	Document Scope: Departmental	
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	Hypoxic Ischemic Encephalopathy Clinical Pathway	Version: 5

1.0 Introduction

Hypoxic ischemic encephalopathy (HIE) is defined as an abnormal neurologic state in the neonatal period arising as a result of a hypoxic-ischemic insult. The long-term neurodevelopmental outcome for neonates who have suffered brain injury from a birth related hypoxic-ischemic insult is often poor. There is evidence from both animal and human studies that induced hypothermia provides a mechanism for neuroprotection reducing the severity of brain injury leading to an improved neurological outcome in many patients.⁶⁻⁹ All infants with HIE should be assessed for eligibility to receive total body cooling. Evidence suggests that hypothermia in neonates with moderate to severe HIE reduces the severity of brain injury and leads to improved neurological outcome. Therapeutic hypothermia is considered to be the standard of care treatment in perinatal asphyxia of the term newborn.

Target Patient Population

- The commencement of hypothermia **within 6 hours of birth**, for eligible patients, is the *desirable target*. Ideally this should be initiated **as soon as possible** as earlier cooling can improve its effectiveness¹². However due to challenges with clinical assessment of encephalopathy within the first 6 hours of life **ALL** babies with HIE irrespective of the inclusion and exclusion criteria, who are referred to SickKids within 12 hours of birth, should be considered as potentially eligible for therapeutic hypothermia, in consultation with the staff neonatologist⁵.
- **In the presence of severe encephalopathy where the risk of death or adverse neurodevelopmental outcome is assessed to be high, the responsible physician(s) may choose to not offer hypothermia treatment if the plan is not to pursue aggressive treatment.**
- **Initiation of hypothermia does not preclude a decision to withdraw life-sustaining therapy at a later time.**


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 **EITHER**:
Cord or postnatal blood gas within one hour of birth with pH less than or equal to 7.00 OR base deficit of greater than or equal to -16 **OR** If pH 7.01-7.15 or BD -10 to 15.9, or if no blood gas available then must have evidence of an acute perinatal event (abruption, uterine rupture, maternal trauma or cardiopulmonary arrest, late or variable decelerations) and Apgar score 5 or less at 10 minutes or need for continued ventilation or resuscitation at 10 minutes
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 or a Thompson score of >8.

***The neurological examination must be performed by a physician/NP skilled in neurological assessment to determine the degree of encephalopathy.**

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	Document Scope: Departmental	
	Document Type: Clinical Practice Guideline	
	Approved on 2020-07-28 Next Review Date: 2023-07-28	
Hypoxic Ischemic Encephalopathy Clinical Pathway		Version: 5


Modified Sarnat Score

Category	Mild Encephalopathy	Moderate Encephalopathy	Severe Encephalopathy
1. Level of consciousness	Hyperalert	Lethargic	Stupor/coma
2. Spontaneous activity	Normal	Decreased	No activity
3. Posture	Mild distal flexion	Strong distal flexion Truncal extension	Decerebrate (arms extended and internally rotated, legs extended with feet in forced plantar flexion)
4. Tone	Normal	Mild hypotonia	Flaccid tone
5. Primitive reflexes Suck Moro	Weak Strong	Weak Incomplete	Absent Absent
6. Autonomic system Pupils Heart rate Respirations	Dilated, responsive Tachycardia Normal	Constricted Bradycardia Periodic breathing	Skew deviation, dilated/non-reactive to light Variable HR Apnea

Thompson Score

Score	0	1	2	3
Tone	___ Normal	___ Hypertonic	___ Hypotonic	___ Flaccid
LOC	___ Normal	___ Hyper alert stare	___ Lethargic	___ Comatose
Seizures	___ None	___ Infrequent < 3/day	___ Frequent > 2/day	
Posture	___ Normal	___ Fisting, cycling	___ Strong 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	
SUB-TOTAL				
TOTAL				

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	Document Scope: Departmental	
	Document Type: Clinical Practice Guideline Approved on 2020-07-28 Next Review Date: 2023-07-28	
	Hypoxic Ischemic Encephalopathy Clinical Pathway	Version: 5

Exclusion Criteria

1. Neonate less than 1.8 kg
2. Clinically significant coagulopathy despite treatment
3. Moribund neonates, or neonates with major congenital or genetic abnormalities, in whom no further aggressive treatment is planned

2.0 Ancillary monitoring during Whole Body Cooling

1. All cooled patients should receive aEEG (amplitude integrated electroencephalography) monitoring during the cooled period. Continuous EEG monitoring should be considered if there is discontinuity on the aEEG or a seizure history
2. The following **laboratory monitoring** is recommended as a minimum, and will be ordered by the medical team. Additional laboratory tests may be ordered as needed.

On admission

- Gas, lactate, CBC, coagulation, electrolytes, LFTs, urea & creatinine, ammonia, calcium, glucose

At 12 hrs

- Gas, lactate, electrolytes, CRP

At 24 hours of cooling

- Gas, lactate, CBC, coagulation, electrolytes, LFTs, bilirubin, urea & creatinine, ammonia, calcium, phosphate

AT 48 hours of cooling

- Electrolytes, urea and creatinine, bilirubin

AT 72 hours of cooling

- Glucose, electrolytes, bilirubin and CBC

AT 24 hours post rewarming


- Glucose, electrolytes, calcium and bilirubin

***POC Blood glucose monitoring should occur every 6 hours throughout the cooling process**


3. Adjustments to **alarm limits for continuous cardiorespiratory monitoring** should be documented in the doctor's orders (*i.e low resting heart rates*)

3.0 Patient Considerations

- **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.

	Document Scope: Departmental	
	Document Type: Clinical Practice Guideline Approved on 2020-07-28 Next Review Date: 2023-07-28	
	Hypoxic Ischemic Encephalopathy Clinical Pathway	Version: 5

- **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. Fluid and nutritional requirements may need modification, as metabolic activity is likely to be significantly reduced. **Patients should remain NPO during cooling and re-warming phase.**
- **Analgesia / Sedative treatment:** 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 dexmedetomidine (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. In addition, potentially toxic serum concentrations of morphine may occur with moderate hypothermia and infusion rates >5 micrograms/kg per hour ¹².
- **Concurrent AED and Sedative Use:** 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.
- **HOLDING:** Patients MAY be eligible for holding during cooling. Refer to **NICU Holding Guidelines** for eligibility and procedure.
- **Subcutaneous Fat Necrosis:** Once target temperature has been reached **Do not use additional ice packs** on the skin-this may pose an additional risk for subcutaneous fat necrosis (see 5.3 #10, below).

	Document Scope: Departmental
	Document Type: Clinical Practice Guideline Approved on 2020-07-28 Next Review Date: 2023-07-28
	Version: 5

Hypoxic Ischemic Encephalopathy Clinical Pathway

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	<ol style="list-style-type: none"> 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) 	<ol style="list-style-type: none"> 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 	<ol style="list-style-type: none"> 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 	<ol style="list-style-type: none"> 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	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • 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 / DIAGNOSTICS	<ul style="list-style-type: none"> • Head ultrasound • X-ray to confirm lines and tubes placement • Neurology consult within 24 hours of admission or within 1 hour if seizures present 	<ul style="list-style-type: none"> • If ongoing hemodynamic instability, consider echocardiogram • Complete MRI checklist 	<ul style="list-style-type: none"> • Initiate lactation consult (if required) 	<ul style="list-style-type: none"> • OT consult if feeding difficulties • Consider pediatrician for follow-up in community
FAMILY/CAREGIVER EDUCATION	<ul style="list-style-type: none"> • Introduce team and review plan of care • Ensure that mum is encouraged to start pumping and storing breast milk 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Bedside RN to continue seizure teaching • Order teaching meds (if required) • Provide follow-up package • Facilitate infant holding by parent 	<ul style="list-style-type: none"> • 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)

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	Document Scope: Departmental	
	Document Type: Clinical Practice Guideline	
	Approved on 2020-07-28 Next Review Date: 2023-07-28	
Hypoxic Ischemic Encephalopathy Clinical Pathway		Version: 5

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.	<i>Low water indication/warning message</i> will alarm if water level is too low. If in operation and this alarm occurs press SILENCE ALARM button. Pour distilled water into reservoir until it is visible touching the strainer. The status display will change to show CHECK SET PT. All 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°C by first operating in the Manual Control Mode. <ul style="list-style-type: none"> ▪ 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.


	Document Scope: Departmental	
	Document Type: Clinical Practice Guideline	
	Approved on 2020-07-28 Next Review Date: 2023-07-28	
Hypoxic Ischemic Encephalopathy Clinical Pathway		Version: 5

Important Steps		Key Points
		Skin temperature should be monitored as a safety measure, in case the rectal thermometer becomes dislodged.
3.	<p>Insert the rectal/esophageal temperature probe to the appropriate depth.</p> <p>a. Rectal insertion:</p> <p>i. Lubricate probe with water-based lubricant. Gently insert temperature probe to 3 cm into infant's rectum. Secure probe to infant's leg to avoid probe dislodgement.</p> <p>b. Esophageal insertion:</p> <p>i. Submerging probe in warm water will make probe more pliable.</p> <p>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.</p> <p>iii. Lubricate probe with sterile water or infant's saliva.</p> <p>iv. Insert esophageal probe into nare. Do not push past resistance. Attempt opposite nare or insert orally and secure probe with tape.</p> <p>v. Confirm placement with a 2 view x-ray.</p> <p>vi. Secure probe to infant's face to avoid dislodgement.</p>	Utilize esophageal placement for infants with anorectal malformations/injuries.
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.	<p>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.</p> <p>An infant's body temperature is more responsive to surface heating and cooling than adults related to their higher ratio of skin contact</p>


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Hypoxic Ischemic Encephalopathy Clinical Pathway		Version: 5

	Important Steps	Key Points
		area to body mass. Prevent excessive and/or prolonged tissue pressure and shearing forces, especially over bony prominences, to prevent skin damage.
6.	<p>Active cooling will be reduced when the rectal/esophageal temperature falls below or meets 34.5 °C.</p> <ul style="list-style-type: none"> ▪ Press TEMP SET button. ▪ Use the up/down arrows to change the SETPT temperature to 33.5°C. ▪ Press the GRADIENT 10C* button, then press the SMART MODE button. <p>The target rectal/esophageal temperature is 33.0°C-34.0°C which is consistent with published trials of whole body hypothermia.^{10; 11}</p> <p>*In GRADIENT 10C MODE the unit monitors the patient's temperature and maintains the circulating water temperature at a maximum of 10°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°C the blanket temperature will not fall below 23.5°C. If a 10°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).</p> <p>To set GRADIENT VARIABLE MODE:</p> <ul style="list-style-type: none"> ▪ Press TEMP SET button. ▪ Use the up/down arrows to change the SET PT temperature to desired patient temperature. ▪ Press GRADIENT VARIABLE button. 	<p>Commencement of 72 hour cooling period begins when target temperature is reached.</p> <p>Notify physician immediately if temperature increases or decreases outside of the 33.0°C-34.0°C target.</p> <p>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.</p> <p>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.</p>

	Document Scope: Departmental
	Document Type: Clinical Practice Guideline Approved on 2020-07-28 Next Review Date: 2023-07-28
	Version: 5
Hypoxic Ischemic Encephalopathy Clinical Pathway	

Important Steps		Key Points																
	<ul style="list-style-type: none"> Use the up/down arrows to change the gradient to the desired value (0 to 20). Press GRADIENT VARIABLE button. 																	
7.	<p>Rectal/esophageal, skin and blanket/water temperatures are to be assessed and recorded at specified frequencies:</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th></th> <th>Rectal/esophageal</th> <th>Skin</th> <th>Blanket</th> </tr> </thead> <tbody> <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> </tbody> </table> <p>The probe used to record skin temperature should be placed on the abdomen, not the extremities. Monitor the skin temperature as follows:</p> <ul style="list-style-type: none"> 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 		Rectal/esophageal	Skin	Blanket	q15min	x4hrs	x4hrs	x4hrs	then q1hr	x12hrs	x12hrs	x12hrs	then q2hr	x72hrs (until cooling completed)			<p>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.</p>
	Rectal/esophageal	Skin	Blanket															
q15min	x4hrs	x4hrs	x4hrs															
then q1hr	x12hrs	x12hrs	x12hrs															
then q2hr	x72hrs (until cooling completed)																	
8.	<p>Notify physician immediately if:</p> <p>Under physician's order active cooling will be reduced if:</p> <ul style="list-style-type: none"> Oxygen requirements increase by more than 20% The infant is treated with anticonvulsants or muscle relaxants. <p>Under physician's order cooling will be stopped if:</p> <ul style="list-style-type: none"> Persistent hypoxemia despite 100% oxygen and pulmonary vasodilator treatment. Life threatening coagulopathy. Arrhythmia requiring medical treatment (not sinus bradycardia). 	<p>Notify physician/nurse practitioner immediately of any changes in the infant's condition.</p> <p>*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</p>																

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Hypoxic Ischemic Encephalopathy Clinical Pathway		Version: 5


Important Steps		Key Points
	<ul style="list-style-type: none"> Decision made by responsible physician to withdraw intensive care support on the basis of poor neurodevelopmental outcome. 	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.
9.	<p>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.</p> <ul style="list-style-type: none"> Hats, socks, and a thin sheet ON TOP of the patient are acceptable as long as the core temperature is within expected range. 	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 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.	<p>Rewarming of Infants Following Body Cooling Each hour increase the Blanketrol III Set point temperature:</p> <ul style="list-style-type: none"> 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	Avoid more rapid re-warming. Continue to care for infant's thermoregulation as per Electronic


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Hypoxic Ischemic Encephalopathy Clinical Pathway		Version: 5

Important Steps	Key Points
(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.	Patient Monitoring Guideline for the NICU and Vital Sign Monitoring Policy.

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	Hypoxic Ischemic Encephalopathy Clinical Pathway	Version: 5

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Attachments:

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