

THERAPEUTIC HYPOTHERMIA IN THE NEWBORN

PRACTICE GUIDELINE[®]

DOCUMENT SUMMARY/KEY POINTS

Induced hypothermia reduces the secondary neuronal loss that follows asphyxia-related primary neuronal loss in the experimental animal. There is now sufficient evidence that early therapeutic 'cooling' of the newborn infant with moderate/severe Hypoxic Ischaemic Encephalopathy [HIE] results in a modest reduction in HIE-related death and long-term moderate-severe disability.

Key performance Indicators

- Skin integrity over cool pack sites is checked every 60 minutes and skin integrity is maintained
- Active cooling is commenced if the rectal temperature is not $<35.0^{\circ}\text{C}$ after 30 minutes of passive cooling.
- Active cooling is reduced if the rectal temperature is $<34.5^{\circ}\text{C}$.
- Active cooling is ceased if the rectal temperature is $<34.0^{\circ}\text{C}$

CHANGE SUMMARY

- N/A – new SCHN guideline.
- Replaces GCNC Whole Body Cooling Guideline – CHW.
- **Note:** the SCH CICU guideline "[Surface Cooling and Therapeutic Hypothermia](#)" does not cover the management of neonates with hypoxic ischaemic encephalopathy [HIE].

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1 st February 2016	Review Period: 3 years
Team Leader:	Staff Specialist, Neonatology	Area/Dept: GCNC and NETS

READ ACKNOWLEDGEMENT

- Staff caring for the neonatal HIE patients are to read and acknowledge they understand the contents of this document.

TABLE OF CONTENTS

Indications for Therapeutic Hypothermia (TH)	3
Relative contraindications to Therapeutic Hypothermia	4
Procedure for Therapeutic Hypothermia	4
<i>When should cooling be commenced?</i>	4
<i>Target temperature</i>	4
<i>Equipment and monitoring</i>	4
Cool-Pak cooling	4
Passive cooling	4
Active cooling	5
<i>Step summary</i>	5
<i>Caveat</i>	5
Duration of Therapeutic Hypothermia	5
Rewarming	5
Tolerance to Therapeutic Hypothermia	6
Monitoring.....	6
Neurodevelopmental follow up	6
References	7

Background

Moderate/severe Hypoxic Ischaemic Encephalopathy [HIE] following perinatal asphyxia contributes significantly to neonatal mortality and morbidity including long-term neurodevelopmental sequelae in 25%-60% of survivors.

Evidence from high quality studies including systematic reviews of randomised controlled trials indicate that Therapeutic Hypothermia [TH] in neonates \geq 35 weeks gestation with **moderate** to **severe** HIE is safe and reduces the risk of death or disability at 18 to 22 months of age. There is no evidence to support cooling of infants with mild HIE or safety in those born before 35 weeks gestation.

Indications for Therapeutic Hypothermia (TH)

Note: Informed procedure-specific parental consent is required before therapeutic hypothermia can be instituted.

All of the following four criteria must be met:

1. More than or equal to 35 weeks gestational age.
2. Less than 6 hours post birth.
3. Evidence of asphyxia as defined by the presence of at least two of the following:
 - a) Apgar less than 6 at 10 min or continued need for resuscitation with positive pressure ventilation +/- chest compressions at 10 mins.
 - b) Any acute perinatal event that may result in HIE (i.e. abruptio placentae, cord prolapse, severe FHR abnormality etc).
 - c) Cord pH less than 7.0 or base excess of -12mmol/L or less.
 - d) If cord pH is not available, arterial pH less than 7.0 or BE less than -12mmol/L within 60 mins of birth.
4. The presence of moderate/severe HIE; defined as seizures OR presence of signs in at least three of the six categories given below:

Category	Moderate encephalopathy	Severe encephalopathy
Level of consciousness	Lethargy	Stupor/coma
Spontaneous activity	Decreased activity	No activity
Posture	arms flexed, legs extended (decorticate)	arms and legs extended (decerebrate)
Tone	Hypotonia	Flaccid
Primitive reflexes	Weak suck, incomplete Moro	Absent suck, absent Moro
Autonomic system. Any one of: <i>Pupils</i> <i>Heart rate</i> <i>Respirations</i>	Constricted Bradycardia Periodic breathing	Dilated/non - reactive Variable heart rate Apnoea

Relative contraindications to Therapeutic Hypothermia

1. More than 6 hours of birth
2. Oxygen requirement greater than 80%
3. Major congenital abnormalities
4. Severe clinical coagulopathy - low platelet count or clinical evidence of abnormal clotting and/or clotting studies which has not responded to appropriate therapy.
5. Baby unlikely to survive.

Procedure for Therapeutic Hypothermia

When should cooling be commenced?

- For eligible neonates, hypothermia should be started within 6 hours of birth.

Target temperature

- The aim is to maintain the rectal temperature at $33.5 \pm 0.5^{\circ}\text{C}$.

Equipment and monitoring

- The infant should be nursed under a servocontrolled radiant warmer.
- The infant should have venous and arterial cannulas or catheters.
- Infants receive routine clinical care, including the monitoring of vital signs and surveillance for organ dysfunction.

Cool-Pak cooling

- The aim is to achieve a rectal temperature of $33.5 \pm 0.5^{\circ}\text{C}$ ($33.0\text{--}34.0^{\circ}\text{C}$) within 60 minutes using passive cooling and, if necessary, active cooling.
- The infant's rectal temperature is measured 5 cm from the anal verge.

Passive cooling

- Switch off radiant heater and gel mattress heating.
- Nurse the baby completely naked.
- Institute active cooling if the rectal temperature is not less than 35.0°C within 30 minutes.

Active cooling

Wrap the 'Cool Paks', which are stored in the refrigerator (NEVER the freezer), with a cotton cover or Rediwipe and place 'Cool Paks' **(1)** under the shoulders/upper back, **(2)** under the head and/or **(3)** across the chest/body. The 'Cool Paks' should be 'refreshed' every 1–2 hours.

Active cooling should be reduced by removing one or more 'Cool Paks' when the rectal temperature is less than 34.5°C and stopped when the temperature is less than 34.0°C.

If the rectal temperature is below 33.5°C, the overhead radiant warmer should be set at the lowest temperature required to maintain the rectal temperature at 33.5 ± 0.5°C.

Step summary

- Commence active cooling if the rectal temperature is not less than 35.0°C after 30 minutes of passive cooling.
- Reduce active cooling if the rectal temperature is less than 34.5°C.
- Cease active cooling if the rectal temperature is less than 34.0°C
- Turn on the overhead heater if the rectal temperature is less than 33.0°C.

Caveat

- Consider reducing the rate of active cooling if the oxygen requirement increases by more than 20% or if the infant is being treated with anticonvulsants or muscle relaxants.

Duration of Therapeutic Hypothermia

- Therapeutic Hypothermia is usually continued for 72 hours.
- Therapeutic Hypothermia may be ceased earlier under the following circumstances:
 - Persistent hypoxaemia (PaO₂ <50 mmHg or SaO₂ <85%).
 - Persistent coagulopathy despite corrective treatment.
 - Cardiac arrhythmia requiring drug treatment.
 - Severe encephalopathy and a joint parental and medical decision to forego life sustaining treatment. Note the baby should be rewarmed prior to cessation of life sustaining treatment.

Rewarming

- The infant should be rewarmed slowly over approximately 12 hours. Hyperthermia should be strictly avoided.
- Apply the abdominal wall skin probe and turn on the radiant warmer with the servocontrol set to 34.5°C. Turn on the gel mattress.
- Increase the set temperature by 0.5°C every 2 hours until it is set at 36.2–36.5°C and the rectal temperature is 37.0°C.
- The abdominal wall skin temperature should be measured continuously. The axillary temperature should be measured one hourly when the rectal temperature approaches 37.0°C.

- The standard nursery practice for measuring, controlling and maintaining body temperature should be reinstated once the infant has been rewarmed.

Tolerance to Therapeutic Hypothermia

In general, infants tolerate Therapeutic Hypothermia without serious adverse consequences. If analgesia sedation is being used during mechanical ventilation, the morphine infusion rate should be set at 10micrograms/kg/hr because morphine excretion is delayed in hypothermic infants. Phenobarbitone may be preferred as a sedative.

Monitoring

- The infant's rectal and abdominal wall skin temperatures are monitored continuously and recorded every 15 minutes for the first 4 hours and then every hour during the remaining period of cooling. The axillary temperature should be measured and recorded every 4 hours throughout the cooling period.
- Check the condition of the infant's skin in contact with the Cool-Paks every 60 minutes.
- Arterial blood gas and acid base status (including glucose, lactate and ionised calcium) should be measured 4 hourly for the first 24 hours and then 8 hourly for 3–5 days.
- Serum electrolytes should be measured 8 hourly for the first 24 hours and then 12–24 hourly for 3–5 days.
- Full blood count should be measured 8 hourly for the first 24 hours and then 12–24 hourly for 3–5 days
- Coagulation studies (INR and APPT) should be measured daily for 3–5 days.
- Liver function tests should be measured 48 hourly for 2–4 days.
- The amplitude integrated EEG (aEEG) must be recorded continuously in all the infants undergoing Therapeutic Hypothermia. If the aEEG becomes normal and the infant is no longer as encephalopathic by 6 hours of age, the need for continuing Therapeutic Hypothermia can be reconsidered. Apparent improvement of the aEEG alone after 6 hours of age is not an indication for discontinuing Therapeutic Hypothermia. Subsequent brain MRI and standard EEG are recommended.
- Serum phenobarbitone levels should be monitored in infants treated with this drug.

Neurodevelopmental follow up

Surviving infants should be enrolled in the SCH or the Grace Developmental Follow up Clinic for ongoing assessment of their mental and psychomotor development.

References

1. Barks, J. D. E. (2008). Current controversies in hypothermic neuroprotection. *Seminars In Fetal & Neonatal Medicine*, 13, 30-34.
2. Gunn, A. J., Wyatt, J. S., Whitelaw, A., Barks, J., Azzopardi, D., Ballard, R., et al. (2008). Therapeutic hypothermia changes the prognostic value of clinical evaluation of neonatal encephalopathy. *Journal of Pediatrics*, 152, 55-58.
3. Jacobs, S., Hunt, R., Tarnow-Mordi, W., Inder, T., & Davis, P. (2007). Cooling for newborns with hypoxic ischaemic encephalopathy. [update of Cochrane Database Syst Rev. 2003;(4):CD003311; PMID: 14583966]. *Cochrane Database of Systematic Reviews*, CD003311.
4. Perlman, M., & Shah, P. (2008). Time to adopt cooling for neonatal hypoxic-ischemic encephalopathy: response to a previous commentary. [comment]. *Pediatrics*, 121, 616-618.
5. Schulzke, S. M., Rao, S., & Patole, S. K. (2007). A systematic review of cooling for neuroprotection in neonates with hypoxic ischemic encephalopathy - are we there yet? *BMC Pediatrics*, 7, 30.
6. Shah, P. S., Ohlsson, A., & Perlman, M. (2007). Hypothermia to treat neonatal hypoxic ischemic encephalopathy: systematic review. *Archives of Pediatrics & Adolescent Medicine*, 161, 951-958.
7. NSW Health Policy Directive PD2010_0006 Whole Body Cooling - Neonates - Suspected Moderate or Severe Hypoxic Ischaemic Encephalopathy (HIE):
http://www0.health.nsw.gov.au/policies/pd/2010/pdf/PD2010_006.pdf (accessed 25/01/2016)

Copyright notice and disclaimer:

The use of this document outside Sydney Children's Hospitals Network (SCHN), or its reproduction in whole or in part, is subject to acknowledgement that it is the property of SCHN. SCHN has done everything practicable to make this document accurate, up-to-date and in accordance with accepted legislation and standards at the date of publication. SCHN is not responsible for consequences arising from the use of this document outside SCHN. A current version of this document is only available electronically from the Hospitals. If this document is printed, it is only valid to the date of printing.