

Hypoxic-Ischemic Encephalopathy (HIE)

Inclusion Criteria

- Infants ≥ 36 0/7 wks estimated GA at birth and < 24 hours old

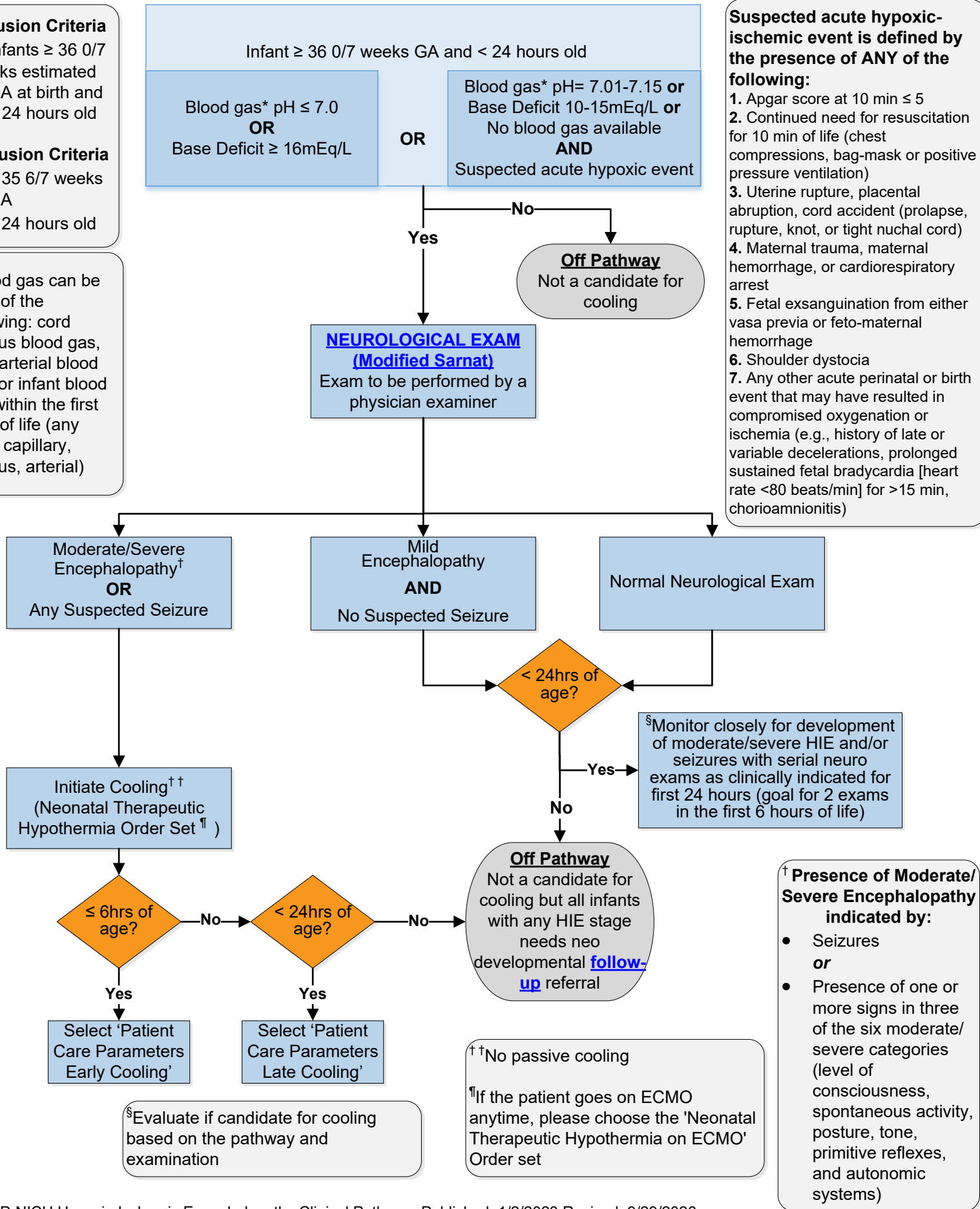
Exclusion Criteria

- ≤ 35 6/7 weeks GA
- ≥ 24 hours old

*Blood gas can be ANY of the following: cord venous blood gas, cord arterial blood gas, or infant blood gas within the first hour of life (any type- capillary, venous, arterial)

Suspected acute hypoxic-ischemic event is defined by the presence of ANY of the following:

1. Apgar score at 10 min ≤ 5
2. Continued need for resuscitation for 10 min of life (chest compressions, bag-mask or positive pressure ventilation)
3. Uterine rupture, placental abruption, cord accident (prolapse, rupture, knot, or tight nuchal cord)
4. Maternal trauma, maternal hemorrhage, or cardiorespiratory arrest
5. Fetal exsanguination from either vasa previa or feto-maternal hemorrhage
6. Shoulder dystocia
7. Any other acute perinatal or birth event that may have resulted in compromised oxygenation or ischemia (e.g., history of late or variable decelerations, prolonged sustained fetal bradycardia [heart rate <80 beats/min] for >15 min, chorioamnionitis)



Diagnosis & Definition

- Neonatal encephalopathy (NE) - heterogeneous, clinically defined syndrome characterized by disturbed neurologic function in the earliest days of neonatal life and 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 NE 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 ~33.5°C to mitigate the neurologic sequelae of an acute hypoxic ischemic event

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Differential Diagnoses

- If there was need for assisted ventilation for >10 minutes of life, review maternal records for suspected acute hypoxic-ischemic event, consider neurologic exam and/or other causes as mentioned below
- Neonatal stroke
- Metabolic conditions/ inborn errors of metabolism
- Sepsis $\pm$ meningitis
- Brain malformations
- Genetic conditions

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Severity Assessment and Neurological Exam

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

NEUROLOGIC EXAM (Modified Sarnat) CERTIFICATION FORM

Seizures? Y N

See definitions for Neurologic Examination on page 2

Modified Sarnat Examination Examiner _____ Date/Time of Birth _____ Date/Time of Exam _____ Age (hours) _____

	Normal (0)	Mild (1)	Moderate (2)	Severe (3)	Score
Level of consciousness	0- When awake, alert, fixes on visual stimuli	1- Irritable, hyperalert, poor feeding, excess crying alternating with sleeping	2- Lethargic: delayed but complete response to external stimuli (start with mild stimuli first then proceed to more noxious stimuli)	3- Stupor or coma: infant is not arousable and is non-responsive to external stimuli; may have a delayed but incomplete response to stimuli	
Spontaneous activity	0- Frequent spontaneous movements	1- Increased and exaggerated movements, jittery	2- Decreased activity	3- No activity	
Posture	0- Extremities flexed toward the trunk, infant is moving around or does not maintain one posture	1- Mild distal or arm flexion with leg abduction or slight extension	2- Distal flexion, complete extension or 'frog-legged' position (complete abduction)	3- Decerebrate	
Tone	0- Normal tone	1- Slightly increased tone	2a- Hypotonia (focal or general) 2b- Hypertonia	3- Flaccid or rigid	
Primitive reflexes				*code highest level	
Suck	0- Strong coordinated suck	1- Uncoordinated suck	2- Suck is weak/unsustained or only has bite	3- Absent suck	
Moro	0- Complete response (full abduction then smooth adduction)	1- Exaggerated	2- Incomplete (partial abduction at shoulder and extension of arms)	3- Absent moro	
Autonomic system				*code highest level	
Heart rate	0- Normal	N/A	2- Bradycardia	3- Variable HR	
Respiration	0- Normal	1- Irregular and/or tachypneic (RR >60)	2- Periodic breathing	3- Apnea or requires ventilator 3a = on vent with spontaneous breaths 3b = on vent without spontaneous breaths	
Pupils	0- Reactive	1- Dilated, but reactive	2- Constricted, but reactive	3- Deviated, dilated, or non-reactive to light	

- CATEGORYSIGNS OF HIE IN CATEGORY
1. Level of Consciousness

2. Spontaneous Activity

3. Posture

4. Tone

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 ____:____

Documentation of the Sarnat examination is detailed in [Appendix C](#)

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Admission Criteria

Therapeutic Hypothermia is offered only in the NCH Main Campus NICU

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Transport Considerations

- Arrange for the infant to be transported expeditiously
- Request that the transport team takes the cooling equipment with them to the referral hospital
- Cooling can be initiated by the transport team preferably at <6 hours.
- Ask referral physician to maintain the infant's temperature from 36.0-36.5°C until transport team arrives
- Do not passively cool the baby
- Ask the referral physician/transport team that the placenta is sent to pathology (preferred to NCH pathology)
- Ask the referral physician to obtain glucose, blood gas, CBC with platelet count and calcium if able
- Inform NCH charge RN and NNP to begin set-up for therapeutic hypothermia per clinical protocol
- Inform neurology about the potential admit and the need for EEG

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Monitoring

- While the patient receives TH, every effort should be made to prevent hyperthermia (temperature $\geq 37.5^{\circ}\text{C}$)
- 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 $33.0\text{-}34.0^{\circ}\text{C}$
- 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 $87\text{-}94^{\circ}\text{F}$
- 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°C every 1 hour until esophageal temperature at 36.5°C is reached
- Discontinue esophageal probe and cooling blanket only when infant temperature stable at $36.5\text{-}37.0^{\circ}\text{C}$ for 4 consecutive hours
- Turn on radiant warmer and set at 36° once esophageal temperature is at 36.5°C
- Avoid over-heating and elevated esophageal temperatures $>37.3^{\circ}\text{C}$ and notify the resident/NNP/neonatologist for instructions
- Assess skin condition every hour and document
- **Early discontinuation of hypothermia therapy** before 72 hours (early cooling) or 96 hours (late cooling) may be indicated if an alternative diagnosis other than HIE is the cause of the encephalopathy, need for surgical procedure, or redirection of care by family. In addition, early discontinuation may be considered with severe coagulopathy, hypotension, or pulmonary hypotension despite optimal management.

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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°C every 1 hour until esophageal temperature at 36.5°C is reached
- Obtain Point of Care Testing (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°C for 4 consecutive hours
- Turn on radiant warmer and set at 36°C once esophageal temperature is at 36.5°C
- Avoid over-heating and elevated esophageal temperatures >37.3°C 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:
 - CBC
 - Electrolytes and creatinine
 - Lactate
 - Ionized calcium
 - 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
 - Long-Term Monitoring (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, consider waiting until DOL 10 or later due to risk of pseudo-normalization 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

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 through completion of rewarming
- Fluid and nutritional management
 - Consider initiating enteral feeding (orogastric/nasogastric) with maternal or donor human milk starting at 20.0 ml/kg/day and increase by 20.0 ml/kg/day as tolerated
 - 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 medications should include PharmD expertise
- Treatment of shivering/irritation for patients undergoing therapeutic hypothermia
 - Continue to [Appendix A](#)

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Treatments Not Recommended

- Erythropoitein
- Avoid benzodiazepines if possible

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Discharge Criteria & Follow-Up

ALL infants with a diagnosis of HIE (mild, moderate, or severe) need neonatology follow-up in the Early Development Follow-Up Clinic:

- Neonates with history of seizure, contact neurology prior to discharge for seizure teaching, first follow up appointment at 4 weeks post discharge
- Neonates without seizures: first follow-up appointment at 3-4 months corrected chronological age

Referral order instructions:

1. Place order for "Referral to Neonatology Follow Up" (REF 225)

Outpatient Procedures						
Px Code	Name		Type	Class	Frequency	Pref List
REF225	Referral to Neonatology Follow Up		Outpat Ref	Internal Referral		REFERRALS

2. Under "What clinic is requested" — click "Early Development Follow-Up Clinic" and answer the questions
 - a. "Has the patient experienced seizures" **YES/NO**
 - b. "Has the patient experienced HIE" — **YES** (all stages of HIE, mild, moderate, or severe)
 - c. "Did the patient require cooling" **YES/NO**

Referral to Neonatology Follow Up Accept Cancel

Class: Internal Referral External Referral

Referral: To Department Specialty: Neonatology Reason: Specialty Services Required

Priority: Routine STAT

What clinic is requested?
Early Development Follow-Up Clinic BPD

Discharge Date:

Interpreter Needed? Yes No

Has the patient been diagnosed with BPD? Yes No

Is the patient on Oxygen? Yes No

Was the patient discharged on 2 or more inhaled respiratory medications? Yes No

Has the patient received Synagis or Nirsevimab? Yes No

Has the patient experienced seizures? Yes No

Has the patient been diagnosed with NAS due to IUDE? Yes No

Has the patient experienced HIE? Yes No

Did the patient require cooling? Yes No

Has the patient been diagnosed with Deep Medullary Venous Thrombosis? Yes No

Does the patient have congenital abnormalities with greater than 3 different systems? Yes No

Does the patient have a trach? Yes No

Has the patient been diagnosed with IVH grade 3-4? Yes No

Next Required

Accept Cancel

Patient & Caregiver Education

Whole Body Cooling – Therapeutic Hypothermia

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Risk Awareness & Zero Hero

- Avoid hyperthermia (temperature $\geq 37.5^{\circ}\text{C}$) and hypothermia (temperature $< 33^{\circ}\text{C}$). Evaluate for malfunctioning of equipment
 - [Therapeutic Hypothermia Protocol \(Medical\).doc](#)

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Key References

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Quality Measures

Outcome Measure:

1. Percentage of infants with concerns for HIE admitted to the NCH main campus NICU within 6 hours
2. For infants who are admitted to the NICU within 6 hours with moderate/severe HIE, 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, the time of initiation of cooling from the time of arrival to NCH

Process Measure:

- Neurological exam documentation rate in the NCH 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

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Pathway Team & Process

Pathway Development Team:

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Advisory Committee Date: *November, 2022*

Origination Date: *January, 2023*

Next Revision Date: *January, 2031*

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 associated 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.

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For more information about our pathways and program please contact:
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Appendix A

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 > 5 x ULN

b. Dose escalation:

- Increase dose in **increments of 0.1mcg/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 0.5mcg/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

References:

1. Cosnahan AS, Angert RM, Jano E, Wachtel EV. Dexmedetomidine versus intermittent morphine for sedation of neonates with encephalopathy undergoing therapeutic hypothermia. *J Perinatol*. 2021;41(9):2284-2291. doi:10.1038/s41372-021-00998-8
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Appendix B

Helping Hands:

[Whole Body Cooling \(Therapeutic Hypothermia\)](#)

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Appendix C

Documentation

NCH:

- Documentation of Sarnat Exam
- Use the "Modified Sarnat Exam" navigator to fill out the exam. Then, can pull your documentation of the exam into a progress note using .neosarnat (need to have first filled out your exam in the navigator)

Summary Chart Review Results Review Intake/Output Problem List Notes Charges (Provider) Orders MAR NICU Navigator Flowsheets Immunizations **Modified Sarnat Exam** Flowsheets

Modified Sarnat Exam

Assessment

+ New Reading

Assessment

Admission (Current) from 2255 in C04B

General Information

Date of Exam 2030

Time of Exam No

Does the infant have seizures? No

Is the infant sedated/paralyzed? No

Therapeutic Hypothermia Categories

Level of Consciousness 2 - Lethargic

Spontaneous Activity 2 - Decreased activity

Posture 2 - Distal flexion, complete extension, "frog-legged" position

Tone 2a - Hypotonia (focal or general)

Suck 2 - Weak, unsustained, bite

Moro 2 - Incomplete (partial abduction at shoulder and extension of arms)

Highest Primitive Reflexes Level 2 - Moderate HIE

Pupils 0 - Reactive

Heart Rate 0 - Normal

Respiration 1 - Irregular and/or tachypneic (RR>60)

Highest Autonomic System Level 1 - Mild HIE

Total Level of HIE

+ New Reading

No data found.

Total Abnormal Values

+ New Reading

No data found.

OSU

- Dot phrase for documentation of the Sarnat exam in OSU IHIS EPIC .neocoolingexam

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