CLINICAL PRACTICE GUIDE

Hypoxic ischaemic encephalopathy in newborns – recognition, monitoring and early management

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NSW GOVERNMENT
AGENCY FOR CLINICAL INNOVATION
The Maternity and Neonatal Network

The information in this document should not replace a clinician's professional judgement.

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At a glance

This clinical practice guide provides guidance on recognition, monitoring and early management of newborns with hypoxic ischaemic encephalopathy (HIE) who may benefit from therapeutic hypothermia (cooling). Therapeutic hypothermia has been found to be safe for term and late preterm infants (≥35 weeks gestation) with moderate or severe HIE.

Clinical management of newborns with HIE

Recognition

Use the Newborn Encephalopathy Pathway to identify encephalopathy during labour and birth, and manage appropriately

Assessment and monitoring of encephalopathy severity

Use the Encephalopathy Severity Tool to assess the severity of encephalopathy in newborns every hour in the first six hours of birth

Therapeutic hypothermia

Initiate therapeutic hypothermia for newborns who meet **all of the three** criteria:

GA ≥35 weeks and ≥1,800g and <6 hours old

AND

Evidence of severe acidosis or depression at birth, with any ONE of:

- pH <7.00 or a BE equal to or worse than –12mmol/L on any cord or newborn blood gas in first hour
- Apgar score <6 at 10 minutes
- Ongoing resuscitation (positive pressure ventilation or cardiac massage) for ≥10 minutes

AND

Presence of moderate/severe encephalopathy with any **ONE** of:

- three or more moderate or severe features of encephalopathy (Sarnat criteria) identified at any time from 1 to 6 hours of life

OR

- two moderate or severe features of encephalopathy and abnormal aEEG (e.g. aEEG lower margin <5μV for >1 hour)

OR

- Seizures (witnessed by a medical officer/nurse/midwife or seen on aEEG/EEG)

For newborns who meet two or more criteria for moderate or severe encephalopathy OR seizures at any time from one to six hours of life:

- consider therapeutic hypothermia
- request senior medical review
- seek NETS advice.

If uncertain about the need for therapeutic hypothermia, **transfer the newborn to a neonatal intensive care unit.**

Contraindications for therapeutic hypothermia

No absolute contraindications but relative contraindications include:

- uncontrolled bleeding
- uncontrolled severe hypoxia due to persistent pulmonary hypertension
- imminent end of life care planned.

Introduction

This clinical practice guide provides guidance on recognition, monitoring and early management of newborns with hypoxic ischaemic encephalopathy who may benefit from therapeutic hypothermia. The guide replaces the NSW Health Policy Directive PD2010 006: Whole Body Cooling – Neonates Suspected Moderate or Severe Hypoxic Ischaemic Encephalopathy (HIE).[1] Changes since PD2010 006 are documented in Appendix 1.

Background

Hypoxic ischaemic encephalopathy (HIE) is a type of neonatal encephalopathy caused by systemic hypoxaemia and/or reduced cerebral blood flow resulting from an acute peripartum event.[2] It can be the result of perinatal and/or neonatal asphyxia.[3] HIE is classified as mild, moderate or severe based on the Sarnat score for encephalopathy.[4]

Evidence from high-quality, multi-centred trials and meta-analysis supports that therapeutic hypothermia is safe for term and late preterm infants (≥35 weeks gestation) with moderate or severe HIE. It reduces the risk of death or disability at 18 to 22 months if commenced within six hours of birth.[5-10] In 2020, 358 (6.0%) of the Australian and New Zealand Neonatal Network (ANZNN) registrants born at more than 34 weeks gestation received therapeutic hypothermia.[11]

Intended audience

This guide is intended for clinicians in all facilities caring for newborns.

Methods

The NSW Health Hypoxic Ischaemic Encephalopathy Expert Advisory Group was established in March 2021 at the request of the Clinical Excellence Commission (CEC) and the Agency for Clinical Innovation (ACI) to standardise the definition, documentation and clinical assessment of neonates with neonatal encephalopathy, and update the NSW Health Policy Directive PD2010.006. The advisory group consisted of senior medical, nursing and midwifery clinicians with expertise in obstetrics, neonatology and paediatrics from NSW, together with observers from Victoria and the Australian Capital Territory (ACT), and was supported by executive sponsors and staff from the CEC and the ACI.

An evidence review was used to inform this update, and a report of this group was published as the NSW Consensus Statement: Newborn Hypoxic Ischaemic Encephalopathy (HIE).[12]

General principles of management of newborns at risk of HIE

Identify all newborns at risk of HIE at birth and undertake ongoing monitoring

- Identify all newborns at risk of HIE at birth and commence monitoring using the Newborn Encephalopathy Pathway and Assessment of Encephalopathy Severity Tool.

Prioritise resuscitation and stabilisation before commencing therapeutic hypothermia

- Identify acute peripartum events for HIE (refer to Box 1).[13]
- Ensure appropriate resuscitation and stabilisation of the newborn, paying close attention to airway, breathing, circulation and glucose levels before considering therapeutic cooling.[14]
- Always avoid hyperthermia. A core temperature of >37.5C increases the risk of death and disability.[15]
- Prioritise attention to basic pathophysiology supports for all newborns who are at risk of HIE, including any cardio-respiratory and fluids and glucose needs.[7, 16] Exercise caution with fluid boluses.[17, 18]
- Therapeutic hypothermia is an adjunct therapy and must only be considered after initial resuscitation and stabilisation.[1]
- The ability to provide therapeutic hypothermia should not influence decisions about cessation of resuscitation attempts at birth.[19]

Do not commence therapeutic hypothermia without a Newborn and Paediatric Emergency Transport Service consultation

- Initiate early discussion with a neonatologist or Newborn and Paediatric Emergency Transport Service (NETS) for all newborns who meet two or more criteria of moderate or severe encephalopathy or seizures at any time from one to six hours of birth (see Criteria for Therapeutic Hypothermia).
- Therapeutic hypothermia must **not** be commenced without discussion with NETS and a tertiary centre neonatologist.
- All newborns for whom therapeutic hypothermia is commenced should be transferred to a neonatal intensive care unit (NICU) for continuing management.[20]
- If the need for therapeutic hypothermia is uncertain (e.g. if the newborn has two, but not three, features of moderate or severe encephalopathy), it may also be appropriate to transfer the newborn to a NICU for further assessment, including electroencephalogram (EEG) or amplitude integrated EEG (aEEG) monitoring.

Clinical management

Recognition: The Newborn Encephalopathy Pathway

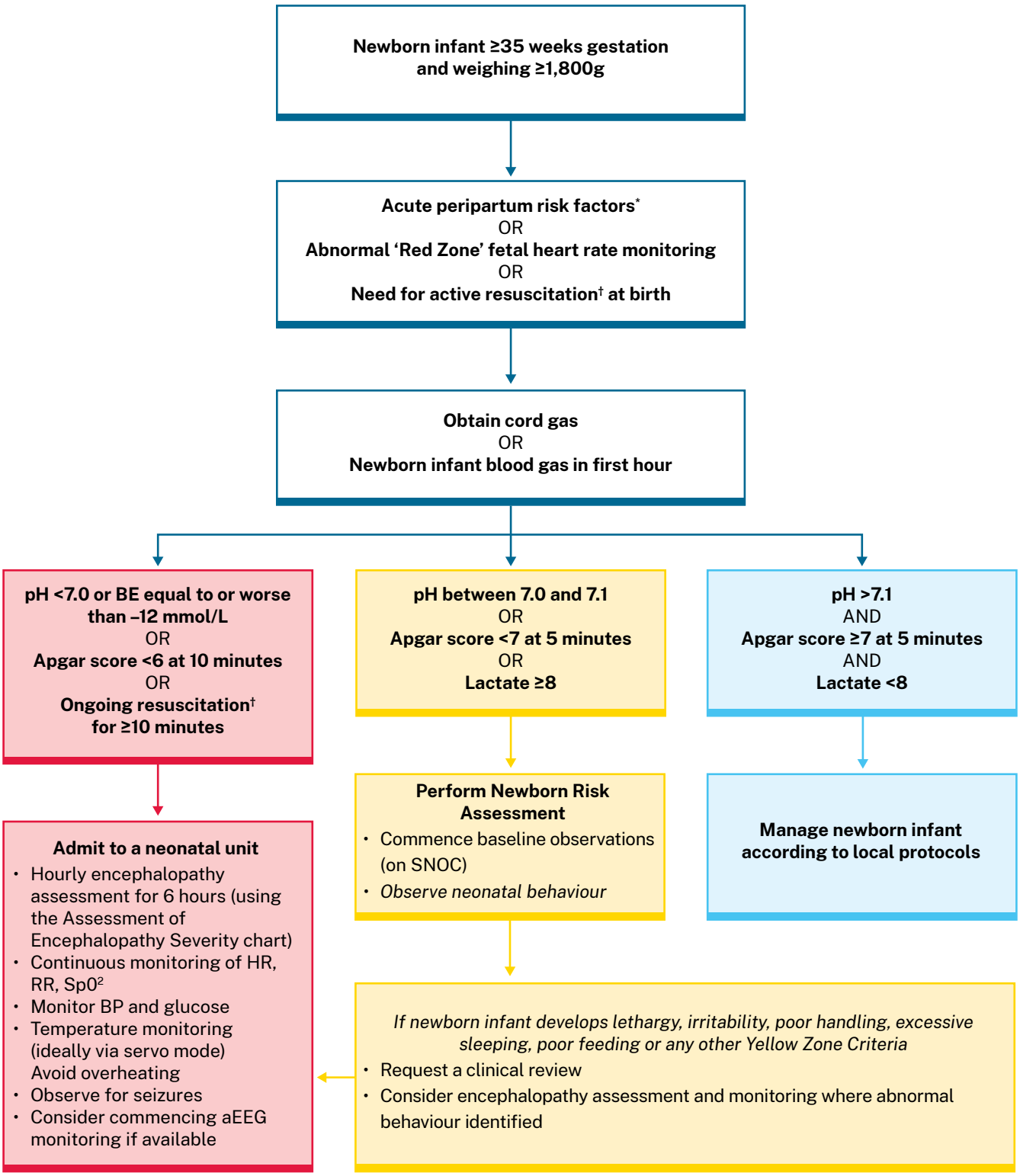
- Acute peripartum events (see Box 1) for encephalopathy should be identified during labour and birth[21] and managed appropriately.[22]

Box 1: Examples of acute peripartum events

- Uterine rupture
- Placental abruption
- Cord prolapse
- Maternal collapse
- Fetal exsanguination, e.g. with vasa praevia
- Amniotic fluid embolism
- Severe maternal hypotension
- Prolonged labour with transverse arrest
- Prolonged shoulder dystocia
- Difficult instrumental delivery

- For newborns with acute peripartum risk factors, abnormal 'Red Zone' fetal heart monitoring or active resuscitation at birth, perform
  - paired cord blood gases or
  - a neonatal blood gas in the first hour of life (where paired cord gases are unable to be collected).
- Follow the Newborn Encephalopathy Pathway (Figure 1) for all newborns with any of the following:
  - pH <7.1mmHg
  - Base Excess (BE) equal to or worse than -12mmol/L
  - Apgar score <7 at 5 minutes
  - Lactate ≥8mmol/L
  - Ongoing resuscitation for ≥10 minutes.
- The Newborn Encephalopathy Pathway may also be used to monitor and assess newborns who experience a sudden unexpected postnatal collapse (SUPC) in the birthing unit or post-natal environment.[23]

Figure 1: Newborn Encephalopathy Pathway



*Examples of acute peripartum risk factors include uterine rupture, placental abruption, cord prolapse, fetal exsanguination from vasa praevia, shoulder dystocia, maternal collapse.

†Resuscitation defined as need for: **positive pressure ventilation** OR **cardiac massage** (excludes known surgical infants requiring planned intubation).

Assessment and monitoring

Monitor airways, breathing, circulation, glucose and temperature

- Admit to neonatal unit for close observation and encephalopathy, monitoring:
  - all 'Red Pathway' newborns
  - 'Yellow Pathway' newborns if concerned about lethargy, irritability, poor feeding, etc.

  (See Newborn Encephalopathy Pathway for Red Pathway and Yellow Pathway criteria.)
- Assess airway, breathing, circulation and glucose
- Monitor respiratory rate, oxygen saturation, heart rate, temperature, blood pressure and glucose
- Monitor blood gases as required for clinical condition
- Monitor temperature hourly. Increase frequency if indicated by clinical condition
- Target:
  - Oxygen saturation: 91%–95%, when receiving supplemental oxygen
  - Partial pressure of carbon dioxide (PaCO2): 35–45mmHg for mechanically ventilated patients
  - Mean blood pressure: 40-50mmHg (consider inotropes for low blood pressure)
  - Blood glucose: 3–7mmol/L
  - Temperature: 36.5°C to 37.0°C (unless therapeutic hypothermia has commenced).
- Always avoid hyperthermia, as temperature >37.5°C increases the risk of morbidity and mortality.

Note: Blood glucose and temperature targets differ from the Standard Neonatal Observation Chart (SNOC) targets due to greater vulnerability of this cohort. Altered SNOC calling criteria may be required.

Assess newborns at high risk of encephalopathy using the Assessment of Encephalopathy Severity tool every hour in the first six hours of birth

- The level of encephalopathy cannot be accurately assessed during resuscitation or while a newborn is either critically hypoxic or hypotensive. Encephalopathy should be assessed as soon as possible after the newborn has stabilised.
- Hourly neurological assessment from one to six hours of life is recommended because of the evolving nature of HIE in the first hours after birth.[8] Over time some newborns may deteriorate and others improve and so therapeutic hypothermia must be considered for all newborns who meet criteria at any time in the first six hours after birth, even if their condition subsequently improves.[24]
- Contact NETS for advice for all newborns with evidence of two or more features of moderate or severe encephalopathy or seizures at any time from one to six hours of life.
- Newborns with mild encephalopathy may have some normal features (e.g. normal posture, tone). If present, these should be documented as normal.

- Consider alternate and additional diagnoses (e.g. subgaleal haemorrhage, sepsis other central and peripheral nervous system disorders, metabolic syndromes, cardiovascular abnormalities). Consider investigations as per the Queensland Health HIE clinical features investigations and management.[4]
- Newborns who require sedation (e.g. opiates) or muscle relaxation (e.g. pancuronium, vecuronium) for management of severe respiratory illness require careful assessment, including neurological examination, before initiating muscle relaxation and amplitude-integrated electroencephalography (aEEG) or electroencephalography (EEG) monitoring in a NICU to assess for evidence of encephalopathy or seizures.[10]
- Anticonvulsant medications can make assessment of encephalopathy more difficult. If there is concern that the newborn may be having subtle or uncertain seizures, consider discussing with a neonatologist before commencing anticonvulsant medications.
- A video demonstrating the neurological examination of a baby with suspected HIE can be found at Scottish Neuroprotection Care Pathway (NCP) for Infants with Hypoxic-Ischaemic Encephalopathy (HIE).[25] This site also provides useful videos on supporting communication skills with parents.
- Consider aEEG monitoring or a formal EEG. Starting therapeutic hypothermia should not be delayed while waiting for these investigations.

Figure 2: Assessment of Encephalopathy Severity Tool

Modified Sarnat Criteria

Assess neonatal signs against each criterion (N = Normal / MILD = Mild / MOD = Moderate / S = Severe / or N/A = Not Available)

Assessment Criteria	Encephalopathy Severity				Hours post birth Record severity of each criterion hourly (N, Mild, Mod, S or N/A)					
	Normal (N)	Mild (MILD)	Moderate (MOD)	Severe (S)	0-1hrs	1-2hrs	2-3hrs	3-4hrs	4-5hrs	5-6hrs
Alertness / Level of consciousness	Alert Arouses appropriately	Hyperalert	Lethargic Difficulty waking	Stupor or coma						
Spontaneous activity	Normal	Normal or increased	Decreased activity	No activity						
Posture	Normal	Normal	Distal flexion*	Decerebrate†						
Tone	Normal	Normal or increased tone in limbs or trunk	Hypotonia (focal or general) in limbs, trunk or neck	Flaccid						
Suck reflex	Normal	Normal or incomplete suck or biting	Weak suck	Absent						
Moro reflex	Normal	Exaggerated, low threshold	Incomplete	Absent						
Autonomic: **Normal:** pupils equal/reactive, normal HR, normal RR **Mild:** Pupils equal/reactive, increased HR, normal RR **Moderate:** Pupils constricted or bradycardia or periodic/irregular breathing **Severe:** Pupils dilated or deviated, or variable HR or apnoea										
Total moderate or severe features										
Seizures (tick if observed)										
Date and time of assessment										
Clinician signature and designation (hourly)										
Telehealth / Video assessment (tick if undertaken)										

Request Senior Medical Review, discuss with Tertiary Centre Neonatologist/NETS consultant and consider Therapeutic Hypothermia if the newborn has 2 or more features of moderate or severe encephalopathy OR has seizures at any time from 1 to 6 hours post birth

References: Sarnat HB and Sarnat MS Neonatal Encephalopathy following Fetal Distress. Arch Neurol 1976:33,696-705 Queensland HIE Guideline 2019, NZ Consensus Statement for Treatment of Encephalopathy

* Thumb flexed under fingers or decorticate - arms flexed/legs extended

† arms and legs extended or sustained tonic postures

Criteria for therapeutic hypothermia for newborns with HIE

All of the following three criteria (Table 2) must be met for the newborn to be eligible for therapeutic hypothermia.

Table 2: Criteria for therapeutic hypothermia

1. GA ≥35 weeks and ≥1,800g and <6 hours old
AND
2. Evidence of severe acidosis or depression at birth, with any ONE of: • pH <7.00 or a BE equal to or worse than –12mmol/L on any cord or newborn blood gas in first hour • Apgar score <6 at 10 minutes • Ongoing resuscitation (positive pressure ventilation or cardiac massage) for ≥10 minutes
AND
3. Presence of moderate/severe encephalopathy with any ONE of: • three or more moderate or severe features of encephalopathy (Sarnat criteria) identified at any time from 1 to 6 hours of life OR • two moderate or severe features of encephalopathy and abnormal aEEG (e.g. aEEG lower margin <5μV for >1 hour) OR • Seizures (witnessed by a medical officer/nurse/midwife or seen on aEEG/EEG)
Therapeutic hypothermia may also be considered for newborns with **moderate or severe encephalopathy AND other features of hypoxia/ischaemia**, including: • pH 7-7.1, Apgar <7 at 5 mins or lactate >8mmol/L in the first hour OR • sudden unexpected post-natal collapse with pH <7.1
CONTRAINDICATIONS
There are no absolute contraindications to therapeutic hypothermia; however, relative contraindications include: • uncontrolled bleeding • uncontrolled severe hypoxia due to persistent pulmonary hypertension • imminent end of life care planned.

- Request Senior Medical Review, discuss with a tertiary centre neonatologist/NETS consultant and consider therapeutic hypothermia for all newborns who meet two or more criteria of moderate or severe encephalopathy (e.g. decreased lethargy, decreased activity, decreased muscle tone, abnormal postures or reflexes, weak or absent suck) OR seizures at any time from one to six of life (see Criteria for therapeutic hypothermia).
- If the need for therapeutic hypothermia is uncertain (e.g. if newborn has two, but not three, features of moderate or severe encephalopathy), it may be appropriate to transfer the newborn to a NICU for further assessment, including aEEG/EEG monitoring.
- There is insufficient evidence from clinical trials to provide clear guidance for several subgroups of newborns, including:
  - newborns with pH 7 to 7.1, Apgar <7 at 5 minutes or lactate >8mmol/L in the first hour of life[26]
  - Sudden Unexpected Postnatal Collapse (SUPS) in the newborn period (usually <48 hours)[27, 28]
  - newborns with borderline criteria, e.g. born at 34 weeks gestation, birth weight 1,750g-1,880g, encephalopathy or seizures identified at 6-12 hours of life.
- Therapeutic hypothermia may be considered on a case-by-case basis for these newborns after discussion with a tertiary centre neonatologist. However, it should only be commenced the potential benefits outweigh the risks.
- For newborns with SUPC, therapeutic hypothermia (if considered appropriate) must be commenced within six hours of the SUPC episode.[27, 28]

Therapeutic hypothermia – initial management

General principles

- Therapeutic hypothermia must not be commenced without discussion with NETS and with a tertiary centre neonatologist.
- The decision to provide therapeutic hypothermia must be made within the first six hours after birth and should be initiated as soon as possible after this decision has been made.
- Attention must be paid to other aspects of care for all newborns who are at risk of HIE, including cardio-respiratory, intravenous fluids and glucose needs. Caution must be exercised with fluid boluses outside of blood products. If the infant requires respiratory support, normal humidifier settings should be used.
- Active bleeding should be investigated and therapy provided, where needed. If there is no active bleeding, therapeutic hypothermia should not be delayed while waiting for coagulation investigations.
- Further information on early management can be found in the Hypoxic Ischaemic Encephalopathy in the Newborn - NETS Practice Guideline.[29]

Temperature monitoring and therapeutic hypothermia ('cooling') methods

Refer to Figure 3 – Therapeutic hypothermia flowchart

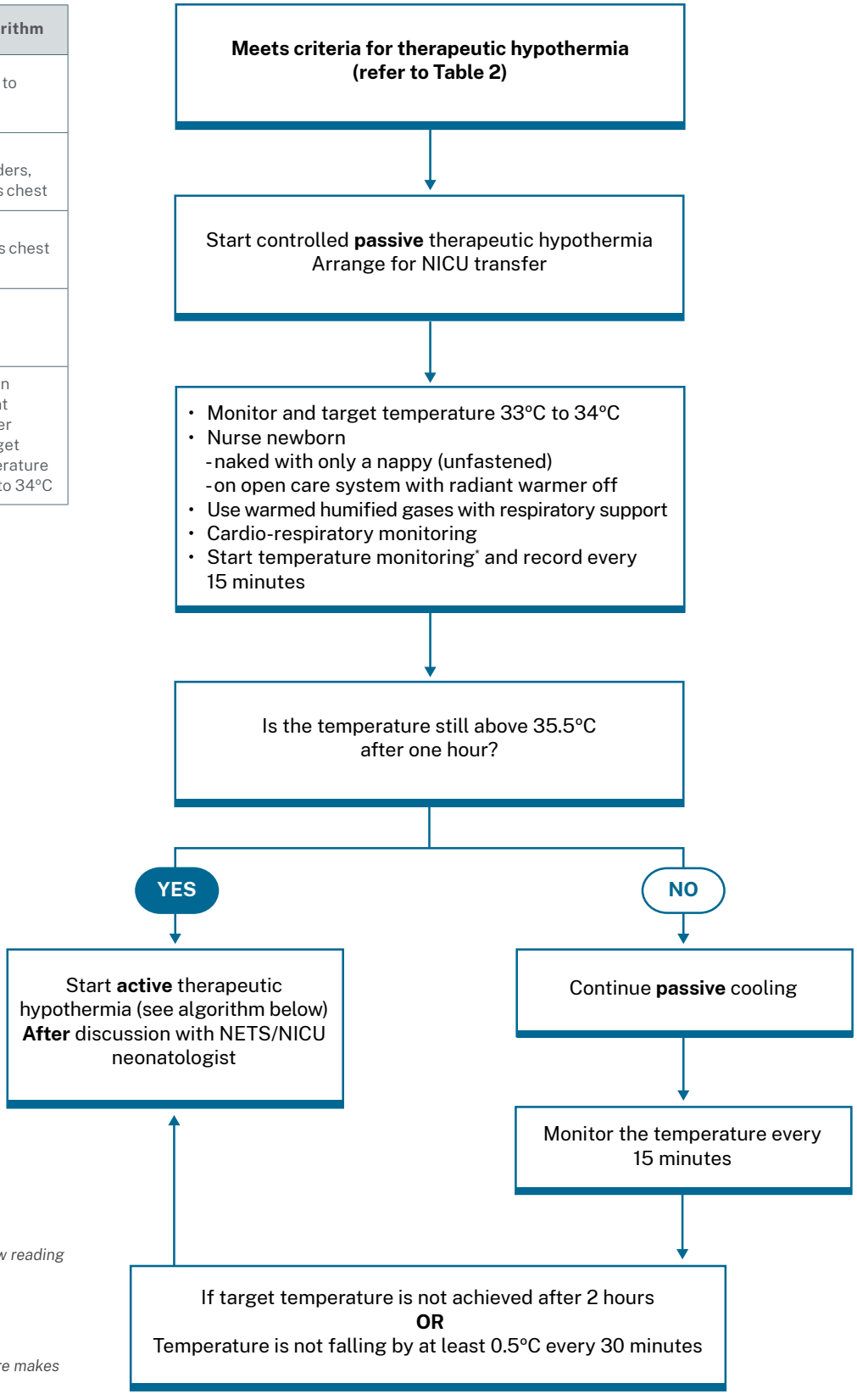
- Cardio-respiratory monitoring with continuous rectal temperature monitoring is recommended.
- If continuous rectal monitoring is not available, intermittent axillary temperatures should be performed every 15 minutes (using a low reading thermometer).
- Place nil by mouth.
- Active therapeutic hypothermia can also be provided using a Total Body Therapeutic Hypothermia System ('cooling blanket'). Use local protocols if a Total Body Therapeutic Hypothermia System is available.
- Observation and documentation of skin condition should occur every 15 minutes with active therapeutic hypothermia.[30]

Considerations

- If the newborn's temperature drops below 33.5°C:
  - During passive cooling: commence low radiant heater to maintain rectal or axillary temperature within target range.
  - Active cooling: remove one or both cool packs and, if necessary, turn on low radiant heater to maintain temperature within target range.
- If the newborn develops signs of distress or shivering that results in difficulties maintaining temperature, consider appropriate pharmacological support in consultation with a neonatologist.
- Consider stopping therapeutic hypothermia before 72 hours in consultation with the neonatologist if the following occur:
  - life-threatening coagulopathy
  - uncontrolled pulmonary hypertension
  - pathological cardiac arrhythmia requiring treatment (not sinus bradycardia)
  - deterioration that leads to redirection to end-of-life care based on discussions between the family, treating team and the neonatologist.

Figure 3: Therapeutic Hypothermia ('Cooling') Pathway

Active therapeutic hypothermia algorithm		
Rectal/ axillary temperature	Number cool packs[†]	Areas to apply
≥35.5°C	2[‡]	Under shoulders, across chest
34.0 to 35.5°C	1	Across chest
<34.0°C	0	Nil
<33.5°C	0	Turn on radiant warmer to target temperature 33°C to 34°C



** Use rectal monitoring if possible. Use a low reading thermometer if axillary*

† Using refrigerated cool packs with cotton sleeve/cover

‡ More than 2 packs prevent radiant heat loss into the environment and therefore makes cooling the newborn increasingly difficult.

Care of the family

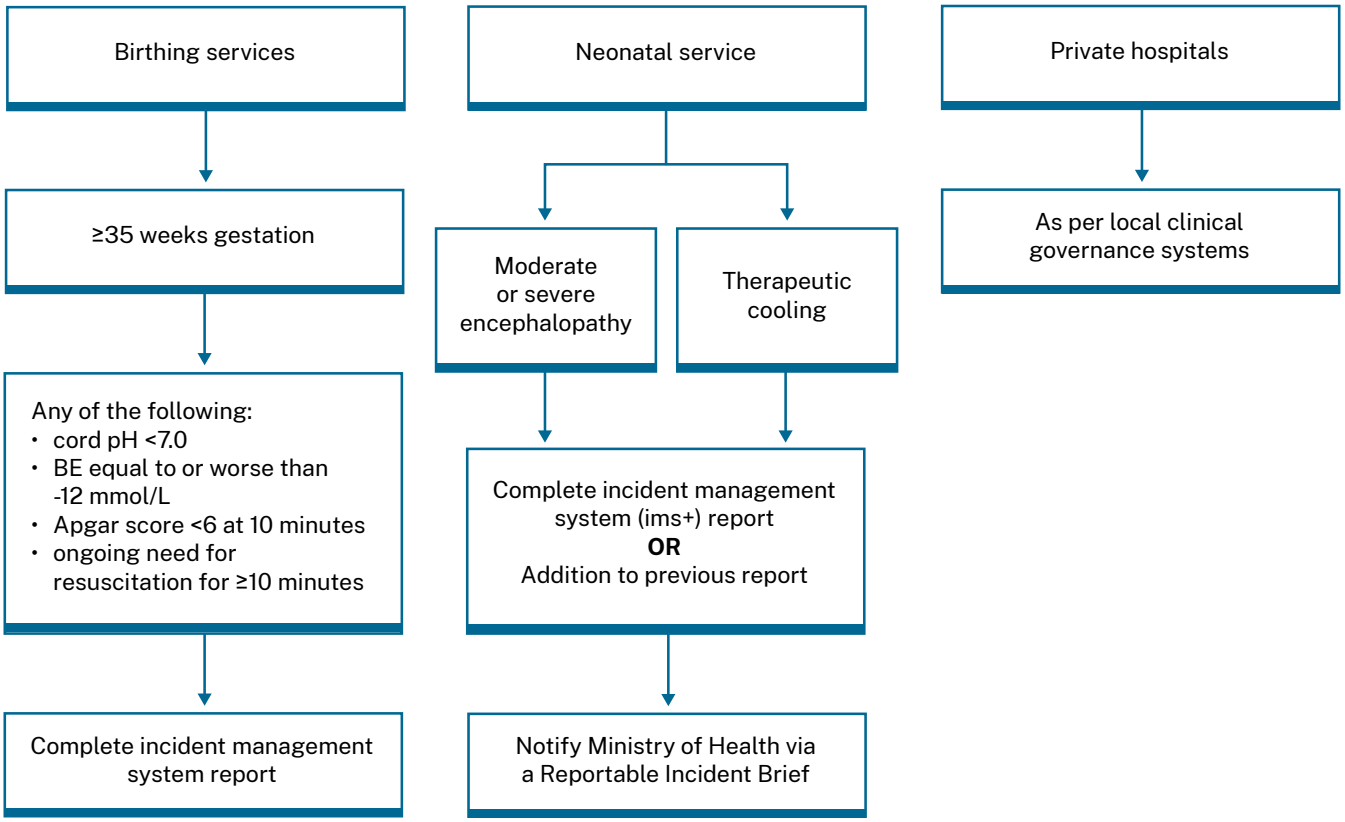
- Parents of newborns with HIE experience trauma both from the birth and from their concern about their baby and need for therapeutic hypothermia treatment.
- Face-to-face meetings with clinicians with clear, compassionate and transparent communication about their newborn's condition and need for therapeutic hypothermia, together with encouraging parental involvement, can help to reduce this trauma.[31]
- Provide parent information sheet on Therapeutic Hypothermia ('cooling') to Protect Newborns with Hypoxic Ischaemic Encephalopathy (HIE).
- Advise/reassure parents about their newborn's appearance and that they will feel cool to touch.
- Provide opportunities to bond by encouraging parents to provide care, e.g. nappy changes.
- Discuss and encourage breast milk expression.
- Provide immunosupportive oral care.
- Separation or isolation from their newborn may be a trigger for some parents, including Aboriginal families and refugees. Identify parents and families that may require additional support and provide referral early in the admission.
- Provide families with information about transfer, hospital name and location, contact numbers.
- A video resource on 'Supporting Communication Skills' (Video 2) can be found at Scottish Neuroprotection Care Pathway (NCP) for Infants with Hypoxic-Ischaemic Encephalopathy (HIE).[25] This video is designed to assist thinking about how and what you might say during early conversations with parents of a baby with suspected HIE.

Reporting

Reporting processes should be in place to monitor incidence of newborns with moderate or severe encephalopathy (see Figure 4).

- Birthing services to complete an incident management system (ims+) report for all newborns ≥35 weeks gestation identified with high risk of neonatal encephalopathy following birth, including newborns with:
  - cord pH <7.0
  - BE equal to or worse than –12 mmol/L
  - Apgar score <6 at 10 minutes
  - ongoing need for resuscitation for ≥10 minutes.
- Neonatal services to complete an incident management system (ims+) report (or addition to a previously submitted ims+ report) for newborns who develop:
  - moderate or severe HIE
  - who receive treatment with therapeutic hypothermia.
- Reporting for newborns born in a private hospital should occur through similar clinical governance systems within the newborn's hospital of birth.
- Serious incidents, including term newborns diagnosed with severe HIE or who receive therapeutic hypothermia, should be notified to the Ministry of Health via a Reportable Incident Brief in accordance with NSW Health Policy Directive, Incident Management PD2020_047 32 for all newborns born in NSW.

Figure 4: Reporting process for newborns with moderate or severe encephalopathy



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Appendix: Changes in guidance since 2010 NSW Health Policy Directive PD 2010: 006

The clinical practice guide replaces the NSW Health Policy Directive, PD2010 006: Whole Body Cooling - Neonates Suspected Moderate or Severe Hypoxic Ischaemic Encephalopathy (HIE).[1]

Changes since 2010 include:

- Addition of Newborn Encephalopathy Pathway to assist in recognition of newborns with HIE.
- A recommendation for continuous monitoring and frequent review of newborns at high risk of HIE (Newborn Encephalopathy Red Pathway). The management should be in a neonatal unit and last at least six hours.
- The expansion of NSW Newborn Encephalopathy Severity Tool to include criteria for mild, moderate and severe encephalopathy and recording of seizures.
- Hourly neurological assessment from one to six hours after birth using the Assessment of Encephalopathy Severity Tool.
  - Minor changes to criteria for therapeutic hypothermia, including: need for only one feature of depression at birth in addition to (previously required two features).
  - Addition of option to use EEG or aEEG assessment to help determine moderate or severe encephalopathy.[33]
- Option for therapeutic hypothermia to be considered for newborns with moderate or severe encephalopathy and pH 7 to 7.1, or lactate ≥8.0 OR following post-natal collapse, when it is considered that hypoxia/ischaemia is the most likely cause of the encephalopathy.
- Introduction of the option for telehealth/video assessment with tertiary centres to aid in assessment of encephalopathy severity.

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