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COOLING FOR NEONATAL HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE) - GUIDELINE

P&N-1-0014

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Background

The Cochrane Library systematic review '[Cooling for newborns with hypoxic ischaemic encephalopathy' \(HIE\)](#)¹ includes eight randomised controlled trials, comprising 638 term infants with moderate or severe encephalopathy and evidence of intrapartum asphyxia.

Therapeutic hypothermia (cooling) resulted in a statistically significant and clinically important reduction in the combined outcome of mortality or major neurodevelopmental disability to 18 months of age with a relative risk reduction of 24%, absolute risk reduction of 15%, and number needed to treat (NNT) of 7. Cooling also resulted in statistically significant reductions in mortality and in neurodevelopmental disability in survivors.

Adverse effects of hypothermia can include:

- sinus bradycardia;
- borderline increase in the need for inotrope support, and
- increase in the incidence of thrombocytopaenia (platelet count below $150 \times 10^9/L$).

There was no significant increase in major adverse effects from cooling in these trials.

The Cochrane review¹ concluded that ***therapeutic hypothermia is beneficial to term newborns with HIE. Cooling reduces mortality without increasing major disability in survivors. The benefits of cooling on survival and neurodevelopment outweigh the short-term adverse effects.***

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Objective(s)

To treat term and near-term infants with **moderate or severe HIE** with **whole body therapeutic hypothermia**, according to the protocol as used in the ICE (Infant Cooling Evaluation) trial.

Equipment

1. Radiant warmer
2. Rectal thermistor (temperature probe)
 - Vital Temp™ General Purpose Probe, 9 FR, Vital Signs Colorado, Inc. (disposable /single use)
3. Cable to connect rectal thermistor to temperature module (e.g. to Blanketrol III, or to monitor (e.g. to Propaq for NETS transports) as appropriate)
4. Lubricant
5. Slick tape
6. Cold gel packs (6) **at refrigerator temperature (NEVER from the freezer).**
7. Disposable covers for cold packs
8. Blanketrol III with infant cooling mat (for cooling at the RHH NPICU)
9. Small 'cool box' ('Esky') with frozen 'ice brick' for transport of cold gel packs (i.e. for NETS transfers).

Indications

CRITERIA FOR THERAPEUTIC COOLING

1. Gestational age greater than or equal to 35 weeks
2. Less than 6 hours of age
3. Moderate or severe HIE:

Sign	Moderate HIE	Severe HIE
Consciousness	Lethargic	Comatose/ obtunded
Activity	Decreased	Absent

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Posture	Distal flexion	Decerebrate (complete extension)
Tone	Hypotonic	Flaccid
Primitive reflexes	Weak suck, gag & Moro	Absent suck, gag & Moro
Pupils	Constricted	Deviated, dilated, non-reactive
Heart rate	Bradycardia	Variable
Respiration	Periodic	Apnoeic

4. Evidence of peripartum hypoxia-ischaemia, **at least 2 of:**

- a. Apgar score of 5 or less at 10 minutes
and / or
- b. Mechanical ventilation (bag / Neopuff via mask or ETT) **or** need for resuscitation at 10 minutes
and / or
- c. Cord pH less than 7.0 **or** blood gas pH less than 7.0 **or** base deficit greater than or equal to 12 within 1 hour of birth

Contraindications to therapeutic cooling

- a. Cooling cannot be initiated within 6 hours of birth
- b. Birth weight less than 2 kg
- c. Oxygen requirement greater than 80%
- d. Major congenital abnormalities
- e. Severe clinical coagulopathy
- f. Death appears inevitable

Imperforate anus is not an absolute contraindication as placement of an oesophageal thermistor may be considered.

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When to initiate cooling in NPICU

1. **Inborn** infants at RHH: Do not actively re-warm ventilated near-term infants with moderate/severe HIE when admitted to NPICU
 - a. If ineligible for therapeutic cooling when all criteria are determined, then warm according to normal procedure.
 - b. If there is rapid improvement in the neurological status such that the infant is no longer encephalopathic, discuss discontinuation of cooling with the on-call NPICU Consultant.
 - c. If the infant does not meet all of the criteria (e.g. infant greater than 6 hours of age, postnatal hypoxic-ischaemic event) and therapeutic cooling is considered, discuss with the on-call NPICU Consultant before initiating cooling.
2. **Outborn** infants transported by NETS: continue therapeutic cooling in NPICU if commenced by NETS during transport.

Procedure for therapeutic cooling

- Admit to NPICU.
- Nurse infant on a **radiant warmer** bed (whether ventilated or not).
- Nurse infant naked:
 - No nappy or wraps.
 - No hat.
 - Do not nurse on a sheepskin, or on a water bag.
 - Do not use plastic wrap.
- If ventilated, maintain **humidifier** at usual temperature.
- Continuous invasive blood pressure monitoring by indwelling **arterial line** (preferably umbilical) for the 72 hours duration of cooling and for the 12 hours of re-warming.
 - Capillary blood acid-base may be affected by decreased peripheral perfusion during cooling.
- All arterial **blood gases analyses at 37°C** (i.e. Do not adjust for baby's actual temperature).
- Insert lubricated **Rectal Thermistor / Probe** into anus at least 5 cm and tape with sleek at the 10 cm (first) mark to the upper inner thigh.
 - It is very important that the probe is inserted at least this far to accurately measure the baby's core temperature – the probe is designed for this purpose and will not cause mucosal trauma.

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- Leave the probe in for 84 hours (72 hours cooling and 12 hours re-warming).
- The probe does not need to be removed for cleaning.
- Connect the rectal probe to its cable and Blanketrol III [see [Blanketroll III for Therapeutic Cooling](#)], or patient monitor (as appropriate).
- Set temperature alarm limits at 33°C (low) and 34°C (high) during the 72 hour cooling period.
- Documentation (nursing):
 - Maintain a separate **Seizure** chart.
 - Record **rectal temperature** hourly, in addition to NPICU routine.
 - If in use, record the number of cold packs required hourly
 - All other documentation as per routine.
- Documentation (medical):
 - Clearly document the clinical history (including the antenatal history, labour, delivery, and resuscitation details) and the degree of encephalopathy (see [Appendix 1](#)).
 - **Rectal temperature to be maintained at 33 to 34°C for 72 hours**
 - Duration of cooling (72 hours) and re-warming (12 hours) as detailed in [Appendix 2](#).
- Unless specified, medical and nursing care are as usual (e.g. fluid management, anticonvulsants, blood gases and blood glucose levels)
- Guideline for investigations / assessment in cooled infants (suggested):

?Test	Admission	Day 1	Day 2	Day 3	Day 4 - 7
ABG	✓	✓	✓	✓	
Lactate	✓	✓	✓		
FBE	✓	✓	✓	✓	
PT, PTT	✓	✓	✓	±	
Glucose	✓	✓	✓	✓	
LFTs	✓	✓	✓		
UEC, Ca, Mg	✓	✓	✓	✓	
ECG		✓	±		
Echocardiogram	±	±	±	±	±
aEEG (i.e. BRAINZ monitoring)	✓	✓	✓	✓	(✓)
Conventional EEG					✓
Sarnat Stage	✓	✓	✓	✓	
Cranial U/S		✓			
MRI					✓

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INITIATION OF THERAPEUTIC COOLING WITH COLD PACKS

- **Initiation of cooling:**
 - Turn radiant warmer OFF and expose the infant to normal ambient temperature (**passive cooling**).
- **Active cooling:** If rectal temperature **more than 35.5°C**, place 2 cold packs:
 - 1st pack: under the shoulders/ upper back/ head.
 - 2nd pack: across the chest/body.
- **Adjustment and maintenance of cooling:**
 - When the rectal temperature falls **below 34.5°C**, reduce active cooling by removing one cold pack.
 - When the rectal temperature **below 34°C**, stop active cooling by removing all cold packs.
 - If the rectal temperature falls **below 33.5°C**, set radiant warmer on manual and gradually adjust heater output to maintain rectal temperature 33.0 to 34.0°C.
 - If the rectal temperature reaches **34°C and the radiant warmer is off**, recommence active cooling with one or two cold packs as required.

INITIATION OF COOLING WITH THE BLANKETROL III

[please see [Blanketroll III for Therapeutic Cooling](#)]

- **Initiation of cooling:**
 - Turn the radiant warmer OFF and expose the infant to normal ambient temperature.
 - Place the infant on the infant cooling blanket and ensure proper connection of the blanket to the Blanketrol III unit.
 - Insert the rectal thermistor as detailed above and connect to the Blanketrol III with the appropriate cable.
 - Initiate cooling with the Blanketrol III according to the [Blanketroll III for Therapeutic Cooling](#), setting the desired patient core temperature to 33.5 °C (set point).

OTHER COOLING MANAGEMENT ISSUES

- Cooling requirements may decrease and the rectal temperature may fall with treatments that reduce the metabolic rate:
 - Anticonvulsants.
 - Sedatives.
 - muscle relaxants.

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- If the infant appears **uncomfortable**, consider morphine and/or midazolam (if ventilated) or paracetamol (PR administration is allowed when nil orally, even with a rectal thermistor in-situ, and even if not all of the dose is retained in the rectum).
 - Irritability is common and is often related to HIE
 - Shivering, like tremors, are common in infants with milder encephalopathy
- **Stop cooling** following discussion with Consultant if there is any one of these:
 - Worsening or severe persistent pulmonary hypertension of the newborn (PPHN)
 - Severe coagulopathy
 - Arrhythmia requiring medical treatment (not sinus bradycardia)
 - Decision made to withdraw life-support as determined by and at the discretion of the attending NPICU Consultant with the family.

RE-WARMING

After 72 hours cooling using cold packs

- Cease cooling with the cold packs.
- Apply skin temperature probe and turn the radiant warmer on with the servo set at 34.5 °C.
- Increase the set temperature by **0.5 °C every 2 hours** until set at ~36.5 °C and rectal temperature is ~37 °C.
- Re-warming will take 6 to 12 hours.
- Continue rectal temperature monitoring for 12 hours after re-warming is commenced.
- Remove rectal thermistor (temperature probe) and discard.
- **DO NOT** discard the rectal thermistor adaptor cable.

After 72 hours cooling using the Blanketrol III (preferred)

- After 72 hours the temperature should be allowed to rise.
- The rate of rise should be approximately 0.5 °C every 3 hours (i.e. increase the set point on the Blanketrol III by 0.5 °C every 3 hours) and no faster than 0.5°C every 2 hours.
- Re-warming with the Blanketrol III is best achieved using the Gradient 10C mode or the Gradient variable mode.
- Re-warming will take 6 to 12 hours.
- Continue rectal temperature monitoring for 12 hours after re-warming is commenced.
- Remove rectal thermistor (temperature probe) and discard
- **DO NOT** discard the rectal thermistor adaptor cable.

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NETS Transfer Issues

THERAPEUTIC COOLING FOR OUTBORN INFANTS

1. The baby must satisfy the above clinical criteria for therapeutic cooling (see [Indications](#) above).
2. It is not recommended that therapeutic cooling be initiated until the NETS transport team have assessed the baby and discussed the baby with the on-call RHH NPICU Consultant. It is expected that, during the initial triage call, the RHH NPICU Consultant will raise the possibility of cooling and discuss it with the referring doctor. There may be specific circumstances, in discussion with the on-call RHH NPICU Consultant, when cooling can be commenced before the NETS team arrives.
3. It is critical to ensure that for these very sick babies emphasis is placed on addressing the main principles of stabilising a critically ill baby, i.e. airway, breathing, circulation, blood glucose, and so on.
4. In all cases where the baby fulfils the clinical criteria for cooling but cooling is not being commenced immediately, advice is provided about the importance of **avoiding hyperthermia** during the stabilisation period.

TRANSPORT RELATED MANAGEMENT ISSUES

Airway, Breathing, Circulation

- Ensure the airway is secure (intubation is not an absolute prerequisite for cooling), breathing is adequate and any circulatory compromise has been addressed.

Initial investigations

- Minimum investigations required before initiating cooling:
 - arterial blood gas
 - blood glucose level
- A platelet count and clotting studies should be obtained where feasible (often this may be organised before the arrival of the NETS team).

Vascular access

- It is preferable that these babies have a UAC and a dual lumen UVC sited at the referring unit. Inability to place these lines does not absolutely preclude the use of cooling.

Documentation

- Clearly document the clinical history (including the antenatal history, labour, delivery, and resuscitation details) and the degree of encephalopathy (see [Appendix 1](#)).

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INITIATION OF THERAPEUTIC COOLING AT THE REFERRAL HOSPITAL

Procedure for therapeutic cooling for a NETS transport is very similar to the [Procedure for therapeutic cooling](#) (above) with cooling initiated using cold packs. On arrival at the RHH NPICU cooling may be continued with the Blanketrol III with the infant-size cooling mat.

Specific issues relating to NETS transports include:

- The cable to the rectal thermistor must be connected to the Propaq transport monitor.
- **Initiation of cooling:**
 - Turn the radiant warmer **and the transport incubator OFF** and expose the infant to normal ambient temperature (**passive cooling**).
 - The procedure for **active cooling** using cold packs whilst on the radiant warmer at the referring hospital is as per the [Procedure for therapeutic cooling](#) above.
- **When infant is in the transport incubator:**
 - If ventilated, leave transport incubator OFF with the portholes open (when possible).
 - If not ventilated, leave the transport incubator on the lowest possible temperature, with the portholes open (when possible).
 - If the rectal temperature falls **below 33.5°C**, turn the transport incubator heater on and gradually adjust the temperature to maintain the rectal temperature between 33.0 to 34.0°C.
- If the infant is observed to be **uncomfortable**, consider morphine and/or midazolam (if ventilated) or paracetamol (PR administration is allowed when nil orally, even with a rectal thermistor in-situ, and even if not all retained in rectum).
 - Irritability is common and is often related to HIE.
 - Shivering, like tremors, are common in infants with milder encephalopathy
- **Stop** cooling following discussion with Consultant if there is:
 - Worsening or severe persistent pulmonary hypertension of the newborn (PPHN).
 - Severe coagulopathy.
 - Arrhythmia requiring medical treatment (not sinus bradycardia).

Follow-up

All surviving infants treated with therapeutic hypothermia should be referred either to the Neonatal Follow-up Clinic or to their local Paediatrician. When appropriate, consideration should be given to Paediatric Neuropsychological evaluation when at least 2 years of age.

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3. Jacobs S, Stewart M, Presbury F. Therapeutic Hypothermia for near-term Infants with moderate or severe HIE being retrieved by NETS (Clinical Guideline). NETS Victoria, 2007.
4. [UK Toby Cooling Register, Data Collection Form, v.6, July 2008](#).
5. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress: a clinical and electroencephalographics study. Arch Neurol 1976;33:696.

Acknowledgements

This guideline is based on the protocol developed by Dr Sue Jacobs and the team at the Royal Women's Hospital, Melbourne and NETS Victoria, Melbourne. The cooling protocol is based on that used in the ICE (Infant Cooling Evaluation) trial developed at the same institution.

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Related Documents

- [Blanketroll III for Therapeutic Cooling](#)

Key Words - Intranet Search Function

1. Cooling
2. Hypothermia
3. HIE
4. Asphyxia
5. Encephalopathy



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APPENDIX 1

Therapeutic cooling documentation

(Adapted from the [UK Toby Cooling Register Data Collection Form](#), the ICE trial clinical criteria for moderate to severe HIE and Sarnat et al, 1976⁵)

Clinical Details at Birth (circle where appropriate)

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Hospital of birth:	Cord blood gas: pH: pCO ₂ : pO ₂ : Base deficit:
Date of birth:	
Gestational age at birth:	
Sex: M / F	
Birth weight (g):	Worst blood gas within 60 min of life: Specify: art / ven / cap pH: pCO ₂ : pO ₂ : Base deficit:
Head circumference (cm):	
First gasp (min):	Seizures: Y / N
Resuscitation greater than 10 min (Y / N)	Encephalopathy: Y / N
Apgar score 1 min: 5 min: 10 min: 20 min:	Age when cooling commenced (hrs:mins):

Pregnancy complications (circle all that apply)

None Diabetes Illicit drug use Maternal seizure Placenta praevia

Pre-eclampsia Thyroid disorder *Other significant event

*If other please specify _____

Mode of delivery (circle one)

Pre-labour CS In labour CS SVD cephalic SVD breech

Instrumental delivery

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Delivery complications (*circle all that apply*)

None Head entrapment Placental abruption Prolapsed cord
 Ruptured uterus Shoulder dystocia *Other significant event

*If other please specify _____

Congenital abnormalities noted at birth

Please specify _____

Grade of HIE prior to cooling (*circle appropriate severity for each sign*)

Please note:

- Moderate or severe HIE are a prerequisite for consideration of therapeutic cooling.
- Seizures are a feature of at least moderate HIE.

Sign	Normal	Mild HIE	Moderate HIE	Severe HIE
Consciousness	Normal	Hyper-alert, stare, irritable	Lethargic	Comatose/ obtunded
Activity	Normal	Uninhibited, over-reactive	Decreased	Absent
Posture	Normal	Fisting, cycling	Distal flexion	Decerebrate (complete extension)
Tone	Normal	Hypertonic	Hypotonic	Flaccid
Primitive reflexes	Normal	Partial Moro	Weak suck, gag & Moro	Absent suck, gag & Moro
Pupils	Normal	Dilated	Constricted	Pupils dilated (may be mid-position and unequal), may be non-responsive or poorly reactive to light
Heart rate	Normal	Tachycardia	Bradycardia	Variable
Respiration	Normal	Hyperventilation	Periodic	Apnoeic



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APPENDIX 2

Documentation of cooling duration

Cooling started **Date** : : (e.g. 26 Dec 07)

Time : 24 hour clock (e.g. 16:30)

Re-warming to start **Date** : :

Time :

Re-warming to stop **Date** : :

Time :