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Hypoxic Ischemic Encephalopathy Clinical Pathway

Version: 7

1.0 Introduction

Hypoxic ischemic encephalopathy (HIE) is defined as an abnormal neurologic state that occurs during the neonatal period following a hypoxic-ischemic insult. There is evidence from both animal and human studies that therapeutic hypothermia provides neuroprotection by reducing the severity of brain injury and resulting in an improved neurological outcome[1–7]. All infants with HIE should be assessed for eligibility to receive therapeutic hypothermia. Evidence suggests that hypothermia in neonates with moderate to severe HIE reduces the severity of brain injury and leads to improved neurological outcome[1,2,4]. Therapeutic hypothermia is considered the standard of care in newborns with HIE.

Target Patient Population

- The commencement of therapeutic hypothermia **within 6 hours of birth**, for eligible patients, is the desired target[8]. Recent data showed that therapeutic hypothermia initiated before or after 4 hours of age demonstrated no significant effect on mortality, short-term outcomes, brain injury on MRI, and neurodevelopmental impairment at 2 years of age in infants with HIE (Rao et al. Unpublished data, 2023).

- All term or late-preterm infants ³35 weeks gestation with moderate or severe HIE should be considered for therapeutic hypothermia.

- Therapeutic hypothermia is not recommended for preterm infants and infants with mild HIE as there is currently no evidence that cooling is beneficial for these infants[9–14]. Studies have shown that therapeutic hypothermia in preterm infants less than 35 weeks was associated with increased mortality and adverse effects[9–12]. Similarly, there is insufficient evidence to recommend therapeutic hypothermia for infants with mild HIE, as several studies have shown no difference in long-term outcomes (death and disability) between infants with mild HIE who were cooled and those who received standard care[13,14]. The benefits of therapeutic hypothermia in preterm infants and infants with mild HIE may not outweigh the risks, therefore cooling is currently not recommended for these infants until more evidence is available.

- In the presence of profound encephalopathy where the risk of death or adverse neurodevelopmental outcome is high, the responsible physician may choose not to offer hypothermia treatment if there is no plan to pursue aggressive treatment.

- Initiation of hypothermia does not preclude a decision to withdraw life-sustaining therapy.

Therapeutic Hypothermia Criteria

Inclusion Criteria:

Infant should fulfill all 4 criteria:

1. GA greater than or equal to 35 weeks
2. Less than 6 hours post-delivery
3. Evidence of intrapartum hypoxia defined as:
    a. Cord or postnatal blood gas within one hour of birth with pH less than or equal to 7.00 OR base excess (BE) of greater than or equal to -16.
    b. If pH 7.01-7.15 or BE -10 to 15.9, and Apgar score 5 or less at 10 minutes or need for continued ventilation or resuscitation at 10 minutes.
    c. If no blood gas available then must have evidence of an acute perinatal event ie placental abruption, uterine rupture, maternal trauma or cardiopulmonary arrest, late or persistent variable decelerations in an encephalopathic newborn.
4. Signs of moderate or severe encephalopathy defined as presence of clinical seizures or 3 or more of the items in the moderate or severe categories using the modified Sarnat score.

- **Exclusion Criteria**
    1. Preterm infants born less than 35 weeks gestation
    2. Neonates with mild encephalopathy on Sarnat Scoring
    3. Neonates with a weight less than 1.8 kg
    4. Clinically significant refractroty coagulopathy despite treatment
    5. Moribund neonates, or neonates with major congenital or genetic abnormalities, in whom no further aggressive treatment is planned

Neurological Assessment

Standardized neurological examination must be performed by a physician or nurse practitioner skilled in neurological assessment within the first hour of life to determine the degree of encephalopathy. The gold standard in the assessment is the modified Sarnat Score; however, it is recommended to also perform the Thompson score as an additional tool to trend clinical evolution numerically. Of note, cerebral function monitoring using amplitude-integrated EEG (aEEG) can assist in screening infants for eligibility for therapeutic hypothermia, although this should not be used to exclude otherwise eligible neonates as per Newborn Brain Society Guidelines, 2022.

Modified Sarnat Score

	Normal	Mild	Moderate	Severe
Level of consciousness	☐ Alert and responsive	☐ Hyperalert, jittery, exaggerated responses	☐ Lethargic	☐ Stupor or coma
Spontaneous activity	☐ Normal	☐ Decreased ± periods of hyperactivity	☐ Decreased	☐ No activity
Posture	☐ Predominantly flexed posture	☐ Mild distal flexion	☐ Strong distal flexion or complete extension	☐ Intermittently decerebrate
Tonus	☐ Flexor tone in extremities	☐ Slightly increased peripheral tone	☐ Hypotonia or hypertonia	☐ Flaccid or rigid
Primitive reflexes **1) Suck** **2) Moro**	 ☐ Strong ☐ Strong	 ☐ Weak, poor ☐ Low threshold to elicit	 ☐ Weak or bites only ☐ Incomplete	 ☐ Absent ☐ Absent
Autonomic function **1) Pupils** **2) Heart Rate** **3) Respirations**	 ☐ Normal size, reactive ☐ Normal heart rate ☐ Normal	 ☐ Mydriasis ☐ Tachycardia (>160/min) ☐ Hyperventilation	 ☐ Miosis ☐ Bradycardia (<100/min) ☐ Periodic breathing	 ☐ Skewed/Non-reactive ☐ Variable ☐ Apnea/On ventilator

Thompson Score

Score	0	1	2	3
Tone	Normal	Hypertonic	Hypotonic	Flaccid
Level of consciousness	Normal	Hyper alert stare	Lethargic	Comatose
Seizures	None	Infrequent < 3/day	Frequent > 2/day	
Posture	Normal	Fisting, cycling	Distal flexion	Decerebrate
Moro	Normal	Partial	Absent	
Grasp	Normal	Poor	Absent	
Suck	Normal	Poor	Absent ± bites	
Respiration	Normal	Hyperventilation	Brief apnea	IPPV (apnea)
Fontanel	Normal	Full, not tense	Tense	
TOTAL SCORE				

2.0 Clinical and neurophysiologic monitoring during therapeutic hypothermia

- Modified Sarnat score and Thompson score should be administered daily and documented on EPIC in all newborns undergoing therapeutic hypothermia until the end of rewarming.
- Newborns receiving therapeutic hypothermia should receive aEEG monitoring during the cooling and rewarming periods.
- Continuous EEG should be considered if there is a concern for seizures or suppressed background patterns (discontinuous normal voltage, burst-suppression, continuous low voltage, isoelectric trace) on aEEG.
- Near-infrared spectroscopy (NIRS) should be connected to newborns undergoing therapeutic hypothermia to optimize brain hemodynamics.
- Adjustments to alarm limits for continuous cardiorespiratory monitoring should be documented (i.e low resting heart rates).

- The following **laboratory monitoring** is recommended as a minimum to be ordered by the medical team. Additional laboratory tests may be ordered as needed.

Laboratory Monitoring	
POCT glucose	Every 6 hours throughout the cooling process
On admission	Gas, lactate, CBC, coagulation, electrolytes, ALT, AST, urea, creatinine, ammonia, calcium, glucose
12 hours after initiation of cooling	Gas, lactate, electrolytes, C-reactive protein
24 hours after initiation of cooling	Gas, lactate, CBC, coagulation, electrolytes, LFTs, bilirubin, urea & creatinine, ammonia, calcium, phosphate
48 hours after initiation of cooling	Electrolytes, urea and creatinine, bilirubin
72 hours after initiation of cooling	Glucose, electrolytes, bilirubin, CBC
24 hours after rewarming has been completed	Glucose, electrolytes, calcium, bilirubin

- In infants presenting without a clear sentinel event, other causes of neonatal encephalopathy should also be considered and investigated appropriately. Possibility of a systemic and/or central nervous system infection should be ruled out. Placental pathology should be sent and pathology results should be monitored closely. Neurometabolic disorders are a frequent cause of neonatal encephalopathy, so a metabolic/genetic consultation for further testing with whole exome sequencing is strongly advised in these infants in consultation with the neonatal neurology team.

3.0 Patient Considerations

- **Rewarming:** Rewarming should occur no faster than 0.5 degrees Celsius/hour, even if rewarming is occurring for other clinical indications such as hemodynamic instability or persistent coagulopathy. – see rewarming section.

- **Venous/arterial Access**
  Consider venous/arterial access needs for patient monitoring prior to the cooling process as difficulties in obtaining access may occur related to decreased perfusion secondary to hypothermia.

- **Fluid and Nutritional Requirements**
  Fluid and nutritional requirements should be assessed daily and when there are changes to the level of patient sedation. Hypothermia, sedation, and the effects of a hypoxic ischemic insult have an additive effect on the infant's metabolic activity.

- **Enteral feeding during therapeutic hypothermia**
  - Patients with moderate-severe HIE will remain NPO during cooling.
  - Patients with milder HIE may be eligible for tropic feeds – Enteral Feeding During Therapeutic Hypothermia

- **Minimizing the risk of subcutaneous fat necrosis**
  - Once target temperature has been reached **do not use additional ice packs** on the skin as this increases the risk for subcutaneous fat necrosis (see 5.3 #10, below) – Subcutaneous Fat Necrosis
  -
- **Analgesia and sedation management**
  - Indications for sedation include agitation or shivering response. Shivering leads to increased peripheral muscle oxygenation consumption. Neonates with excessive shivering should be considered for treatment with dexmeditomidine (please see formulary for dosing details).
  - Analgesia may be used instead of a sedative in the case of patients who have pain due to trauma at delivery, with low dose morphine infusion. Infants with hypoxic ischemic encephalopathy have reduced morphine clearance and elevated serum morphine concentrations.
  - Potentially toxic serum concentrations of morphine may occur with moderate hypothermia and infusion rates >5 micrograms/kg per hour [12].

- **Concurrent use of anti-epileptic drugs (AED) and sedative medications**
  Caution should be used in patients who are receiving anticonvulsants in addition to sedative or opioid agents. Please discontinue sedatives for patients receiving Phenobarbital or midazolam infusions for seizures. Please refer to the SickKids Neonatal Seizure Management Guidelines for the management of seizures and consult Neonatal Neurology service for further guidance

- **Holding during therapeutic hypothermia**
  Patients MAY be eligible for holding during cooling. Refer to **NICU Holding Guidelines** for eligibility and procedure.

4.0 Process for Management of HIE in NICU

Hypoxic Ischemic Encephalopathy (HIE) **Expected Date of Discharge: 8 days post admission**

	DAY OF ADMISSION (0-24 HOURS POST BIRTH)	1-2 DAYS POST ADMISSION (24-48 HOURS POST BIRTH)	DAY 3 (72 HOURS POST-BIRTH)	DAY 4-8 POST-BIRTH
GOALS	1. Complete HIE admission order ("HIE" order set) 2. Complete baseline vitals and blood work 3. Ensure neonate is monitored closely for seizure activity 4. If ventilated, assess for ongoing respiratory support 5. Initiate/maintain cooling protocol (if indicated)	1. Monitor ins and outs 2. Ensure neonate is voiding 3. Maintain therapeutic hypothermia 4. Control seizures as required 5. If intubated, complete spontaneous breathing trial 6. Book MRI for day 4/5 post rewarming 7. Book family meeting with both parents	1. Rewarm to normothermic (if cooled) 2. Prepare for MRI 3. Confirm family meeting for day 4-5 (post MRI) 4. Review enteral nutrition status 5. Continue to assess for readiness for extubation	1. MRI on day 4/5 2. Discuss prognosis with parents/caregivers 3. Initiate enteral/oral feeds 4. Discuss day 8 discharge and disposition
ROUTINE MANAGEMENT	• Complete full neurological examination and document level of encephalopathy • Ensure continuous cardiorespiratory monitoring • Follow cooling protocol • Maintain BLANKETROL at 33.5°C (if cooled) • Establish central venous and arterial access • Assess need for urinary catheter • Cerebral Function Monitoring (CFM) • If seizure activity/depressed background on CFM, initiate seizure management and continuous EEG monitoring • Assess need for low dose sedation • Maintain NPO status • Start TPN • Restrict fluid intake to 40-60 mL/kg/day	• Complete full neurological examination and document level of encephalopathy • Complete labs as per HIE protocol • Ensure urine output is > 1mL/kg/hr • Stop antibiotics if blood cultures negative at 48 hours • Reassess TPN orders • Follow-up on blood cultures • Discuss lactation status with parents • Start mouth care if on breast milk	• Complete full neurological examination and document level of encephalopathy • Monitor hemodynamics closely in rewarming phase • Discontinue CFM if no seizure activity 6 hours post rewarming • Determine discharge destination • Keep NPO if MRI within 12 hours; otherwise start enteral feeds • Prepare sedation orders for MRI • Ensure team is available for MRI • Remove foley catheter • Remove arterial line • Attempt oral feeding • Initiate discharge summary	• Complete full neurological examination and document level of encephalopathy • Complete follow-up blood work for any previous abnormalities • Discontinue umbilical lines • Day 4, discontinue sedation medications (post MRI) • Day 5, complete follow-up EEG (if required) • Ensure nutritional goals are being met
CONSULTS / DIAGNOSITICS	• Head ultrasound • X-ray to confirm lines and tubes placement • Neurology consult within 24 hours of admission or within 1 hour if seizures present	• If ongoing hemodynamic instability; consider echocardiogram • Complete MRI checklist	• Initiate lactation consult (if required)	• OT consult if feeding difficulties • Consider pediatrician for follow-up in community
FAMILY / CAREGIVER EDUCATION	• Introduce team and review plan of care • Ensure that mum is encouraged to start pumping and storing breast milk	• Update parents re: neonate clinical status and expectations for the next 48 hours • Book for follow-up meeting on day 4/5 (post MRI) • If neonate has seizure activity, bedside RN to initiate seizure teaching to discuss prognosis and long term outcomes • Teach mouth care with EBM • Initiate EBM teaching	• Bedside RN to continue seizure teaching • Order teaching meds (if required) • Provide follow-up package • Facilitate infant holding by parent	• Complete hydration status teaching • Complete Well Baby Care teaching • Confirm follow-up plans: Neonatal Follow-up Clinic, Neurology Clinic and Pediatrician

Printable Version of Process for Care Coordination

5.0 Procedure

5.1 Equipment

- Blanketrol III unit (located in the link room) Hypo/hyperthermia blanket – should be attached to Unit (do not remove unless leak/defect)
- Disposable rectal probe – supply room (special order item – inventory monitored by Patient Information coordinator)

5.2 Preparing Blanketrol III unit

	Important Steps	Key Points
1.	Check the level of distilled water in the reservoir. To do so, lift cover of the water fill opening and check if the water is visibly touching the strainer. If needed, carefully add distilled water.	*Low water indication/warning message* will alarm if water level is too low. If in operation and this alarm occurs press SILENCE ALARM button. Pour distilled water into reservoir in until it is visible touching the strainer. The status display will change to show CHECK SET PT. All

Important Steps		Key Points
		parameters will need to be reset to proceed (see below)
2.	Lay the hypo/hyperthermia (rubber blanket) flat on the Overbed warmer with the hoses lying without kinks, towards the Blanketrol III unit.	Ensure hoses are not twisted to allow for unrestricted circulation of water through the unit to the hypo/hyperthermia blanket.
3.	If hoses from hypo/hyperthermia blanket are not connected attach return and outlet couplings to Blanketrol III unit.	Do not disconnect hoses from Blanketrol III after use.
4.	Check that the power switch is OFF prior to inserting the electrical plug into a properly grounded hospital grade receptacle (**red electrical outlet**).	
5.	Turn power switch ON. Water will be circulated through the blanket. Check that there are no leaks in the blankets or hoses.	Water leaks present a risk of infection to the patient and should not be used. Obtain alternate blanket from another Blanketrol III supply box.
6.	Set the Celsius/Fahrenheit switch so that Celsius is displayed.	
7.	Pre-cool the blanket to **33^{0}C** by first operating in the Manual Control Mode. ▪ Press the MANUAL CONTROL button. ▪ Press the TEMP SET button	Allow 15 minutes to pre-cool the hypo/hyperthermia blanket prior to use.

5.3 Cooling the Infant

Important Steps		Key Points
1.	Place infant on a radiant over-bed warmer.	Allows for easy access to the infant.
2.	Ensure radiant warmer on over-bed is OFF. Monitor skin temperature with skin temperature probe.	Exposure to the environment assists in maintaining hypothermic state. Skin temperature should be monitored as a safety measure, in case the rectal thermometer becomes dislodged.
3.	Insert the rectal/esophageal temperature probe to the appropriate depth. **a. Rectal insertion:** i. Lubricate probe with water-based lubricant. Gently insert temperature probe to 3 - 5 cm into infant's rectum. Secure probe to infant's leg to avoid probe dislodgement. **b. Esophageal insertion:** i. Submerging probe in warm water will make probe more pliable. ii. Measure distance from the tip of the nose to the earlobe to the xyphoid process then **subtract** 2 cm from the length to approximate distance to lower esophagus. iii. Lubricate probe with sterile water or infant's saliva. iv. Insert esophageal probe into nare. Do not push past resistance. Attempt opposite nare or insert orally and secure probe with tape. v. Confirm placement with a 2 view x-ray. vi. Secure probe to infant's face to avoid dislodgement.	Utilize esophageal placement for infants with anorectal malformations/injuries.

	Important Steps	Key Points
4.	Insert temperature probe plug into Blanketrol III unit patient probe jack on the right side of the unit.	
5.	Position the pre-cooled hypo/hyperthermia blanket fully unfolded under the infant such that the infant is supine with the occiput resting on the blanket.	This exposes the greatest amount of body surface area of the infant to the hypo/hyperthermia blanket. The Blanketrol III system is used either: to lower or to raise a patient's temperature and/or maintain a desired patient temperature through conductive heat transfer. An infant's body temperature is more responsive to surface heating and cooling than adults related to their higher ratio of skin contact area to body mass. Prevent excessive and/or prolonged tissue pressure and shearing forces, especially over bony prominences, to prevent skin damage.
6.	Active cooling will be reduced when the rectal/esophageal temperature falls below or meets 34.5 ^{o}C. ▪ Press TEMP SET button. ▪ Use the up/down arrows to change the SETPT temperature to **33.5^{0}C.** ▪ Press the GRADIENT 10C* button, then press the SMART MODE button. The target rectal/esophageal temperature is **33.0^{o}C-34.0^{o}C** which is consistent with published trials of whole body hypothermia. [10; 11] *In GRADIENT 10C MODE the unit monitors the patient's temperature and maintains the circulating water temperature at a maximum of 10^{o}C different from the patient's temperature in order to gradually adjust the patient's temperature to a set point determined by the operator. When the patient reaches set point, the unit continues to circulate the water but the water is not heated or cooled. If the patient's temperature falls outside the set point range, the unit resumes operation in GRADIENT 10C MODE. Therefore, if the patient temperature is set for 33.5^{0}C the blanket temperature will not fall below 23.5^{0}C. If a 10^{o}C gradient is not maintaining the patient's temperature at the desired level a variable gradient can be selected using the GRADIENT VARIABLE MODE, whereby a gradient value can be set (range from 0 to 20 degrees Celsius gradient). To set GRADIENT VARIABLE MODE: ▪ Press TEMP SET button.	Commencement of 72 hour cooling period begins when target temperature is reached. Notify physician immediately if temperature increases or decreases outside of the **33.0^{o}C-34.0^{o}C** target. Once you activate the SMART Mode function, the unit will evaluate whether or not the patient's current temperature is the same as their target temperature every 30 minutes. If they are not the same then the unit will respond by adjusting the water temperature by 5 degrees (warmer or cooler) until the patient reaches their target temperature. Once the patient reaches the target temperature the SMART Mode will turn off and the Blanketrol III will default back to the original Gradient setting. If the patient's temperature deviates by 0.2 degrees C (+/-) the SMART Mode will be activated.

<table>
<tr><th colspan="2">Important Steps</th><th>Key Points</th></tr>
<tr><td></td><td>

Use the up/down arrows to change the SET PT temperature to desired patient temperature.
Press GRADIENT VARIABLE button.
Use the up/down arrows to change the gradient to the desired value (0 to 20).
Press GRADIENT VARIABLE button.

</td><td></td></tr>
<tr><td>7.</td><td>Rectal/esophageal, skin and blanket/water temperatures are to be assessed and recorded at specified frequencies:
<table>
<tr><th></th><th>Rectal/esophageal</th><th>Skin</th><th>Blanket</th></tr>
<tr><td>q15min</td><td>x4hrs</td><td>x4hrs</td><td>x4hrs</td></tr>
<tr><td>then q1hr</td><td>x12hrs</td><td>x12hrs</td><td>x12hrs</td></tr>
<tr><td>then q2hr</td><td colspan="3">x72hrs (until cooling completed)</td></tr>
</table>
The probe used to record skin temperature should be placed on the abdomen, not the extremities.
Monitor the skin temperature as follows:

Insert skin temp module into bedside monitor
Insert metal end of skin temp probe into module
Secure pt end of probe onto infant’s abdomen (over liver).
Apply silver dot over probe to hold probe in place
Skin temp should appear on VS monitoring screen

</td><td>An infant’s body temperature is more responsive to surface heating and cooling than adults related to their higher ratio of skin contact area to body mass. Prevent excessive and/or prolonged tissue pressure and shearing forces, especially over bony prominences, to prevent skin damage. Frequent skin assessments should be conducted (manufacturer’s recommendations indicate as frequently as q20 minutes and more frequently for pediatric patients) of areas in contact with the hypo/hyperthermia blanket for skin damage. Neonates are at risk for developing fat necrosis.</td></tr>
<tr><td>8.</td><td>Notify physician immediately if:
Under physician’s order active cooling will be reduced if:

Oxygen requirements increase by more than 20%
The infant is treated with anticonvulsants or muscle relaxants.

Under physician’s order cooling will be stopped if:

Persistent hypoxemia despite 100% oxygen and pulmonary vasodilator treatment.
Life threatening coagulopathy.
Arrhythmia requiring medical treatment (not sinus bradycardia).
Decision made by responsible physician to withdraw intensive care support on the basis of poor neurodevelopmental outcome.

</td><td>Notify physician/nurse practitioner immediately of any changes in the infant’s condition.
*The infant’s rectal/esophageal temperature will begin to decrease soon after initiation of the cooling therapy. Within the first 30-45 minutes on the blanket, it is expected for the infant’s esophageal temperature to drop below the eventual desired temperature of 33.5°C. The Blanketrol system adjusts quickly and will warm the blanket water to raise the infant’s temperature to 33.5°C by approximately 90-120 minutes from initiation of the cooling therapy. While maintaining the infant’s temperature at 33.5°C, the blanket itself will feel warm to the touch. Once stable at 33.5°C, some rectal/esophageal temperature fluctuation around the Set point is to be expected, but should not be greater than +/- 0.5°C.</td></tr>
<tr><td>9.</td><td>During cooling therapy there should only be a thin sheet between the infant and the hypothermia blanket. Rolled cloth blankets and other positioning aids may be used but should be placed under the cooling blanket.</td><td>In some infants there is difficulty maintaining the target temperature. For those infants ensure serum magnesium levels are in the normal range, try lowering the gradient temperature to 15 degrees</td></tr>
</table>

Important Steps		Key Points
	▪ Hats, socks, and a thin sheet ON TOP of the patient are acceptable as long as the core temperature is within expected range.	Celsius, **Do not use additional ice packs** on the skin-this may pose an additional risk for subcutaneous fat necrosis, try warming the infants hands and feet to reduce shivering
10.	Monitor skin for signs of Subcutaneous Fat Necrosis	Subcutaneous Fat Necrosis

6.0 Rewarming of Infants Following Body Cooling

Upon completion of the 72-hour period of cooling, the infant will be re-warmed gradually, increasing the core body temperature at the rate of 0.5°C per hour over a 6-hour period.

Important Steps		Key Points
1.	**Rewarming of Infants Following Body Cooling** Each hour increase the Blanketrol III Set point temperature: • Press the TEMP SET switch. • Press the Up arrow to increase the SETPOINT by 0.5°C. • Press the GRADIENT 10C button.	**Re-warming the infant's temperature should not exceed at the rate of 0.5°C per hour over a 6-hour period.**
2.	**At the end of the 6-hour re-warming period, the infant's thermoregulation will be returned to the Overbed warmer servo-control with skin probe placed on the infant's abdomen**; set the initial radiant warmer set point (skin/control) temperature 0.5°C higher than the infant's current skin temperature. Press the Blanketrol III TEMP SET switch, remove the blanket from under the infant, remove the esophageal probe, and turn the Blanketrol III unit power switch to OFF. The radiant warmer set point temperature should be increased by 0.5°C every hour until a set point of 36.5°C is reached, or until the infant has achieved an axillary temperature of 36.5°C.	Avoid more rapid re-warming. Continue to care for infant's thermoregulation as per Electronic Patient Monitoring Guideline for the NICU and Vital Sign Monitoring Policy.

7.0 References

1. Gluckman, P. D., J. S. Wyatt, D. Azzopardi, R. Ballard, A. D. Edwards, D. M. Ferriero, R. A. Polin, C. M. Robertson, M. Thoresen, A. Whitelaw, and A. J. Gunn. 2005. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicoated randomised trial. *Lancet* 365:663-670.
2. Jacobs, S., R. Hunt, W. Tarnow-Mordi, T. Inder, and P. Davis. 2003. Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane.Database.Syst.Rev.*CD003311.
3. Shah, P. S., A. Ohlsson, and M. Perlman. 2007. Hypothermia to treat neonatal hypoxic ischemic encephalopathy: systematic review. *Arch.Pediatr.Adolesc.Med.* 161:951-958.
4. Shankaran, S., A. R. Laptook, R. A. Ehrenkranz, J. E. Tyson, S. A. McDonald, E. F. Donovan, A. A. Fanaroff, W. K. Poole, L. L. Wright, R. D. Higgins, N. N. Finer, W. A. Carlo, S. Duara, W. Oh, C. M. Cotten, D. K. Stevenson, B. J. Stoll, J. A. Lemons, R. Guillet, and A. H. Jobe. 2005. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N.Engl.J.Med.* 353:1574-1584.
5. Shankaran, S., A. R. Laptook, R. A. Ehrenkranz, J. E. Tyson, S. A. McDonald, E. F. Donovan, A. A. Fanaroff, W. K. Poole, L. L. Wright, R. D. Higgins, N. N. Finer, W. A. Carlo, S. Duara, W. Oh, C. M. Cotten, D. K. Stevenson, B.

J. Stoll, J. A. Lemons, R. Guillet, and A. H. Jobe. 2005. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N.Engl.J.Med.* 353:1574-1584.
6. Thoresen, M., J. Penrice, A. Lorek, E. B. Cady, M. Wylezinska, V. Kirkbride, C. E. Cooper, G. C. Brown, A. D. Edwards, J. S. Wyatt, and . 1995. Mild hypothermia after severe transient hypoxia-ischemia ameliorates delayed cerebral energy failure in the newborn piglet. *Pediatr.Res.* 37:667-670.
7. Thoresen, M. and J. Wyatt. 1997. Keeping a cool head, post-hypoxic hypothermia--an old idea revisited. *Acta Paediatr.* 86:1029-1033.
8. Thoresen, M., S. Satas, M. Puka-Sundvall, A. Whitelaw, A. Hallstrom, E. M. Loberg, U. Ungerstedt, P. A. Steen, and H. Hagberg. 1997. Post-hypoxic hypothermia reduces cerebrocortical release of NO and excitotoxins. *Neuroreport* 8:3359-3362.
9. Vannucci, R. C. and J. M. Perlman. 1997. Interventions for perinatal hypoxic-ischemic encephalopathy. *Pediatrics* 100:1004-1014.
10.Roka A, Melinda KT, Vasarhelyi B, Machay T, Azzopardi D, Szabo M. Elevated morphine concentrations in neonates treated with morphine and prolonged hypothermia for hypoxic ischemic encephalopathy. *Pediatrics* 2008; 121(4):e844-e849
11. Blanketrol III Operation Manual. Model 233 Hyper-Hypothermia Units.

8.0 Guideline Group and Reviewers

*This guideline was critically reviewed and revised by SickKids Neonatal Neurocritical Care Team in May 2023.
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