GUIDELINE

Hypoxic Ischaemic Encephalopathy (HIE) and Therapeutic Hypothermia

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations.

Read the full statement here:
CAHS Child Safe Organisation Commitment Statement.

This document should be read in conjunction with this disclaimer

Please refer to NETS WA Guidelines for the retrieval of neonates with suspected HIE and instructions on Therapeutic Hypothermia.

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Aim

To facilitate early recognition, diagnosis and treatment of infants >35 weeks GA with HIE that require therapeutic hypothermia (TH).

Background

HIE is suppression of brain activity with possible brain injury due to inadequate oxygen and/or perfusion to the brain. The brain injury may occur immediately (primary neuronal death) due to primary energy failure; or during the secondary phase (latent period, 6-100 hours) due to cytotoxic oedema, mitochondrial failure or build-up of excitotoxins leading to cell death. Evidence from high quality RCTs indicates that **therapeutic hypothermia** (TH), of neonates with moderate to severe HIE is relatively safe and reduces the risk of death or disability.

Relative contra-indications to Therapeutic Hypothermia

- Severe coagulopathy or active bleeding (Mosalli 2012, Jacobs, Berg et al. 2013).
- Persistent pulmonary hypertension (PPHN)
    - Pulmonary hypertension itself is a relative contraindication (Thoresen 2008, Jacobs, Berg et al. 2013).
    - Refractory hypoxaemia despite maximal medical therapy (due to the shift in the oxyhaemoglobin dissociation curve to the left with hypothermia), e.g. Oxygen requirement greater than 80% (Dyson 2017, Yum, Seo et al. 2018).
    - Cooling might worsen PPHN and meconium aspiration syndrome
- Consider partial TH with a target temperature between 34-35 degrees Celsius until correction of coagulopathy of persistent pulmonary hypertension

Key Points

- The positive effects of TH are optimised when started prior to 6 hours of age
- The following four essential inclusion criteria should be met to be eligible for TH
    1. >35 weeks gestational age
    2. < 6 hours post birth
    3. Biochemical and/or clinical evidence of asphyxia
    4. Clinical evidence of moderate or severe HIE
- If a neonate meets eligibility criteria but is 6-12 hours of age, delayed initiation of TH may be considered at the discretion of the attending neonatologists
- Avoid hyperthermia (>37.5 C)

Diagnosis and Initiation of TH

- Follow the TH eligibility checklist (MR461.00) for infants with suspected HIE
- For ***outborn infants*** discuss management with NETS WA
- For ***inborn infants*** (KEMH) contact the senior registrar or consultant to discuss therapeutic hypothermia

If eligible for TH commence as below.

If not eligible for TH follow Principles of Management

Commencing Therapeutic Hypothermia

Active phase (72 hours from initiation)

- Aim to reach target range of 33-34°C (rectal temperature) within 1 hour using an
    - automated servo-controlled TH device i.e. Arctic Sun
    - Cool packs (not automated, requires close monitoring)
- Infants that become irritable or start shivering during TH:
    - Consider non-pharmacological soothing methods
    - Consider low dose morphine or dexmedetomidine infusion
    - Encourage cuddles with parents during TH and advise/reassure parents re: appearance, cool to touch.

Documentation

- Neurological observations on Neurological Observation Chart MR494.00
- HIE stage daily on MR461.00

For Rewarming see **Arctic Sun**

- Rewarming phase is over 12 hours

Principles of Management in HIE

General management strategies

General Management	• Transfer to NICU and commence cardiorespiratory monitoring • Commence aEEG/EEG monitoring • Confirm vitamin K has been given
Airway and Breathing	• Assess and support respiration, maintain SaO2 92-98% • Continuous CO2 monitoring if intubated

	• Avoid periods of prolonged hypoxia or hyperoxia • Avoid fluctuations in PaCO2

Circulation	• Central venous access and intra-arterial monitoring
	• POC echocardiogram may be useful to assess fluid status and cardiac function
	• Cautious fluid resuscitation
	• Avoid fluctuations of blood pressure/prolonged hypotension
	• Infants with cardiac dysfunction:
	  ○ Optimise fluid status
	  ○ Inotrope: low dose adrenaline or dobutamine
	  ○ Dopamine may worsen pulmonary hypertension
	  ○ Consider hydrocortisone for inotrope resistant hypotension

Fluids	Commence 10% dextrose at 40-60mL/kg/day
Metabolic	Regular blood sugar monitoring (aim for > 2.5mmol/L) Aim for normoglycaemia, glucose: 3.0mmol/L to 8mmol/L). Avoid hypo or hyperglycaemia
Infection	• Septic screen with blood culture. Incidence of culture positive sepsis is increased (~23/1,000 cases) • Commence empiric antibiotics (benzylpenicillin, gentamicin)
Investigations	• FBC, UEC, LFT, group and hold, coagulation profile, blood gas • Send placenta for histology and MC+S • Maternal blood for cross match • See below for Day 1-5 investigations

aEEG monitoring

- aEEG monitoring should be applied after stabilisation and should continue until the baby is rewarmed
- the aEEG monitor will display background pattern, sleep-wake cycling (SWC), and presence of seizures
    - Background: Continuous, discontinuous, burst-suppression, low voltage, flat trace
    - SWC: no SWC, developing SWC, developed SWC
    - Seizures: laterality; single seizure, repetitive seizures, status epilepticus

Seizure Management

- Higher seizure burden may be associated with worse outcomes in HIE (Kharoshankaya 2016)
- For acute prolonged seizure (>5 minutes) treat with stat dose of midazolam
- For symptomatic, recurrent or prolonged seizures follow Seizure management, neonatal medication protocols and discuss with neurologist

Skin Care

- Frequent repositioning and monitoring of dependent areas
- Increased risk of subcutaneous fat necrosis which may lead to hypercalcaemia, hyperlipidaemia and thrombocytopaenia.
- Assess NSCS and GS as per Neonatal Skin Care guideline and document on the MR489.00

Feeding

- In general, keep the infant nil by mouth during TH and rewarming phase. If considering enteral feeds, use expressed breast milk and minimal volumes (5-10 ml/kg/day).
- A recent retrospective study found that administration of minimal enteral feeds is safe in infants undergoing therapeutic hypothermia for HIE (Thyagarajan 2015)

Investigations

Investigations	D1	D2	D3	D4	D5
Bloods (daily during active and rewarming) ○ FBP, UE&C, calcium, magnesium, LFT, coagulation profile, blood gas monitoring	Y	Y	Y	Y	-
Neurological assessment	Y	Y	Y	Y	Y
aEEG Monitoring (Brainz Monitor)	Y	Y	Y	Y	-
Formal EEG if ○ persistent seizures detected or possible status epilepticus ○ abnormal neurology after rewarming ○ abnormal MRI brain ○ or at discretion of treating team	-	-	-	Y	-

MRI • Received TH - arrange post warming ideally on day 4 or 5 and before day 8	-	-	-	-	Y
• Did not receive TH (moderate to severe HIE) consider day 3-7 of age	-	-	Y	-	-

Complications of TH

- Worsening of coagulopathy - may decrease platelet function and counts.
- Worsening of pulmonary hypertension
- Subcutaneous fat necrosis

Follow-Up

All infants that are admitted with moderate to severe HIE regardless of whether they received cooling should have 4 and 8-month appointment followed by a formal assessment at 12 months and 24 months.

Related CAHS internal policies, procedures and guidelines

Neonatology Clinical Guidelines

- Hypoglycaemia
- Seizures: Neonatal
- Sepsis: Neonatal

Neonatal Medication Protocols

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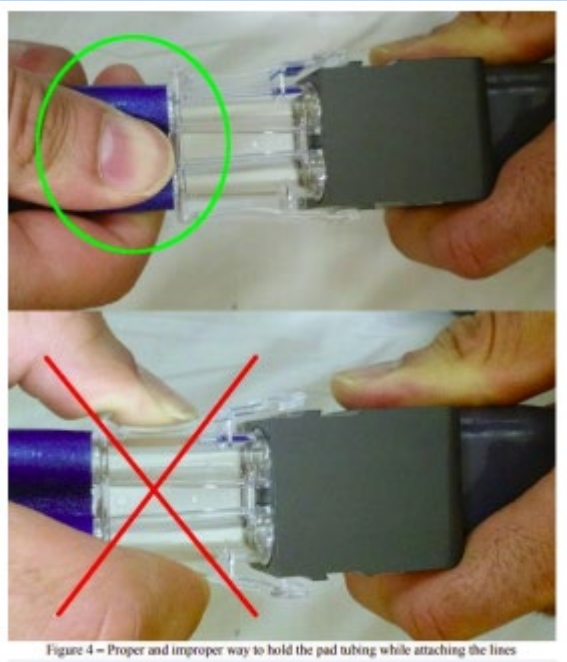
Appendix 1: Artic Sun Cooling and Warming Machine

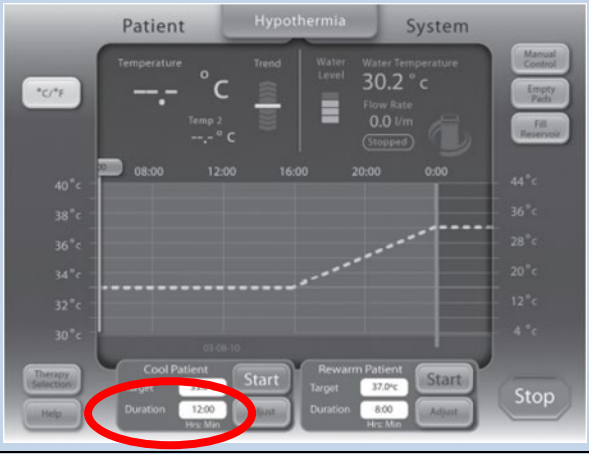
ARCTIC SUN COOLING MACHINE	PROCEDURE
Infant identified for therapeutic cooling. Target Rectal Temperature for 72 Hours Therapeutic hypothermia should not be stopped earlier than the 72-hour period unless attending neonatal consultant decides to cease earlier. The reason for stopping must be documented in the medical records. When hypothermia has been achieved and temperature range is stable, apply BRAINZ Monitor.	○ Nurse the infant on a radiant warmer with the warmer off. ○ Full cardiopulmonary monitoring including invasive blood pressure. ○ If ventilated, leave ventilation humidity at normal temperature. ○ Obtain Arctic Gel Neonatal Pad and machine. ○ Place the Arctic Gel Pad underneath the infant, a single sheet can be used over the mattress if required. ○ Do not dress. Keep nappy on but leave unfastened. ○ Consider use of abdominal straps for nesting and infant comfort.
Connect the machine to power and turn the system on by using the switch at the back of the machine	Plug into essential power. No battery back up is available on Artic Sun.
	Do not remove or cover the white protective cover.
Connect fluid delivery line to pad. Connection is critical for optimal infant therapy. 1. When connecting the gel pad to the grey fluid delivery line grip the blue foam at the base of the gel pad clip, DO NOT connect whilst holding the clear clip. (Refer to picture) 2. Ensure an audible click is heard on both sides. 3. Visually check the clear plastic clip is over the dark grey ridge on both sides of the fluid delivery line.	 Figure 4 – Proper and improper way to hold the pad tubing while attaching the lines
Insert rectal temperature probe and tape the 10 cm mark to the upper inner aspect of the thigh. This depth will give an accurate core temperature. The probe remains in situ for the duration of the cooling period.	Cable is at the back of the machine. Machine is pre-programmed with Neonatology Cooling Protocol for Cooling and Rewarming. The entire process will take 84 hours.

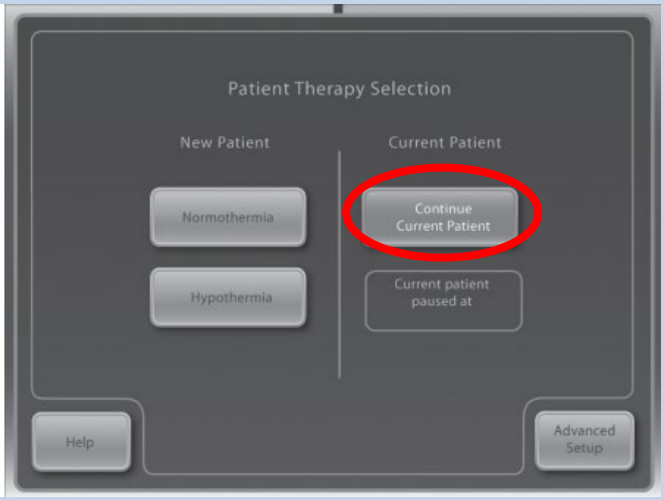
<table>
<tr><td>Connect to Arctic Sun Temperature Cable</td><td rowspan="3">Please note Cooling start time is when Active Cooling Commences.
Automatic temperature adjustments are made by the device. Operator changes are not required.

Document the time of cooling commencement on the MR489/461. If the infant is actively cooled prior to admission you can alter the start time. See below troubleshooting section for how to adjust.</td></tr>
<tr><td>Select “Hypothermia” Mode on front screen.</td></tr>
<tr><td>Select the Green “Start” Button</td></tr>
<tr><td>The programmed machine will alert staff when therapy is completed.
Staff are required to press ‘Stop” on the machine at completion of therapy (Cooling and Rewarming).
The machine will ask you to empty the water from the Artic Sun Gel Pad, press “Start” when prompted. The water will take approximately 40 seconds to empty back into the system.
Rewarming (12 hours): Aims to increase rectal temperature by 0.5° C every 2 hours with a target of 37° C +/- 0.5. System is fully integrated.</td><td>Pads are XRAY/MRI/CT safe so no need to stop therapy or empty pads, they can be left insitu for the procedure.

The Artic Sun machine is not MRI/CT safe. Stop Therapy, empty the water from the pad, disconnect the pad from the machine but leave in place.

CPR can be performed with the pad left insitu. Automatic Defibrillation pads can be placed underneath the Arctic Gel Pad. The system does not need to be stopped if the infant requires defibrillation.</td></tr>
<tr><td>Disconnect the fluid delivery lines after the water is emptied from the Arctic Sun Gel Pad.
1. Pinch the clear plastic clip (Refer to picture)
2. Push the pad and fluid line together,
3. The clips will pop out of the dark grey ridges.</td><td> </td></tr>
<tr><td>Remove the infant from the pad and discard.</td><td>Artic Sun Gel Pads are disposable.</td></tr>
<tr><td colspan="2">TROUBLESHOOTING</td></tr>
<tr><td>FILL RESERVIOR</td><td>PROCEDURE</td></tr>
</table>

At times the water level of the Arctic Sun may drop and require the reservoir to be filled. The machine can be filled from the Hypothermia or Normothermia screen by pressing the fill reservoir button. Machine should be checked by MTMU as soon as therapy ceases if Reservoir has required to be filled.	1. Press the Fill Reservoir button. 2. Ensure only sterile water is used to refill the machine. 3. Follow the directions on the screen to fill the reservoir.
ADJUSTING THE START TIME	**PROCEDURE**
A infant may have commenced active cooling prior to admission. If this has occurred the start time may be adjusted after commencement of therapy so the infant can be rewarmed at the correct time. The Arctic Sun is pre-programmed and will prompt the user to commence rewarming when it is due.	1. Note the time of hours the infant has already been actively cooled. 2. From the Hypothermia Screen press the adjust button. 3. Alter the duration time of hours cooled to the correct amount. 
FLOW RATE TROUBLESHOOTING	**PROCEDURE**

The machine should reach a flow rate of 1.5l/min. If the machine is not reaching this flow rate staff should check for obstructions to the flow.	1. Flow rate not reaching 1.5l/min. 2. Check for obstruction to fluid delivery i.e. kinking or twisting of fluid delivery lines. DO NOT DISCONNECT FLUID DELIVERY LINES WITHOUT EMPTYING THE ARCTIC GEL NEONATAL PAD. 3. Ensure appropriate water level. If not see Fill Reservoir troubleshooting above.
MOVING AN INFANT	**PROCEDURE**
At times there may be a requirement to move an infant who is receiving treatment. It is important to empty the arctic gel pad prior to disconnecting the machine for movement.	1. Infant identified to move. 2. Note the duration of cooling or rewarming left to complete. 3. From the Hypothermia screen press Stop to complete the therapy. 4. When prompted empty the arctic gel pad. This should take around 40 secs. 5. Disconnect the gel pad from the machine as per normal procedure. 6. Unplug the machine and move to where infant will be located. 7. Once infant in new bedspace connect arctic gel pad to machine as per normal procedure. 8. Turn on Arctic Sun machine. 9. Select continue current infant.  10. Should there be any issue with choosing the current infant select new infant for Hypothermia and adjust the cooling/rewarming time as above.

Appendix 2: Active Cooling Phase with Cool Packs

TH using cool packs should only be done when automated machines are unavailable. TH should not be delayed or withheld because of unavailability of automated machines.

Nursing care:

- Set alarm limits for rectal temp at 33.0-34.0ºC.
- Use cold packs from the fridge, **never** frozen.
- Always put cold packs in cotton bags.

Temperature algorithm	Number of cool packs to be applied	Areas to apply
> 37.0	4	Head, shoulders, neck, trunk
36.1 - 37.0	3	Shoulders, neck, trunk
35.1 - 36.0	2	Shoulders, trunk
34.1 - 35.0	1	Trunk
33.0 - 34.0	0	Nil

- When rectal temp < 33.0, set radiant warmer on manual and gradually adjust heater output to maintain rectal temp at 33.0-34.0ºC. Turn off the heater once temperature reaches 33.5.
- Caution: watch temperature range more closely in infants treated with anticonvulsants or muscle relaxants as they may cool much quicker.

Rewarming Phase

This Phase will take up to 12 Hours

- Apply skin temperature probe and turn radiant warmer on if switched off.
- Set servo at 34.0ºC.
- Increase servo temp by 0.5 every 2 hours until rectal temperature is 36.5ºC.
- Adjust alarm limits accordingly on rectal temp range as temp increases.
- Record both skin and rectal temp hourly.
- When normothermia has been achieved, **pay attention to avoid overheating the infant above 37ºC.**