encephalopathy examination score, on admission and repeated over the coming hours. Use descriptive neurological exam if score is not available.**
   4. **aEEG monitoring (if available).**

The Neonatology or Pediatric attending will document the rationale for transferring or not transferring the infant for TH evaluation.

3. **Temperature Monitoring:**

   Monitor core (rectal) temperature closely (continuous or intermittent)

   1) Continuous rectal temperature monitoring (preferred method if available)
   - Gently insert lubricated rectal probe to 4-6 cm, tape to thigh
   - Document temperature and vital signs every 15 minutes

   2) Intermittent rectal temperature checks (until transport team arrives)
   - Gently insert lubricated thermometer rectally ~2 cm
   - Document temperature and vital signs every 15 minutes

4. **Temperature Conversion Chart (˚C → ˚F)**

   ^{o}C to ^{o}F Conversion formula: $^{o}C = 5/9 \times (^{o}F-32)$

   - **33.5˚C = 92.3˚F ←Target Temperature**

5. **Passive cooling at referring centers:**
   - **A.** **<u>TURN OFF RADIANT WARMERS *or* TRANSPORT ISOLETTE HEATERS</u>**
   - **B.** Keep baby draped with light bed sheet whenever possible
   - **C.** Target core (rectal) temp is 33.5˚C
   - **D.** **Caution**: Cooled babies have depressed metabolism, so generate less heat. If baby has never been warmed they are easily over-cooled, even passively. Additionally, cooled babies will also have a lower resting heart rate, often in the 80-100 range when adequate core temperature is reached, and sometimes slightly lower. There is no risk associated with this low heart rate >60bpm.
   - **E.** Once rectal temp falls to 34˚C, have external heat sources available
     2) If core temp falls < 33.5˚C, turn on external heat source (incubator or use warmer) to lowest settings
     3) If core temperature < 33˚C, use external heat source or warmed blanket over baby's chest/abdomen until core temperature reaches 33˚C and then remove the external heat source/blanket
   - **F.** Slowly adjust heat sources as needed to achieve target temperature
   - **G.** Continue close monitoring to prevent rapid re-warming
   - **H.** If core temp rises > 34˚C, try opening isolette port(s), door or undraping
   - **I.** Avoid overhead radiant warmers for heat source.

6. **Transport:**

Hypothermia should be continued during transport. Many publications and our regional data show that active cooling during transport is more effective in bringing temperature of infants to target temperature with least variability. Based on this, Boston Medlfight have started using servo-controlled active TH during transport to replace passive cooling:

- Medical Control attending will continue to discuss with referring hospital if based on perinatal events, neurological examination (encephalopathy score) and aEEG (if available), TH is warranted. If yes, referral center will start passive cooling followed by active cooling in transport.
- For the very borderline cases which do not readily fulfill TH criteria, but referral center wants to proceed with transfer for further evaluation by neonatology and neurology including aEEG, transfer will be planned ASAP. These infants will be kept euthermic until further evaluation is completed at BWH. Continuous rectal temperature monitoring will be used during transport and during evaluation to assure that their core temperature does not exceed 36.5 degrees. Once the clinical team at BWH decide to start TH, passive cooling followed by active cooling will be immediately started according to the TH CPG. If decision is taken not to cool, infant will continue under observation at BWH NICU for 18-24 hours per our TH

CPG. If timely transfer is not feasible, passive cooling in referring hospital following by active cooling in transport might still be considered.

7. **On arrival to BWH:**
   - **For infants actively cooled during transport:** BWH NICU will prepare a cooling blanket. On arrival, rectal probe will be replaced (different blanket brand used in transport) and active TH will be resumed up to 72 hours based on BWH TH CPG. Early rewarming will be considered in very selected cases after 24 hours if fulfilling Early Exit Criteria.
   - **For infants passively cooled during transport:** Passive cooling will be continued on admission and active cooling will be started after eligibility criteria are determined by the admitting attending neonatologist.
   - **For infants who are kept euthermic during transport**: Euthermia will be continued on admission and passive then active cooling will be started after eligibility criteria are determined by the admitting attending neonatologist.
8. The infant should be admitted to the NICU for a minimum of 18-24 hours to monitor.
9. All outborn infants transferred for TH evaluation should have a Neurology consultation and aEEG evaluation.

APPENDICES:

Appendix 1- TH evaluation and check list
Appendix 2- Overview and management
Appendix 3- Detailed encephalopathy exam
Appendix 4 Algorithm for Re-warming a Passively Cooled Infant
Appendix 5 Hematological Management during TH
Appendix 6- Billing and Documentation
Appendix 7- Parent Hand Out

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