

TOTAL BODY HYPOTHERMIA PROTOCOL FOR NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY (HIE) FOR TRANSPORTED PATIENTS

The following guidelines are to assist with the assessment of neonates with HIE for total body hypothermia. If deemed eligible, all neonates who receive hypothermia should be transported to a tertiary NICU. Although hypothermia may, in some circumstances, be initiated prior to the arrival of the transport team; it should only be initiated after consultation with the tertiary centre and ongoing management of these neonates should take place only in a tertiary NICU.

Evidence suggests that hypothermia in neonates with *moderate to severe* HIE reduces the severity of brain injury and leads to improved neurological outcome¹⁻⁴. There is no evidence to support hypothermia in neonates with *mild* HIE. It is important for all neonates born with perinatal distress be assessed for risk factors and carefully monitored for signs of HIE immediately after, and for the first few hours after birth. If moderate or severe HIE is suspected, the tertiary centre should be contacted as early as possible in order to assess for eligibility for hypothermia. For eligible neonates, the earlier the initiation of hypothermia, the more likely it is to be effective, and hypothermia should be initiated *within 6 hours of birth*.

1.0 INCLUSION CRITERIA

MUST HAVE ALL 4 INCLUSION CRITERIA

1. Evidence of moderate or severe encephalopathy defined as clinical seizures **OR** presence of **3 or more** of the items in the 6 categories below.

Category	Moderate Encephalopathy	Severe Encephalopathy
1. Level of consciousness	Lethargic	Stupor or coma
2. Spontaneous activity	Decreased activity	No activity
3. Posture	Distal flexion, truncal extension	Decerebrate (arms extended and internally rotated, legs extended with feet in forced plantar flexion)
4. Tone	Hypotonia (focal or general)	Flaccid
5. Primitive reflexes		
Suck	Weak	Absent
Moro	Incomplete	Absent
6. Autonomic system		
Pupils	Constricted	Dilated or non-reactive to light
Gaze		Skew deviation
Heart rate	Bradycardia	Variable HR
Respirations	Periodic breathing	Apnea

***A neurological examination must be performed by skilled personnel to determine the degree of encephalopathy.**

2. Neonate \geq 35 weeks gestational age
3. Less than 6 hours post delivery
4. Evidence of intrapartum hypoxia

EITHER Cord or postnatal blood gas within one hour of birth with $\text{pH} \leq 7.00$, OR base deficit ≥ 16

OR If $\text{pH} 7.01-7.15$ or $\text{BD} -10$ to -15.9 OR no blood gas available:

Evidence of acute perinatal event that may result in HIE (e.g. abruptio placentiae, cord accident, uterine rupture, maternal trauma or cardiorespiratory arrest, late or variable decelerations etc.) **AND** one of the following: Apgar score 5 or less at 10 minutes, need for mechanical ventilation or resuscitation at 10 minutes

2.0 EXCLUSION CRITERIA

1. Neonate < 1.8 kg
2. Clinically significant coagulopathy despite treatment
3. Moribund neonates, or neonates with major congenital or genetic abnormalities, in whom no further aggressive treatment is planned

In the presence of severe encephalopathy where the risk of death or adverse neurodevelopmental outcome is assessed to be high, the responsible physician(s) may choose to not offer hypothermia treatment if the plan is to not pursue aggressive treatment.

Note however, that initiation of hypothermia does not preclude a decision to withdraw life-sustaining therapy at a later time.

3.0 WHEN SHOULD COOLING BE COMMENCED?

Earlier initiation of hypothermia may increase the degree of neuroprotection. For eligible neonates, hypothermia should be started ***within 6 hours of birth***. The decision to start hypothermia after 6 hours of age will be at the discretion of the responsible neonatologist. There is currently no published evidence on the effects of starting hypothermia after 6 hours.

Total body hypothermia to a target core body temperature of **33.0-34.0°C** can be achieved with a cooling blanket or with cool packs. However, use of the cooling blanket is currently not feasible for the transport setting, thus cool packs are used in transport, and in NICUs where the cooling blanket is not available.

4.0 HYPOTHERMIA FOR AN ELIGIBLE PATIENT IN THE REFERRING HOSPITAL IF TRANSPORT TEAM UNABLE TO ARRIVE WITHIN 6 HOURS AFTER BIRTH

1. Ensure that the tertiary centre neonatologist is in agreement with the decision to start hypothermia treatment ***before*** talking to parents.
2. Ensure that the parent(s) are aware that the results from studies have shown improved outcome for many of these babies, but that poor outcome is still possible and that this is a new therapy where long-term outcomes beyond 2 years of age are not known. (See Parent Information Sheet)
3. Staffing and resources must be sufficient for constant monitoring and one to one nursing care until handover to the transport team.
4. The referring hospital staff should be trained in the continuous monitoring of core (rectal/esophageal) temperature in advance. Specific equipment including a rectal/esophageal probe and a special module used to connect the probe to the monitor are required.

If the rectal/esophageal probe is not available, rectal thermometers may be used with extreme caution. Monitor rectal temperatures every 15 minutes and aim for a target temperature of 34°C.

5. Ask your tertiary centre for the detailed hypothermia protocol to be faxed to you.

REFERENCES

1. Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD, Ferriero DM, Polin RA, Robertson CM, Thoresen M, Whitelaw A, Gunn AJ. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. *Lancet* 2005;365(9460):663-670.
2. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, Fanaroff AA, Poole WK, Wright LL, Higgins RD, Finan NN, Carlo WA, Duara S, Oh W, Cotten CM, Stevenson DK, Stoll BJ, Lemons AJ, Guillet R, Jobe AH. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med* 2005;353:1574-1584.
3. Azzopardi DV, Strohm B, Edwards AD, Dyet L, Halliday HL, Juszczak E, Kapellou O, Levene M, Marlow N, Porter E, Thoresen M, Whitelaw A, Brocklehurst P; TOBY Study Group. Moderate hypothermia to treat perinatal asphyxial encephalopathy. *N Engl J Med*. 2009 Oct 1;361(14):1349-58.
4. Jacobs S, Hunt R, Tarnow-Mordi W, Inder T, Davis P. Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane Database Syst Rev* 2007;(4):CD003311.
5. Simbruner G, Mittal RA, Rohlmann F, Mucic R; neo.nEURO.network Trial Participants. Systemic hypothermia after neonatal encephalopathy: outcomes of neo.nEURO.network RCT. *Pediatrics*. 2010 Oct;126(4):e771-8.
6. Jacobs SE, Morley CJ, Inder TE, Stewart MJ, Smith KR, McNamara PJ, Wright IM, Kirpalani HM, Darlow BA, Doyle LW; Infant Cooling Evaluation Collaboration. Whole-body hypothermia for term and near-term newborns with hypoxic-ischemic encephalopathy: a randomized controlled trial. *Arch Pediatr Adolesc Med* 2011;Aug;165(8):692-700.
7. Shah PS, Ohlsson A, Perlman M. Hypothermia to treat neonatal hypoxic ischemic encephalopathy: a systematic review. *Arch Pediatr Adolesc Med* 2007;161:951-958.
8. Sahni R, Sanocka UM. Hypothermia for hypoxic-ischemic encephalopathy. *Clin Perinatol* 2008;35(4):717-34.
9. Thoresen M. Supportive care during neuroprotective hypothermia in the term newborn: adverse effects and their prevention. *Clin Perinatol* 2008;35(4):749-763
10. Barks JD. Technical aspects of starting a neonatal cooling program. *Clin Perinatol* 2008;35(4):765-775
11. Schulzke SM, Rao S, Patole SK. A systematic review of cooling for neuroprotection in neonates with hypoxic ischemic encephalopathy – are we there yet? *BMC Pediatr* 2007;7:30
12. Edwards AD, Azzopardi DV. Therapeutic hypothermia following perinatal asphyxia. *Arch Dis Child Fetal Neonatal Ed* 2006;91(2):F127-31
13. Shah PS. Hypothermia: a systematic review and meta-analysis of clinical trials. *Semin Fetal Neonatal Med* 2010 Oct;15(5):238-46.
14. Perlman JM, Wyllie J, Kattwinkel J, Atkins DL, Chameides L, Goldsmith JP, Guinsburg R, Hazinski MF, Morley C, Richmond S, Simon WM, Singhal N, Szyld E, Tamura M, Velaphi S; Neonatal Resuscitation Chapter Collaborators. Part 11: Neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2010 Oct 19;122(16 Suppl 2):S516-38.

TOTAL BODY COOLING FOR INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY - PARENT INFORMATION SHEET

Background

Your baby is showing the effects of lack of oxygen or blood supply to the brain and is at risk for brain damage. Recent studies have shown that cooling of your baby to a body temperature of 33-34°C for 72 hours *may* protect the brain and decrease the severity of brain damage. These studies have shown that outcomes may be improved for many of these cooled babies; however, for some of the cooled babies, poor outcome is still possible. This is a new therapy where long-term outcomes beyond 2 years of age are not known. Cooling is now an accepted treatment option for these babies in many centres and we would be recommending cooling for your baby.

How We Cool Babies

Your baby will be cooled to a rectal or esophageal temperature of 33-34°C by turning off the warmer, and if necessary by placing cool packs around your baby's body. Your baby will be cooled for 72 hours. During this time, you may touch and hold your baby's hand. However, you will not be able to hold the baby or have skin to skin contact. Your baby will feel cold during this period and may appear dusky, but this is a normal body response to cooling. After 72 hours, we will allow your baby's temperature to return to his/her normal temperature over a few hours by removing any cool packs and adjusting the warmer.

Are There Any Side Effects of Cooling?

Cooling is well tolerated in most babies. Cooling will cause your baby's heart to slow down. Cooling has also been associated with a decrease in the total number of platelets (cells in the blood that help clotting). However, none of these side effects have required treatment in the babies cooled so far. Your baby will be monitored closely for any side effects.

Alternatives

Although cooling is medically recommended, you have the option of refusing this treatment or to stop the treatment at any time, even if cooling has already been started. In addition, your baby's doctor may choose to discontinue cooling if there are any complications or concerns that the cooling may be harmful for your baby or will not benefit your baby.