Therapeutic Hypothermia

Hypoxic-Ischemic Encephalopathy (HIE) in the NICU

Nationwide Children's — When your child needs a hospital, everything matters.

Center for Clinical Excellence

Inclusion Criteria

- Infants ≥ 35 wks estimated GA at birth and ≥ 1800 gms and < 24 hours old

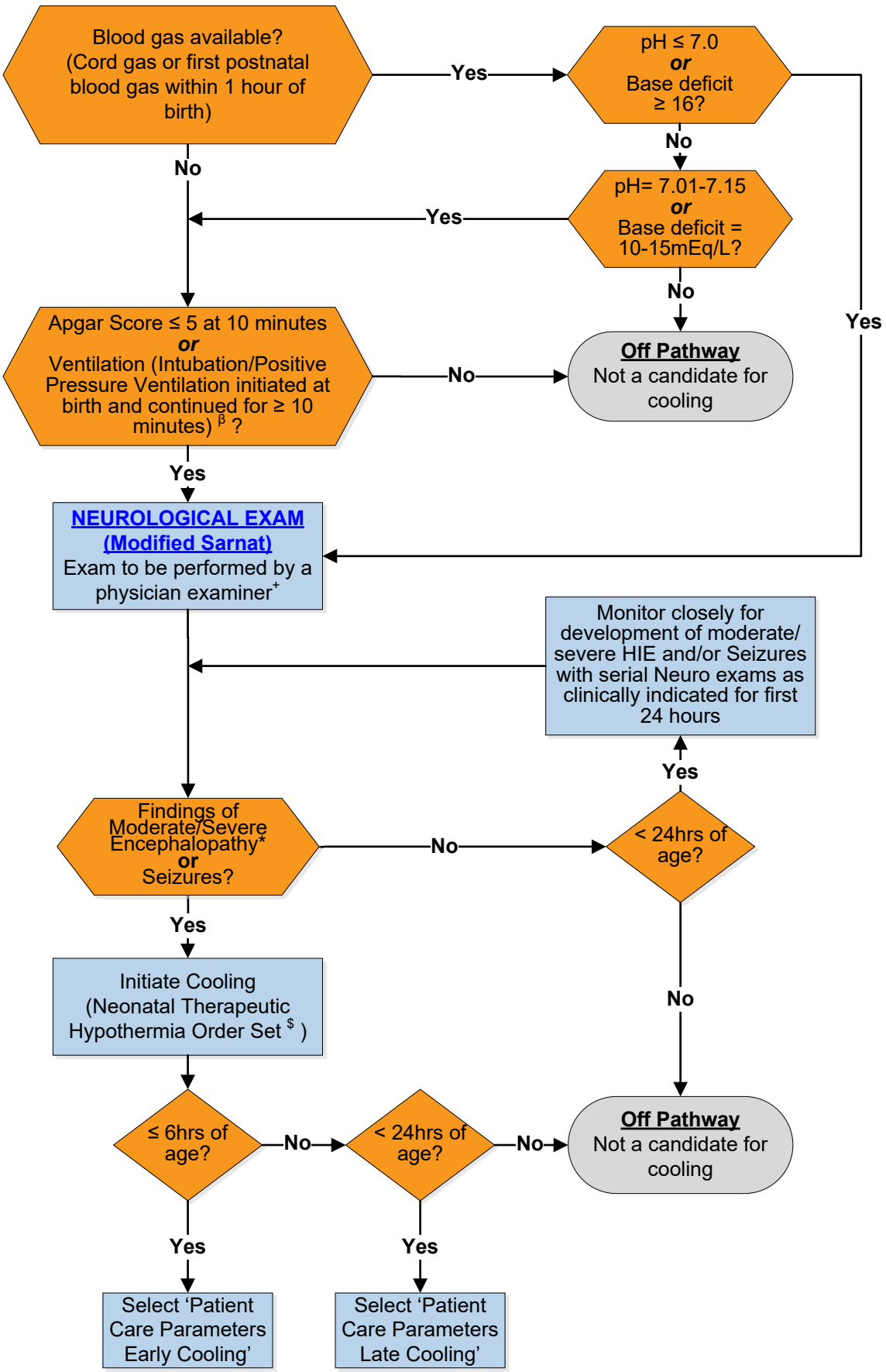
Exclusion Criteria

- ≤ 34 6/7 weeks GA
- Birth Weight <1800g
- ≥ 24 hours old

***Presence of Moderate/Severe Encephalopathy indicated by:**

- Seizures
  or
- Presence of one or more signs in three of the six categories (level of consciousness, spontaneous activity, posture, tone, primitive reflexes, and autonomic systems)

[$] If the patient goes on ECMO anytime, please chose the 'Neonatal Therapeutic Hypothermia on ECMO' Order set



Inclusion & Exclusion Criteria

Inclusion criteria:

- Any neonate (≥ 35 weeks estimated GA at birth and ≥ 1800 grams) with concern for encephalopathy/seizure in the first 24 hours of life

Exclusion criteria:

- ≤ 34 6/7 weeks GA
- Birth Weight < 1800g
- ≥ 24 hours old

Therapeutic Hypothermia Algorithm

Diagnosis & Definition

- Neonatal encephalopathy (NE) - heterogeneous, clinically defined syndrome characterized by disturbed neurologic function in the earliest days of life in an infant born at or beyond 35 weeks of gestation, manifested by a reduced level of consciousness or seizures, often accompanied by difficulty with initiating and maintaining respiration, and by depression of tone and reflexes; 3 in 1000 live births
- Hypoxic ischemic encephalopathy (HIE) – one cause of HIE secondary to acute asphyxia peripartum; 1.5 in 1000 live births
- When a sentinel event is not identified, attention should be made to other possible causes of NE
- Therapeutic hypothermia (TH) – clinical treatment where an infant's body core (esophageal/rectal) temperature is deliberately cooled to ~33.5ºC to mitigate the neurologic sequelae of an acute hypoxic ischemic event

Therapeutic Hypothermia Algorithm

Differential Diagnoses

- Neonatal Stroke
- Metabolic conditions/ Inborn Errors of Metabolism
- Sepsis ± Meningitis
- Brain malformations
- Genetic conditions

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Severity Assessment

Neurological Exam (Modified Sarnat) - serial exam as clinically indicated

- Continue to **Appendix A**

Therapeutic Hypothermia Algorithm

Admission Criteria

Therapeutic Hypothermia is offered only in the Main Campus NICU

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Transport Considerations

- Call Transport and arrange for infant to be transported
- Ask Referral physician what heat source that infant is currently provided with (example: radiant warmer or isolette)
- Ask Referral physician how they will monitor the infant's temperature until transport team arrives, keep the infant's temperature between 36.0-36.5 degrees Celsius
- Ask the Referral physician to obtain glucose, blood gas, CBC with platelet count and Calcium if able
- Routine neonatal care as for any other critically ill infant (ex. Antibiotics, xrays, lines, etc)
- Direct the Referral physician to call directly to NCH physician with any questions
- Inform NCH Charge RN and NNP to begin set-up for therapeutic hypothermia per clinical protocol

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Monitoring

- While the patient receives TH, every effort should be made to prevent hyperthermia (temperature ≥ 37.5C)
- Radiant warmer off
- Place on cooling blanket
- Place esophageal probe (measure tip of nose to ear lobe and down to xiphoid, then subtract 2 cm)
- Confirm placement of esophageal probe with X-ray (~2 cm above diaphragm or lower third of esophagus)
- Esophageal temperature set limits 33.0 to 34.0 degrees Celsius
- Monitor vitals signs including Axillary, Esophageal, Cooling blanket set and Water temperatures every 15 minutes x 4 hours then every 1 hour until protocol discontinued
- Bedside axillary temperature alarm set limits 87-94 degrees Fahrenheit
- Notify Resident/NNP/Neonatologist before starting re-warming
- At 72 hours (Early 6 hours of life or less) OR 96 hours (>6 and <24 hours of life), start re-warming infant by 0.5 degrees Celsius every 1 hour until esophageal temperature at 36.5 degrees Celsius is reached
- Discontinue esophageal probe and cooling blanket only when infant temperature stable at 36.5-37.0 degrees Celsius for 4 consecutive hours
- Turn on radiant warmer and set at 36 degrees once esophageal temperature is at 36.5 degrees Celsius
- Avoid over-heating and elevated esophageal temperatures >37.3 degrees Celsius and notify the Resident/NNP/Neonatologist for instructions
- Assess skin condition every hour and document

Therapeutic Hypothermia Algorithm

Rewarming

- Notify Resident/NNP/Neonatologist before starting re-warming
- At 72 hours (Early: less than 6 hours of life) OR 96 hours (>6 and <24 hours of life), start re-warming infant by 0.5 degrees Celsius every 1 hour until esophageal temperature at 36.5 degrees Celsius is reached
- Obtain POCT Blood Glucose every 2 hours during rewarming phase
- Discontinue esophageal probe and cooling blanket only when infant temperature stable at 36.5-37.0 degrees Celsius for 4 consecutive hours
- Turn on radiant warmer and set at 36 degrees once esophageal temperature is at 36.5 degrees Celsius
- Avoid over-heating and elevated esophageal temperatures >37.3 degrees Celsius and notify the Resident/NNP/Neonatologist for instructions

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Testing

- Consult Pediatric Neurology on admission
- Laboratory:
  - Specific to TH, admission labs to include:
    - Ionized calcium
    - CBC
    - Electrolytes
    - Lactate
    - AST/ALT, Bilirubin, GGTP
    - Neonatal work-up
  - Initial laboratory testing directed at patient clinical picture indicated (i.e blood gas, coagulation studies, sepsis evaluation)
  - Daily laboratory testing directed at clinical picture with attention to routine monitoring of electrolytes, including ionized calcium
- Diagnostic Testing:
  - Head ultrasound at admission
  - LTM for duration of cooling (72 hour course for Early TH, 96 hour for Late TH) and rewarming
  - MRI Head without contrast + MR Spectroscopy
    - Ideal testing is at day of life 4-5
    - If unable to obtain MRI/MRS on DOL 4-5 due to medical condition, strongly consider waiting until DOL 10 or later due to risk of pseudonormalization during intervening days.
    - If infant is still admitted at > DOL 10, consider repeat MRI to evaluate evolution of injury before discharge
  - Every effort should be made to obtain the placental pathology from birth hospital
  - For infants without a sentinel event and/or atypical history and/or course, strong consideration for Genetics consultation and expanding the work-up for other causes of neonatal encephalopathy

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Recommended Treatments

- Therapeutic Hypothermia
  - Early TH: 72 hours
  - Late TH: 96 hours
  - Rewarming is to occur over 6 hours. LTM is to stay in place until 6 hours after rewarming is complete
- Fluid and Nutritional Management
  - NPO for duration of TH and rewarming
  - Maternal breast milk may be used for mouth care
  - Standard fluid and nutritional management to be discussed daily with multidisciplinary team with attention to risk of fluid overload if underlying renal insult as well as alteration of metabolic needs
- Infectious Disease
  - Consider rule out sepsis (bacterial/viral)/ antibiotics
  - Consider obtaining CSF
- Medications commonly used with TH
  - Antiseizure medications may be indicated per clinical course. Co-manage with Pediatric Neurology
  - Routine use of sedation is not recommended. Medical decision-making around these mediations should include PharmD expertise.
- Treatment of Shivering/Irritation for patients undergoing Therapeutic Hypothermia
  - Continue to **Appendix B**

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Treatments Not Recommended

- Erythropoitein
- Avoid Benzodiazepines if possible

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Discharge Criteria & Planning

- For neonates with history of seizure, contact Neurology prior to discharge for seizure teaching
- Follow Up:
  - With seizures: 4 weeks post discharge in Neo Neuro Clinic (part of NICU Early Development Clinic).
  - Without seizures: 3-4 months corrected chronological age in Neo Neuro Clinic (part of NICU Early Development Clinic)

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Patient & Caregiver Education

Whole Body Cooling – Therapeutic Hypothermia

Therapeutic Hypothermia Algorithm

Risk Awareness & Zero Hero

- Avoid Hyperthermia (temperature ≥ 37.5C) and Hypothermia (temperature < 33). Evaluate for malfunctioning of equipment
  - **Therapeutic Hypothermia Protocol (Medical).doc**

Therapeutic Hypothermia Algorithm

Key References

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Therapeutic Hypothermia Algorithm

Quality Measures

Outcome Measure:

1. What percentage of babies with concerns for HIE are admitted to the Main Campus NICU within 6 hours?
2. For infants who are admitted to the NICU within 6 hours with moderate/severe HIE, what is the time of initiation of cooling from the time of arrival to NCH? (Categorize based on cooling initiated during transport)
3. For infants who are admitted to the NICU within 7-24 hours with moderate/severe HIE, what is the time of initiation of cooling from the time of arrival to NCH?

Process Measure:

- Neurological exam documentation rate in Main Campus for all patients receiving TH (regardless of documentation at birthing hospital)

Balancing Measure:

1. Neurological exam documentation for all patients that were referred for evaluation for TH but did not get cooled
2. Infants who did not qualify for TH per Pathway but received TH
   - Had biochemical criteria but did not qualify by exam
   - Or did not have biochemical criteria but encephalopathic on exam

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Potential Areas for Research

- Cooling for mild encephalopathy (Pragmatic Trial Cool Prime)
- Cooling for infants with biochemical criteria but are not encephalopathic on exam
- Neurodevelopmental follow-up of infants by timing of cooling initiation
- Neurodevelopmental follow-up of mild HIE
- Evaluation of cooling during transport
- Standardization of neurological examination following cooling and related neurodevelopmental outcomes

Therapeutic Hypothermia Algorithm

Pathway Team & Process

Pathway Development Team:

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Advisory Committee Date: *November, 2022*

Origination Date: *January, 2023*

Next Revision Date: *January, 2026*

Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

For more information about our pathways and program please contact:
ClinicalPathways@NationwideChildrens.org

Therapeutic Hypothermia Algorithm

Appendix A

+NEUROLOGIC EXAM (Modified Sarnat) CERTIFICATION FORM

- **Seizures?** **Y** **N**

See definitions for Neurologic Examination on page 2

CATEGORY N=6	SIGNS OF HIE IN EACH CATEGORY		
	NORMAL/MILD HIE	MODERATE HIE	SEVERE HIE
1. LEVEL OF CONSCIOUSNESS	1	2 = Lethargic	3 = Stupor/coma
2. SPONTANEOUS ACTIVITY	1	2 = Decreased activity	3 = No activity
3. POSTURE	1	2 = Distal flexion, complete extension	3 = Decerebrate
4. TONE	1	2a = Hypotonia (focal or general) 2b = Hypertonia	3a = Flaccid 3b = Rigid
5. PRIMITIVE REFLEXES			
Suck	1	2 = Weak or has bite	3 = Absent
Moro	1	2 = Incomplete	3 = Absent
6. AUTONOMIC SYSTEM			
Pupils	1	2 = Constricted	3 = Deviation/dilated/non-reactive to light
Heart rate	1	2 = Bradycardia	3 = Variable HR
Respiration	1	2 = Periodic breathing	3 = Apnea or requires ventilator 3a=on vent with spontaneous breaths 3b=on vent without spontaneous breaths

- CATEGORY — SIGNS OF HIE IN CATEGORY

1. Level of Consciousness ____
2. Spontaneous Activity ____
3. Posture ____
4. Tone ____ ____ (Note a or b)
5. Primitive Reflexes (Suck or Moro, code highest level) ____
6. Autonomic System (Pupils, Heart Rate or Respirations, code highest level) ____ If vent, code 3a or 3b

- **Is the infant sedated/paralyzed?** **Y** **N**

Total # Categories should be NO MORE THAN 6 (Count Only the Highest Level in each sign)

The level of encephalopathy will be assigned based on which level of signs (moderate or severe) predominates among the 6 categories. If moderate and severe signs are equally distributed, the designation is then based on the highest level in Category #1: The level of consciousness.

- **Signs of moderate or severe HIE in at least 3 of the 6 categories above?** **Y** **N** (circle one)

If yes, **what is the Level of HIE?** **MODERATE** ***or*** **SEVERE** (circle one)

Name of examiner_____**Exam date & time:** ____/____/____ **at** __ __:__ __

DEFINITIONS FOR NEUROLOGIC EXAMINATION

• Did the infant have documented seizures? Record 'Y" if seizures have been diagnosed or if the infant's chart or verbal summary included the diagnosis of seizures. Seizures can be subtle such as ocular deviation, sucking and lip smacking movements, swimming or "rowing" or "bicycling" movements of limbs. They can be tonic/clonic, localized, multifocal or generalized.

• Does the infant have signs of moderate or severe encephalopathy in > 3 categories (3 of the 6 categories) on the neurologic examination?

1. Level of consciousness: Code "1" if infant arouses to wakefulness, responds appropriately and promptly to external stimuli, or appears hyperalert or inconsolable/irritable, Code "2" if lethargic delayed but complete response to external stimuli (start with mild stimuli first then proceed to more noxious stimuli. Code "3" if stupor/coma (infant is not arousable and is non-responsive to external stimuli. may have a delayed but incomplete response to stimuli).

2. Spontaneous activity: Code "1" if infant is active. Code "2" if activity is decreased. Code "3" if no activity.
Spontaneous Activity Notes: if infant is, sedated clinical judgment has to be used to decide whether the examination is reliable. Paralysis will preclude a meaningful exam.

3. Posture: Code "1" if infant is moving around and does not maintain only one posture, should have flexion or lower extremity at hip and/or knees Code "2" if strong distal flexion, complete extension, or "frog-legged" position. Code "3" if decerebrate with or without stimulation.

Posture Notes: If posture is abnormal, but does not fit 2 or 3, code as 2.

4. Tone: Code "1" if tone is normal (resistance to passive motion). Code "2a" if hypotonic or floppy, either focal or generalized. Code "2b" if hypertonic or increased tone or tension of extremities or trunk upon passive movement. Code "3a" if infant lies like a rag doll with no tone at all (flaccid). Code "3b" if the infant is rigid with extreme stiffness or inflexibility of extremities or trunk upon passive movement.

Tone Notes: Evaluate extremities, trunk and neck tone and make clinical judgment of tone based on tone in these areas. If responses differ in multiple areas, base code on the lower extremity.

5. Primitive reflexes: (remember: count only one sign in this category—the highest level of HIE)

□ Suck: Code "1" if infant vigorously sucks your finger inserted in mouth or around the tube if intubated. Code "2" if suck is weak or infant has bite. Code "3" is suck is absent.

□ Moro: Code "1" if Moro is normal – extension of limbs opening of hands, extension with abduction of UE (flexion of the UE has been removed) Code "2" if incomplete. Code "3" if absent.

Moro Notes: If neonate has fracture of clavicle or brachial plexus injury, evaluate other extremity. Moro has to be done by gently raising and lowering the head when infant is intubated

6. Autonomic system: (remember: count only one sign in this category—the highest level of HIE)

□ Pupils: Code "1" if normal in size and reactive to light. Code "2" if constricted and reacting to light. Code "3" if skew deviation of eyes, pupils are dilated or non-reactive to light.

Pupil Notes: If pupils asymmetric, assign 3. Pupils are difficult to assess in the newborn infant with edema of eyelids---you will need to gently separate the eyelids while a second person shines light.

□ Heart rate: Code "1" if normal heart rate > 100/minute consistently or tachycardia. Code "2" if bradycardia (< 100/minute) with only occasional increases to > 120/minute. Code "3" if heart rate is not constant and varies widely between <100 and > 120

Heart Rate Notes: Heart rate should be evaluated based on documented rate over the previous min/hrs. Do not code heart rate if cooling has been initiated.

□ Respiration: Code "1" if breathing spontaneously. Code "2" if periodic breathing associated with desaturation events (< 80%). Code "3" if apnea or requiring ventilator support.

Therapeutic Hypothermia Algorithm

Appendix B

Treatment of Shivering /Irritation for patients undergoing Therapeutic Hypothermia

Criteria: HIE patients who are being cooled and are shivering and/or have one of the following:

a. NPASS score elevated (> 3)
b. HR continuously > 120 bpm with no other physiologic explanation
c. Clinical pain/agitation perceived by bedside clinician

Recommend the following in a step-wise fashion:

1) **Morphine 0.05 mg /kg x 1 and assess response. If no response within 15 minutes based on criteria above, can trial morphine 0.1 mg /kg IV x 1. If no response noted 15 min after 2nd dose of morphine, then proceed to step #2**
   a. If response is noted, can continue to use the respective prn dose every 3 hours PRN
   b. As cooling continues, if patient no longer is responsive to prn morphine, then proceed to step #2
2) **Dexmedetomidine 0.1 mcg /kg /HR (no loading /bolus dose)**
   - Defined as: ALT 3-5x ULN
   - Consider not using if ALT > 5x ULN

   b. Dose escalation:
   - Increase dose in **increments of 0.1** mcg/kg/HR every **60 minutes**
   - May escalate based off of presence of 1 or more of the following:
     - NPASS score elevated (> 3)
     - HR continuously > 120 bpm with no other physiologic explanation
     - Clinical pain/agitation perceived by bedside clinician
   - Up to a preferred maximum of 0.5 mcg/kg/HR
     - May titrate higher based off of patient's response but use caution (max 1 mcg/kg/HR)

   c. Discontinue dexmedetomidine if one or more of the following are present:
   - Resting HR < 70 bpm
   - Appears over-sedated
   - Not responsive to stimuli

   d. May **restart** dexmedetomidine at 50% of what infusion was stopped if one or more of the following occurs:
   - Shivering
   - HR > 70 bpm
   - Becomes responsive to stimuli

   Dexmedetomidine benefits:
   - Does not interfere with EEG readings (mask seizures)
   - Avoidance of opioids and benzodiazepines
   - Theoretical benefit of neuroprotection

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Therapeutic Hypothermia Algorithm

Appendix C

Helping Hands:
Whole Body Cooling (Therapeutic Hypothermia)

Therapeutic Hypothermia Algorithm