CLINICAL PRACTICE GUIDELINE
Guideline coverage includes NICU KEMH, NICU PCH and NETS WA

Cooling Guideline: Systemic Cooling for Neuroprotection in Neonates > 35 Weeks Gestational Age with HIE

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This document should be read in conjunction with the Disclaimer
This guideline is only for neonates > 35 weeks gestation at birth. Hypothermia is not advisable for preterm neonates < 35 weeks gestation.

HIE following perinatal asphyxia contributes significantly to neonatal mortality and morbidity including long-term neurodevelopmental sequelae in up to 25%-60% of survivors. Evidence from high quality RCTs indicates that cooling of neonates with moderate to severe HIE is safe and reduces the risk of death or disability at 18 to 22 months of age. Therefore, cooling is the first intervention which has been proven in rigorously conducted scientific studies to be beneficial in term and near term neonates with HIE. Target rectal temperatures during the period of cooling: 33.5°C (acceptable range 33-34).

**Guideline for Management in NCCU**

**Essential:** the following four inclusion criteria should be met to be eligible for cooling.

**Inclusion Criteria**

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:
   - Apgar < 6 at 10 minutes or continued need for resuscitation with positive pressure ventilation +/- chest compressions at 10 minutes.
   - Any acute perinatal event that may result in HIE (i.e. abruption of placenta, cord prolapse, severe FHR abnormality etc).
   - 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 based on modified Sarnat Classification (see table below).

If a neonate meets eligibility criteria 1, 3, and 4 but is 6-12 hours of age, delayed initiation of cooling may be considered at the discretion of the attending neonatologists.
The presence of moderate/severe HIE according to the modified Sarnat Classification is defined as seizures OR presence of signs in at least three of the six categories given below:

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<tr>
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<th>Severe encephalopathy</th>
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<td>Periodic breathing</td>
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When screening a neonate for eligibility of cooling, please tick/fill in below list in the medical notes. Use the dedicated stamp. This documentation applies to all neonates with HIE screened for eligibility of cooling, not just the ones who actually meet inclusion criteria and/or receive cooling.

**Individual eligibility criteria checklist (please use stamp and put in medical notes):**

- GA > 35 weeks Yes/no
- Apgar < 6 at 10 minutes Yes/no
- Need for assisted ventilation at 10 mins Yes/no
- Cord pH/postnatal pH < 7 Yes/no
- Cord or postnatal base deficit > 12 Yes/no
- Level of consciousness Awake/lethargy/stupor/coma
- Spontaneous activity Normal/reduced/no activity
- Posture Normal/decerebrate/decorticate
- Tone Normal/hypotonia/hypertonia
- Suck reflex Normal/weak/absent
- Moro’s reflex Normal/weak/absent
- Pupils Normal/constricted/dilated/NR
- Heart rate Normal/bradycardia/variable
- Respirations Normal/periodic/apnoea
- Seizures Yes/no
- Congenital anomaly Yes/no
- Chromosomal anomaly Yes/no
- Severe IUGR (BW < 1800 grams) Yes/no
- In extremis Yes/no
- Ano-rectal anomaly Yes/no
- Suspected head trauma or ICH Yes/no
If the infant meets eligibility criteria for cooling, please follow the guidelines below.

Management

- The decision to cool a neonate with HIE is made by the attending neonatologist or senior registrar.
- In order to be effective, cooling should commence as soon as possible, i.e., within 6 hours of birth.
- Aim is to achieve target temperature range within 1 hour:
  - **Active cooling** - for 72 hours from the initiation of cooling.
  - **Rewarming** - 12 hours of active gradual re-warming time after completion of 72 hours of cooling.

**Note:** The 84 hour period of cooling and re-warming commences from the time cooling begins and not from the time of birth.

**Active Cooling Phase** - Maintenance of Target Rectal Temperature for 72 Hours using the Cincinnati 3 or Meditherm III Servo Controlled Cooling And Warming Machine

- Infant Cooling and rewarming are preferably done using the Cincinnati 3 (PCH) or the Meditherm III (KEMH).
- Manual cooling with cool packs is to be used in the NICU only if all the Cincinnati Meditherm machines are in use for other babies. Cooling should never be withheld or delayed because of unavailability of these machines.
- Place the gel neonatal mattress underneath the baby. A single sheet can be used over the mattress if required.

<table>
<thead>
<tr>
<th>CINCINNATI 3</th>
<th>MEDITHERM III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connect the tubes to the black insulated hose from the machine.</td>
<td>Connect the tubes to the grey insulated hose from the machine.</td>
</tr>
<tr>
<td>Make sure the hoses and gel roll are not kinked. Check the water level at the back of the machine. Water level must be visible at the bottom of the water fill opening.</td>
<td>Make sure all clamps are in the open position, both on the grey hose and on the neonatal mattress. Press the on switch, located at the front lower left of the Meditherm III machine. Select the centre square button, THE AUTOMATIC MODE. Tab to select the speed - choose the middle speed.</td>
</tr>
<tr>
<td>Press the on switch, located at the front lower left of the machine.</td>
<td>Set the target temperature of the patient with the far lower right hand side square button. To cool below 36°C, keep the button depressed to confirm and set the new patient cooling set temperature to 33.5°C.</td>
</tr>
<tr>
<td>Press TEMP SET and use the UP &amp; DOWN buttons to select desired temperature to 33.5°C.</td>
<td></td>
</tr>
<tr>
<td>Select the GRADIENT 10°C and the select SMART MODE.</td>
<td>Cooling will now commence.</td>
</tr>
<tr>
<td>Ensure that paddle wheel is turning. If paddle is not turning check for obstruction</td>
<td>When the infant temperature is approaching the target temp the machine will slow down automatically to prevent significant undershooting and will</td>
</tr>
</tbody>
</table>
such as kinked hose. maintain the target temperature.

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When the infant temperature is approaching the target temp the machine will slow down automatically to prevent significant undershooting and will maintain the target temperature.

**REWARMING PHASE - THIS PHASE WILL TAKE UP TO 12 HRS.**

<table>
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<th>Action</th>
</tr>
</thead>
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<tr>
<td>After the period of cooling, to rewarm the infant, press the TEMP SET button.</td>
<td>After the period of cooling, to rewarm the infant, set the target temperature to the desired temperature 37°C (Core).</td>
</tr>
<tr>
<td>Use the † button to increase the set temperature by 0.3°C every hour until the infant's temperature is 36.5°C over 12 hours.</td>
<td>Continue with the MODERATE rate setting which will rewarm the patient at 0.33°C per hour, i.e. from 33.5 to 36.5°C over 12 hours.</td>
</tr>
<tr>
<td>Every time the TEMP SET is adjusted the GRADIENT 10°C/GRADIENT VARIABLE &amp; SMART button must be pressed to accept the change and to start the unit again.</td>
<td>Once the infant's core temperature reaches 36.5°C at 12 hours the mattress is removed and the machine is turned off. The rectal probe is removed.</td>
</tr>
<tr>
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<td></td>
</tr>
</tbody>
</table>

**Monitor neurological status closely during the rewarming phase.**
Active Cooling Phase - Maintenance of Rectal Temperature Between 33.0 and 34.0 for 72 Hours using Cool Packs

Cooling using cool packs should be done only if all the Meditherm cooling machines are already in use. Cooling should not be delayed or withheld because of unavailability of Meditherm cooling machine. Cool gel packs are also a good method of cooling babies.

- Nurse the infant on a radiant warmer with warmer off.
- Do not nurse on a sheepskin.
- Do not dress.
- Leave nappy unfastened.
- Insert 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.
- Set alarm limits for rectal temp at 33.0-34.0°C.
- Full cardiopulmonary monitoring including invasive blood pressure if possible.
- Use cold packs from the fridge, never frozen.
- Always put cold packs in cotton bags.

<table>
<thead>
<tr>
<th>Temperature algorithm</th>
<th>Number of cool packs to be applied</th>
<th>Areas to apply</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 37.0</td>
<td>4</td>
<td>Head, shoulders, neck, trunk</td>
</tr>
<tr>
<td>36.1 - 37.0</td>
<td>3</td>
<td>Shoulders, neck, trunk</td>
</tr>
<tr>
<td>35.1 - 36.0</td>
<td>2</td>
<td>Shoulders, trunk</td>
</tr>
<tr>
<td>34.1 - 35.0</td>
<td>1</td>
<td>Trunk</td>
</tr>
<tr>
<td>33.0 - 34.0</td>
<td>0</td>
<td>Nil</td>
</tr>
</tbody>
</table>

- 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.
- If infant is ventilated, leave ventilation humidity at normal temperature.
- When hypothermia has been achieved and temperature range is stable, apply BRAINZ Monitor.
- Cooling should not be stopped earlier than the 72 hour period. If the attending neonatal consultant decides to stop cooling earlier the reason 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.
- 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

- Takes place after the completion of 72 hours of cooling and not 72 hours after birth.
- Rewarming process should be gradual and occur over a period of 10-12 hours; rapid rewarming may be harmful.
- 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 particular attention to avoid overheating the infant above 37°C.

**Investigations**

Please ensure below investigations are done and recorded in the medical notes.

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full blood picture</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>U &amp; E’s, Creatinine, Calcium, Magnesium</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Lactate</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>PT, PTT</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Glucose</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Neuro assessment/Modified Sarnat staging*</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>ABG/CBG</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>LFT’s</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>12 ECG (only if concerns)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Brainz Monitor</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>-</td>
</tr>
<tr>
<td>EEG (usually at 72hr)</td>
<td>-</td>
<td>-</td>
<td>Y</td>
<td>-</td>
</tr>
<tr>
<td>MRI (before day 8, ideally on day 4)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Y</td>
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*Modified Sarnat staging:

**Mild:** Hyperalertness, hyper-reflexia, dilated pupils, tachycardia, absence of seizures.

**Moderate:** Lethargy, hyper-reflexia, miosis, bradycardia, seizures, hypotonia with weak suck and Moro.

**Severe:** Stupor, flaccidity, small to midposition pupils which react poorly to light, decreased stretch reflexes, hypothermia, absent Moro.

Follow-up: Please inform the discharge coordinator to ensure appropriate follow up including developmental assessments are arranged.

**The NETS WA team Guideline for Systemic Cooling for Hypoxic Ischaemic Encephalopathy (HIE)**

Once a call has been received from the peripheral hospital, the senior registrar or consultant will discuss with the referring GP/Paediatrician regarding the eligibility and feasibility of cooling the neonate. Once a decision is made to cool the infant, the referring physician will commence cooling using appropriate equipment.

In addition to cooling, the rest of the management is routine and in accordance with the transport protocol.

**Equipment Esky Contents**

- Four cold packs at fridge temp and two frozen cold packs.
- Disposable rectal temperature probe (Mallinckrodt Mon-A-Therm, size 9Fr).
- Cable to connect temperature probe to Propaq monitor.
- Cotton covers for cold packs (always put cold packs in cotton covers).
Management

- In order to be effective, cooling should commence as soon as possible and definitely within 6 hours of birth.
- Please advise the referring physician to avoid overheating the infant and to commence cooling if they have the resources and they are able to do so.
- If the referring team is unable to commence active cooling, discuss the importance of passive cooling and aim to reach the hospital as quickly as possible to commence cooling.
- Insert 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.
- Connect the rectal temperature probe to the monitor (remove T2). Connect to full cardiopulmonary monitoring.
- Arterial line insertion is not a prerequisite for beginning cooling during transport. Insert an arterial line if the overall clinical condition necessitates the presence of a line.

Active Cooling Phase (Aim is to Achieve Target Temperature Range within 1 Hour)

- Do not dress, leave nappy unfastened.
- When rectal temp < 33.0°C, 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.
- Maintain rectal temperatures between 33.0°C and 34.0°C.
- If infant ventilated, leave ventilation humidity at normal temperature.
- Cooling should not be stopped earlier than the 72 hour period. If the attending neonatal consultant decides to stop cooling earlier the reason must be documented in the medical records.
- All other documentation/care/treatment should be as per routine care of infant requiring transport. Advise/reassure parents re: appearance, cool to touch.

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Caution: watch temperature range more closely in infants treated with anticonvulsants or muscle relaxants as they may cool much quicker.
Guideline for Systemic Cooling for Hypoxic Ischaemic Encephalopathy (HIE) for referring hospitals

Dear Doctor/Nurse/Midwife

This guideline is intended for cooling asphyxiated neonates, > 35 weeks gestation at birth, with HIE who are waiting to be transported to Perth Children’s or King Edward Memorial Hospitals for ongoing management. Cooling is not advisable for preterm neonates. All neonates who need cooling should be transported to the neonatal intensive care unit. Do not attempt to manage these sick neonates at your hospital. In addition to cooling, the rest of medical management is the same as any asphyxiated neonate with HIE. Please discuss with the senior registrar or neonatal consultant at Perth Children’s Hospital for overall management of these neonates.

Summary

HIE following perinatal asphyxia contributes significantly to neonatal mortality and morbidity including long-term neurodevelopmental sequelae in up to 25%-60% of survivors. Evidence from high quality studies indicates that cooling of neonates with moderate to severe HIE is safe and reduces the risk of death or disability at 18 to 22 months of age.

If you think, the neonate you are caring for meets all or some of the criteria for cooling, please discuss with the neonatologist or senior registrar on call at PCH.

Essential - The following four inclusion criteria should be met to be eligible for cooling:

1. 35 weeks gestational age (Exclusion criteria < 35 weeks gestation).
2. < 6 hours post birth.
3. Evidence of asphyxia as defined by the presence of at least two of the following four criteria:
   - Apgar <6 at 10 minutes or continued need for resuscitation with positive pressure ventilation +/- chest compressions at 10 minutes.
   - Any acute perinatal event that may result in HIE (i.e. abruption of placenta, cord prolapse, severe FHR abnormality etc.).
   - 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. The presence of moderate/severe HIE is defined as seizures OR presence of signs in at least three of the six categories given below:

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If a neonate meets eligibility criteria 1, 3, and 4 but is 6-12 hours of age, delayed initiation of cooling may be considered at the discretion of the attending neonatologist at PCH.

**Management**

- If the decision is made to initiate cooling at your institution after consultation with the NETS WA Team and prior to the arrival of the NETS Team, cooling should commence as soon as possible and within 6 hours of birth.
- Give the information sheet to parents and discuss with them the benefits of cooling.
- Nurse the infant on a radiant warmer with warmer off, do not nurse in incubator (=PASSIVE cooling). Many asphyxiated babies have poor temperature control, and overheating the baby may worsen existing brain damage. Thus, pay particular attention to avoid body temperature > 36.5°Celsius.
- Do not nurse on a sheepskin.
- Do not dress (=PASSIVE cooling).
- Leave nappy unfastened.
- Full cardiopulmonary monitoring.
- If staffing and resources for monitoring and management are sufficient and if retrieval by the NETS team will be more than 6 hours following birth, continue passive COOLING and initiate ACTIVE cooling as per algorithm, if the axillary temperature after 1 hour of passive cooling is still > 35.0°C.
- Use cold packs from the fridge, never frozen.
- Always put cold packs in cotton bags or wrap in a cotton cover or Chux.

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- Monitor axillary temperatures every 15 minutes.
- WATCH TEMPERATURE CLOSELY. If axillary temp drops to < 33, set radiant warmer on manual and gradually adjust heater output to maintain axillary temp at 33.0-34.0. Turn off the heater once temperature reaches 33.5.
- Aim is to achieve target temperature range within 1 hour but more importantly continue to manage airway, breathing, circulation.
- If ventilated, leave ventilation humidity at normal temperature.
- All other documentation/care/treatment should be the same as in any asphyxiated infant waiting for transport to PCH/KEMH.
- Advise/reassure parents re: appearance, cool to touch.
- Transfer them at the earliest to PCH/KEMH.
- The transport team will bring all the necessary equipment to continue the cooling process during transport.
- For further information on cooling please see the entire protocol.
References