



GUIDELINE

**Hypoxic Ischaemic Encephalopathy (HIE)
and Therapeutic Hypothermia**

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

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this [disclaimer](#)

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

Aim

Outline the criteria and process for Therapeutic hypothermia for infants with Hypoxic Ischaemic Encephalopathy.

Background

Hypoxic ischaemic encephalopathy (HIE) is suppression of brain activity with possible brain injury due to inadequate oxygen 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.

HIE contributes significantly to neonatal mortality and morbidity with adverse neurodevelopmental outcomes seen in up to 25-60% of survivors. Evidence from high quality RCTs indicates that **therapeutic hypothermia** (TH), using whole body or targeted head methods, of neonates with moderate to severe HIE is relatively safe and reduces the risk of death or disability at 18 to 22 months of age.

Criteria for Therapeutic Hypothermia

Key Points

- This guideline is only for newborn infants >35 weeks GA with moderate to severe HIE.
- The positive effects of TH are optimised when started prior to 6 hours of age.
- Avoid hyperthermia (>37.5 C).
- Complete TH Eligibility and Monitoring Chart (MR461.00) if HIE suspected.
- If a neonate meets eligibility criteria 1, 3, and 4 but is 6-12 hours of age, delayed initiation of TH may be considered at the discretion of the attending neonatologists.

Inclusion Criteria

Essential: the following four inclusion criteria should be met to be eligible for TH

1. > 35 weeks gestational age.
2. < 6 hours post birth.
3. Evidence of asphyxia as defined by the presence of at least two of the following four criteria:
 - Any acute perinatal event that may result in HIE (e.g. abruption of placenta, cord prolapse, severe FHR abnormality).
 - Apgar < 6 at 10 minutes or continued need for resuscitation with positive pressure ventilation +/- chest compressions at 10 minutes of age.
 - Cord pH < 7.0 or base deficit of 12 or more.
 - If cord pH is not available, arterial pH < 7.0 or BE > 12 mmol/L within 60 minutes of birth (if able to do gas).
4. Moderate or severe HIE defined by at least one of the following 3 criteria:

- ≥ 3 criteria in moderate/severe category based on modified Sarnat Classification (see [table 1 below](#)).
- Seizures
- Abnormal aEEG (low voltage discontinuous, burst suppression)

Table 1. Clinical features of HIE based on the Sarnat Classification (Sarnat 1976)

Clinical Feature	Stage 1 (mild)	Stage 2 (moderate)	Stage 3 (severe)
Level of consciousness	Alert	Lethargic	Comatose
Spontaneous activity	Normal	Decreased	No activity
Neuromuscular control (A) Muscle tone	Normal or hypertonic	Hypotonic	Flaccid
Neuromuscular control (B) Posture	Normal or mild flexion	Distal flexion	Decerebrate, thumb adduction
Autonomic function Pupils Respiration Heart rate	Dilated, reactive Regular Normal/tachycardia	Small, reactive Periodic Bradycardia	Variable/fixed Ataxic, apnoeic Bradycardia
Primitive reflexes Suck Moro Grasp Oculocephalic	Active Exaggerated Normal/exaggerated Normal	Weak Incomplete Exaggerated Overactive	Absent Absent Absent Reduced/absent

Relative contra-indications to Therapeutic Hypothermia

- Suspected coagulopathy (Mosalli 2012, Jacobs, Berg et al. 2013).
- Passive partial cooling might be considered (to keep axillary or rectal temperatures at 34.5°C) prior to receiving result of the coagulation profile (O'Reilly, Labrecque et al. 2013).
- Persistent pulmonary hypertension (PPHN)
 - Pulmonary hypertension itself is NOT a contraindication (Thoresen 2008, Jacobs, Berg et al. 2013).

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- 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 (need to be guided by clinical condition and echocardiography).

Implementing Therapeutic Hypothermia

Key Points

- Aim of TH is to achieve target range of 33-34°C (rectal temperature) within 1 hour.
- TH is divided into:
 - Active phase: 72 hours from initiation of TH
 - Rewarming phase: 12 hours of rewarming, aiming to increase rectal temperature by 0.5° C every 2 hours with a target of 37° C +/- 0.5.
- Equipment:
 - Automated options: Arctic Sun.
 - Cool gel packs if automated options are unavailable
 - Rectal temperature probe

Initiation of Therapeutic Hypothermia

For further information regarding automated options or cool gel packs, refer to [Appendix 1](#):

Monitoring of Newborn Receiving Therapeutic Hypothermia

General Monitoring

- Continuous intensive care monitoring (ECG, BP, SaO₂, ETCO₂).
- Continuous aEEG monitoring during active and rewarming phase.
- Document neurological observations on Neonatal Neurological Observation Chart MR494.00.
- Document HIE stage daily on Therapeutic Hypothermia Eligibility and Monitoring Form MR461.00.

Temperature Monitoring

- Rectal probe inserted to depth of 5cm.
- Set temperature alarm limits at 33 (low) to 34 (high).

aEEG Monitoring

- aEEG monitoring should be applied after stabilisation of the newborn.
- It is used for early decision making and monitoring of cerebral activity.
- Up to 50% of infants may develop seizures as a result of HIE.

Investigations

1. Complete “HIE bloods” daily during the active and rewarming phase
 - FBP, UE&C, calcium, magnesium, LFT, coagulation profile, blood gas monitoring
 - TH may decrease platelet function and counts.
2. Formal EEG to be arranged (usually post rewarming phase).
3. MRI to be arranged usually post rewarming phase between day 4-8 of age.

Investigations	Day 1	Day 2	Day 3	Day 4	Day 5
Bloods	Y	Y	Y	Y	-
Neurological assessment	Y	Y	Y	Y	Y
aEEG Monitoring (Brainz Monitor)	Y	Y	Y	-	-
EEG (usually at 72hr)	-	-	-	Y	-
MRI (before day 8, ideally on day 4 or 5)	-	-	-	-	Y

Management of Newborn Receiving Therapeutic Hypothermia

General Management Points

- Asphyxia may lead to multi-organ failure (Monitor hepatic, renal, respiratory and cardiac systems regularly).
- TH may lead to reduced platelet function and counts, immune dysfunction.

Cardiac Support

- Volume expansion or Inotrope may be required.
- The infant should remain normotensive to assist in cerebral perfusion.
- If cardiac function is depressed, consider dobutamine or low dose adrenaline.

Fluid and Electrolyte Management

- Total fluid intake early is usually 40-60mL/kg/day.
- Maintain normal electrolyte levels especially sodium to reduce risk of cerebral oedema.

- Strict fluid balance as asphyxia and TH may lead to reduce urine output.

Glucose Homeostasis

- Hypoglycaemia may worsen neurodevelopmental outcomes of infants with HIE.
- Aim for blood glucose levels between 3.5-6 mmol/L.
- Provide 6-8 mg/kg/min of glucose infusion IV.
- Increase concentration of dextrose if fluid restriction required.

Sedation

- Sedation may be required to assist in reducing metabolic rate in infants that have become agitated.

Skin

- Frequent repositioning and monitoring of dependent areas. Documentation of NSCS and GS as per [Neonatal Skin Care](#) guideline.
- Increased risk of subcutaneous fat necrosis
 - This may lead to hypercalcaemia, hyperlipidaemia and thrombocytopenia.

Seizure Control

- Higher seizure burden is known to be associated with worse outcomes in HIE (Kharoshankaya 2016).
- Identify and treat seizures early guided by aEEG and clinical examination.
- Suggested management (Refer to [Seizures: Neonatal](#)):
 - 1st line: phenobarbital.
 - 2nd and/or 3rd line: Leviteracetam, midazolam.
 - 4th line: lignocaine infusion or phenytoin.
- For resistant seizures discuss with neurologist.

Feeding

- Unit practice is to keep the infant nil by mouth during TH and rewarming phase.
- If clinicians would like to give 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).

Follow-Up

- All infants that received TH require developmental follow-up with Griffiths Scales at one year and Bayley Scales at two years of age.

Related CAHS internal policies, procedures and guidelines

Neonatology Clinical Guidelines

- [Hypoglycaemia](#)
- [Seizures: Neonatal](#)
- [Sepsis: Neonatal](#)

[Neonatal Medication Protocols](#)


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This document can be made available in alternative formats on request.

Document Owner:	Neonatology		
Reviewer / Team:	Neonatology Coordinating Group		
Date First Issued:	July 2018	Last Reviewed:	March 2022
Amendment Dates:	March 2023	Next Review Date:	March 2025
Approved by:	Neonatology Coordinating Group	Date:	22 nd March 2022
Endorsed by:	Neonatology Coordinating Group	Date:	
Standards Applicable:	NSQHS Standards:  Child Safe Standards: 1,10		

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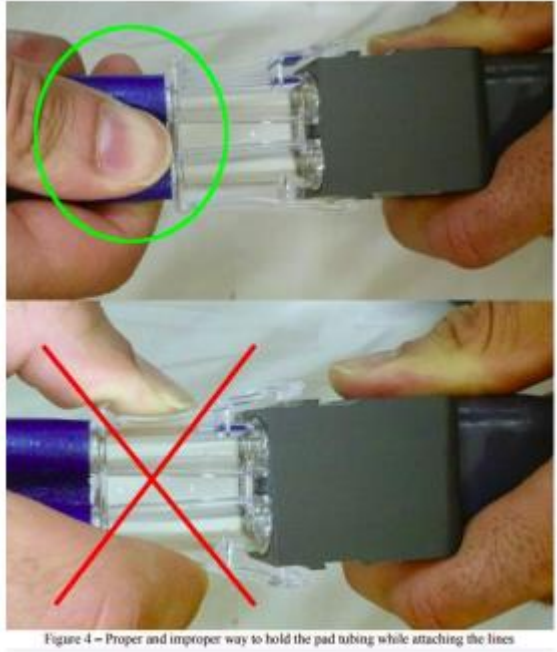
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Appendix 1: Active Cooling Phase

Maintenance of Target Rectal Temperature for 72 Hours using the Artic Sun Cooling and Warming Machine

- Place the gel neonatal mattress underneath the baby. A single sheet can be used over the mattress if required.
 - Consider the use of a pressure mattress.
- Nurse the infant on a radiant warmer with the warmer off.
- Do not dress the infant.
- Leave the nappy unfastened.
- Insert a rectal 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.
- Full cardiopulmonary monitoring including invasive blood pressure if possible.
- If the infant is ventilated, leave ventilation humidity at normal temperature.
- When hypothermia has been achieved and temperature range is stable, apply BRAINZ Monitor.
- 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.
- All other documentation/care/treatment should be as per NICU routine care of infant requiring intensive care.
- Advise/reassure parents re: appearance, cool to touch.

Appendix 2: Cooling and Warming Machines

ARCTIC SUN COOLING MACHINE	PROCEDURE
Patient identified for therapeutic cooling.	Obtain Arctic Gel Neonatal Pad and machine.
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.
Lay the baby on the Artic Gel Pad.	Do not remove white protective cover. Do not cover white protective cover. Keep Nappy on patient. Consider use of abdominal straps for nesting and patient comfort.
<p>Connect fluid delivery line to pad. Connection is critical for optimal patient therapy.</p> <ol style="list-style-type: none"> 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. 	 <p>Figure 4 – Proper and improper way to hold the pad tubing while attaching the lines</p>
Insert rectal temperature probe and connect to Arctic Sun Temperature Cable	Cable is at the back of the machine.
Select “Hypothermia” Mode on front screen.	Machine is pre-programmed with CAHS Neonatology Cooling Protocol for Cooling and Rewarming. The entire process will take 84 hours.
Select the Green “Start” Button	Please note Cooling start time is when Active Cooling Commences.
<p>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.</p>	<p>Automatic temperature adjustments are made by the device. Operator changes are not required.</p> <p>Please note the time of cooling commencement on the MR490 Observation Chart. If the patient is actively cooled prior to admission you can alter the start time. See below troubleshooting section for how to adjust.</p>

Pads are XRAY safe so no need to stop therapy or empty pads.

Pads are MRI/CT Safe and 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 patient requires defibrillation.

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.



Remove the patient from the pad and discard.

Artic Sun Gel Pads are disposable.

TROUBLESHOOTING

FILL RESERVIOR

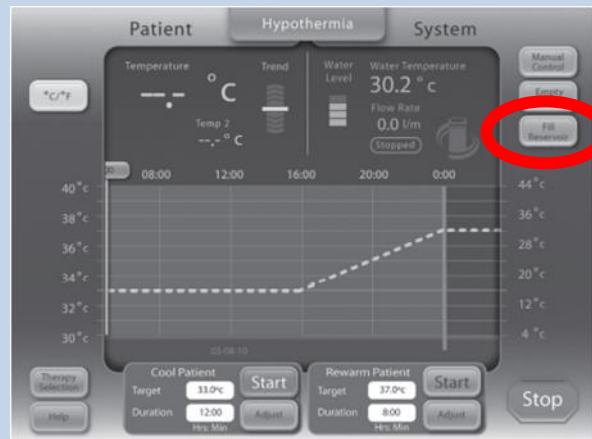
At times the water level of the Arctic Sun may drop and require the reservoir to be filled.


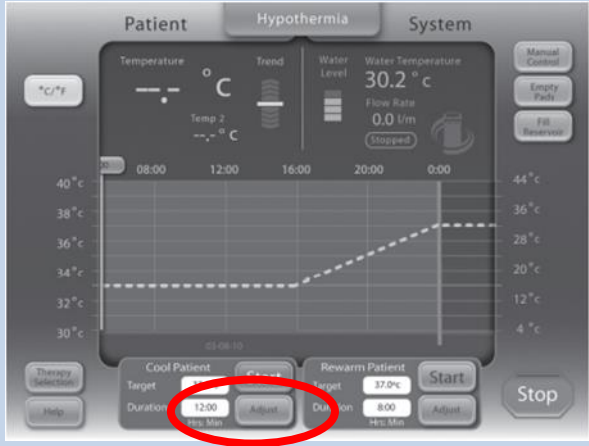
The machine can be filled from the Hypothermia or Normothermia screen by pressing the fill reservoir button.

Machine should be checked by MTMU as soon as therapy ceases if Reservoir has required to be filled.

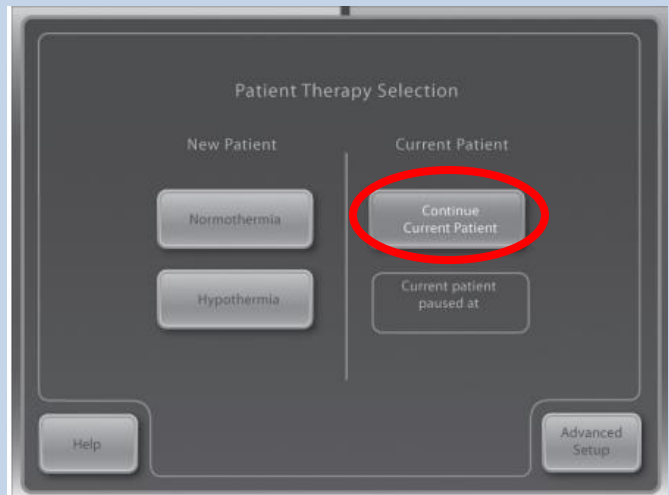
PROCEDURE

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.



	
<p>ADJUSTING THE START TIME</p> <p>A patient may have commenced active cooling prior to admission. If this has occurred the start time may be adjusted after commencement of therapy so the patient 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.</p>	<p>PROCEDURE</p> <ol style="list-style-type: none"> 1. Note the time of hours the patient 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. 
<p>FLOW RATE TROUBLESHOOTING</p> <p>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.</p>	<p>PROCEDURE</p> <ol style="list-style-type: none"> 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.
<p>MOVING A PATIENT</p> <p>At times there may be a requirement to move a patient who is receiving treatment. It is important to empty the arctic gel pad prior to disconnecting the machine for movement.</p>	<p>PROCEDURE</p> <ol style="list-style-type: none"> 1. Patient 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 patient will be located.
 7. Once patient in new bedspace connect arctic gel pad to machine as per normal procedure.
 8. Turn on Arctic Sun machine.
 9. Select continue current patient.



10. Should there be any issue with choosing the current patient select new patient for Hypothermia and adjust the cooling/rewarming time as above.

Appendix 3: 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 is as above under [Active cooling phase](#)

- Set alarm limits for rectal temp at 33.0-34.0°C.
- 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 33.0-34.0°C. 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 after use of cool packs

This Phase will take up to 12 Hours

- Apply skin temperature probe and turn radiant warmer on if switched off.
- Set servo at 34.0°C.
- Increase servo temp by 0.5 every 2 hours until rectal temperature is 36.5°C.
- 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 37°C.**