



Scottish Perinatal Network

Neuroprotection Care Pathway for Infants with Hypoxic-Ischaemic Encephalopathy

NOTE

This guidance is not intended to be interpreted or used as a standard of care. Standards of care are determined based on the full range of clinical information available for an individual case and may change as scientific knowledge, technology, and clinical practice evolve. Following the recommendations in this guidance does not guarantee a successful outcome in every situation, nor does it encompass all appropriate methods of care or exclude other acceptable approaches that may achieve the same results. Clinical judgement remains the responsibility of the healthcare professional(s) involved in the patient's care. Clinicians must also be mindful of the requirements of patient autonomy and patient-centred care, which may involve a patient opting (after discussion of the available treatment options) for a treatment which is not the treatment recommended in the guidance. Where treatment involves deviation from national guidance, or local guidance derived from them, this should be fully documented in the patient's records at the time the decision is made."

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This document has been prepared by Public Services Delivery Scotland (PSD Scotland) on behalf of the Scottish Perinatal Network. Accountable to Scottish Government, PSD Scotland works at the heart of the health service providing national strategic services to the rest of NHS Scotland and other public sector organisations to help them deliver their services more efficiently and effectively. Scottish Perinatal Network is a collaboration of stakeholders who are supported by a PSD Scotland Programme Team to drive improvement across the care pathway.

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Review History

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1.0	April 2015	Final document-initial publication	Scottish Cooling Group (Appendix 6)
2.0	1 st September 2021	Simplification of flowcharts	Scottish Cooling Group (Appendix 6)
3.0	1 st September 2025	Removal of babies <35 weeks from NCP	Scottish Cooling Group (Appendix 6)
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Neuroprotection Care Pathway for Infants with Hypoxic-Ischaemic Encephalopathy

Purpose of pathway

This pathway has been designed to inform the diagnosis, referral, transport and management of infants with moderate and severe hypoxic-ischaemic encephalopathy (HIE) who are born and/or treated in Scotland.

This pathway has been devised to ensure safe, timely, equitable and effective care is available to all infants who may be eligible for therapeutic hypothermia (TH). Guidelines have been developed in accordance with the [Framework for Practice for Therapeutic Hypothermia for Neonatal Encephalopathy, BAPM 2020](#).

The pathway gives guidance in the following areas:

1. Diagnosis and management of HIE
2. Referral and transport of infants with HIE
3. Ongoing management of infants with HIE undergoing therapeutic hypothermia

Location of care

Cooling can be initiated in any hospital setting where rectal temperature monitoring can be carried out. All units (bar Community Midwifery Units, see below) should have servo-controlled cooling equipment to induce hypothermia rapidly where required, whether the baby is in a cooling centre or in a referring unit. It is recommended that units use cerebral function monitoring to optimise decision-making for cooling. Infants who are eligible for ongoing cooling should be transferred to a Cooling Centre ([BAPM 2020](#)) that has facilities for providing neuro-intensive care, prognostic expertise and counselling to parents of brain injured infants. Infants in whom TH has been initiated should be transferred to the appropriate NICU by ScotSTAR with ongoing servo-controlled cooling and intensive care monitoring including rectal temperature. These uplift transfers should be prioritised according to clinical need and should follow local and national transport service guidance regarding timeliness of transfer.

Community Midwifery Units should resuscitate and stabilise the infant and call ScotSTAR to arrange transport to an appropriate care location. Normothermia (36.5-37.4C) should be maintained and hyperthermia should be avoided.

Principles of assessment

Refer to Therapeutic Cooling Decision Aid and [Pre-Cooling Documentation Aid](#) (Appendix 1).

It is a national recommendation that All Special Care Units (SCUs), Local Neonatal Units (LNUs) and NICUs should be able to assess infants and instigate TH using aEEG and servo-controlled cooling equipment as outlined above. Staff in all units should be trained and competent in the neurological assessment of infants, as well as in aEEG monitoring and interpretation ([BAPM 2020](#)).

Cooling is not appropriate if:

- There are other abnormalities indicative of poor long-term outcome e.g. trisomy 18.
- The infant appears 'moribund' and is dying despite intensive care efforts.

Cooling may be appropriate if:

- The infant falls outside of set criteria. See Appendix 3 and contact the Cooling Centre for further advice.
- Infants who are likely to require early surgery should be discussed with the Cooling Centre and Surgery at an early stage. Cooling may still be feasible during surgery, or the surgery may be delayed to accommodate neuroprotective interventions.

Principles of care during and after Therapeutic Hypothermia

General principles

A decision to cool using passive methods is no less significant than a decision involving active methods. Passive cooling is not a 'halfway house' to be used while the baby is still being assessed.

Refer to Management Aids for Referring Centres, Cooling Centres and [Transport Teams](#) (Appendix 2).

Expanded management guidance is provided in Appendix 4.

Complications associated with cooling

Cooling infants to 33-34°C in an intensive care environment can be undertaken safely.

Subcutaneous fat necrosis (SCFN) is a recognised complication of total body cooling. This condition can lead to pain, scarring, and hypercalcaemia that may present after discharge. It may be subtle and occur in any area of the body containing subcutaneous fat and is not restricted to body areas in contact with cooling mats. It is recommended that the infant's skin is closely observed for the development of SCFN both during neonatal stay and after discharge by parents. If it develops, weekly calcium levels should be monitored at least until clinical resolution of SCFN occurs, and in some instances for up to 6 months. Parents should be alerted to the symptoms of hypercalcaemia whether or not SCFN is diagnosed during stay and a parent leaflet with this information should be provided.

Prognostication

An assessment should be made of the likely prognosis into high, moderate and low risk of significant neurodevelopmental impairment, based on the baby's neonatal condition, the evolution of neurological examination, aEEG, MRI and, where available, MRS. If there is overwhelming clinical evidence of very poor prognosis before day 5, an MRI may not be required to support clinical judgement when counselling parents. However, MRI obtained during TH has a sensitivity of 100% (95% CI 84% to 100%) to identify the presence and extent of later brain injury. In general MRI and 1H MRS are most valuable where prognosis is uncertain. Where MRI and 1H MRS are used for

prognostication, clinicians should be aware of the confidence limits around point estimates of predictive values, and efforts made to translate uncertainties in appropriate ways for parents.

Prognosis should be discussed with parents in a timely manner before discharge from the NICU and summarised in a written communication to parents and other health professionals in the referring unit and primary care. Where the result and interpretation of the MR investigations are not available at the time of transfer, specific arrangements should be made to communicate this information to parents and referral teams in a timely manner.

Suggested MR sequences and the prognostic values of MRI and MRS after hypothermia are found in the [BAPM Framework for Practice: Neonatal Brain Magnetic Resonance Imaging: Clinical Indications, Acquisitions and Reporting 2023](#).

Withdrawal of intensive support

In some cases, it may also be apparent soon after delivery that the prognosis of a baby is so poor that ongoing intensive care is likely to be futile. In these circumstances the baby should not be cooled, and it is usually inappropriate to separate the mother and baby by transferring to a Cooling Centre. These cases should be discussed with ScotSTAR and the Cooling Centre.

In infants in whom it is possible to deliver TH with physiological stability; it is recommended that consideration of reorientation of care be delayed for 48 hours to assess recovery. Consideration should be given to any sedative drugs that have been administered and appropriate tests should be undertaken to ensure that the assessment of prognosis has not been modified by drug effects.

If a decision is made to withdraw intensive support during cooling, cooling should be discontinued and, if time allows, the baby re-warmed before intensive care is withdrawn.

Palliative care teams including those from a local children's hospice may provide beneficial support to the infant and their family. The ScotSTAR neonatal transport team can provide transport of an infant planned for palliative care to a hospice or a unit closer to the infant's home. In the event that the infant has died before the hospice team was contacted, the hospice may still be able to offer help and support to the family.

When any baby dies, the parents should be counselled by a Neonatal Consultant about the value of postmortem examination, and this may involve prior discussion with the Procurator Fiscal in certain circumstances. The possibility of organ donation should be explored with the local Specialist Nurse for Organ Donation and discussed with the parents.

Parents

Early open and honest communication by senior members of the neonatal team with parents is an essential part of neonatal care, and there should be no barriers to this. The decision to treat with cooling should be explained to the parents and written parent information should be provided.

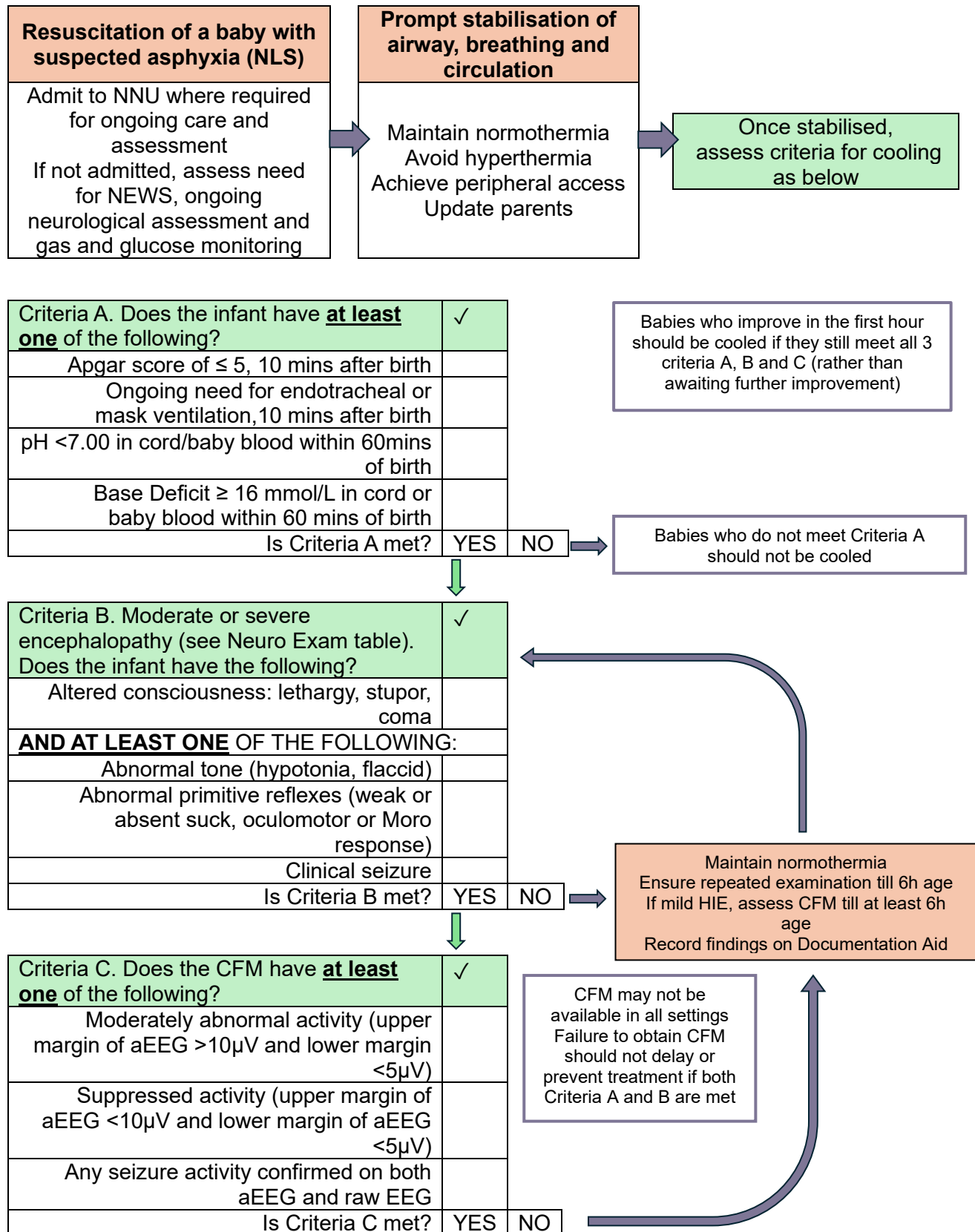
There should be no barriers to parents being with and caring for their baby, aiming for a culture of minimal separation. This will involve timely transfer of the mother after birth. The mother should be encouraged and supported to express breast milk, if they wish to do so.

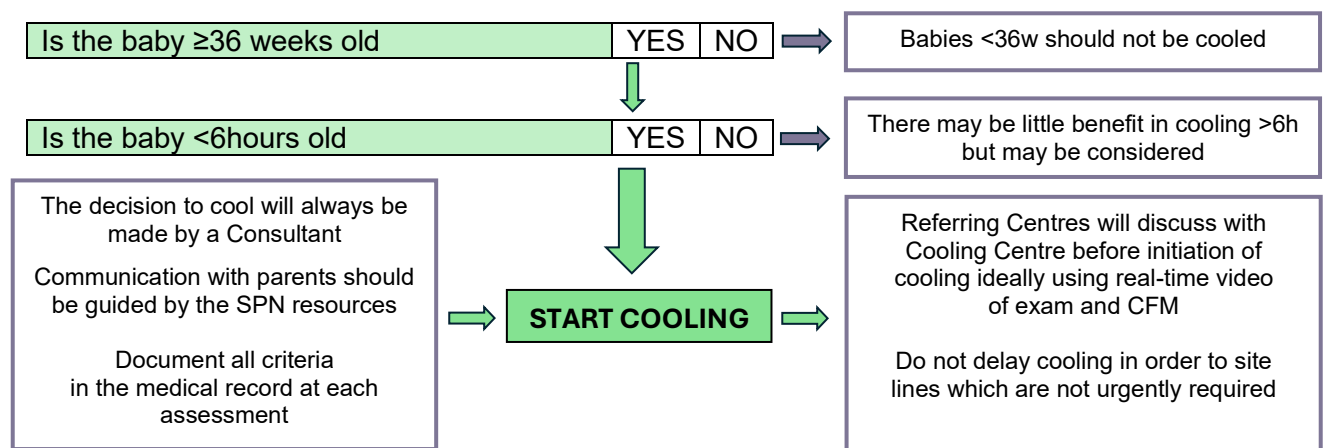
If stable, babies can be held by their parents during therapeutic hypothermia without adverse event. A parent video and a guide to enable the CoolCuddle safely can be found [here](#).

Sensitive and open communication, alongside trauma informed care, needs to be repeated throughout the patient pathway, with parental care being integrated with the clinical care. The clinical team should be responsive to parents' concerns and questions, and to the wellbeing of siblings and the wider family. Parents should be signposted towards support organisations at the earliest, or most appropriate opportunity (Appendix 5).

There should be timely multidisciplinary and multispecialty review of the perinatal care of the mother and baby of any infant who undergoes TH with a particular focus on avoidable factors. This should be discussed with parents in a timely open and honest way, meeting standards of GMC/NMC duty of candour. All parents whose baby has undergone TH should be offered follow up to reflect on antenatal, intrapartum and neonatal care, and the opportunity to ask questions within the review process.

Therapeutic Cooling Decision Aid





Neurological Examination - based on Modified Sarnat scoring

Referring centres are encouraged to use real-time video with the Cooling Centre to aid interpretation of both CFM and of neurological examination.

Domain	Stage 1 (Mild)	Stage 2 (Moderate)	Stage 3 (Severe)
Level of consciousness	Normal Hyperalert	Lethargic or decreased activity in an infant who may be responsive Can be irritable	<u>Stuporose/</u> comatose Not able to rouse and unresponsive to external stimuli
Posture	Flexed with adducted legs	Distal flexion, complete extension or frog-legged	Decerebrate with or without stimulation (all extremities extended)
Spontaneous activity when awake or aroused	Active Vigorous does not stay in one position	Less than active Not vigorous	No activity whatsoever
Autonomic system	Pupils: normal, reactive Heart rate: normal >100 Respirations - normal	Pupils: constricted, reactive Heart rate: bradycardia Respirations: periodic irregular breathing effort	Pupils: fixed dilated, skew gaze, not reactive to light Heart rate: variable may be bradycardic Respirations: completely apnoeic
Tone	Normal – resists passive motion Hypertonic, jittery	Hypotonic or floppy, either focal or general	Completely flaccid like a rag doll
Primitive reflexes	Suck: vigorously sucks finger or ET tube Moro: normal	Suck: weak Moro: incomplete	Suck: completely absent Moro: completely absent
Seizures	None	Common focal or multifocal seizures	Uncommon or frequent refractory seizures

Table 1: From Appendix 3 - Neurological examination on page 29 of BAPM [Framework for Practice for Therapeutic Hypothermia for Neonatal Encephalopathy, BAPM 2020](#)

CFM Criteria for Cooling

CFM should be applied and interpreted by personnel who are trained in its use. This skill includes but is not restricted to:

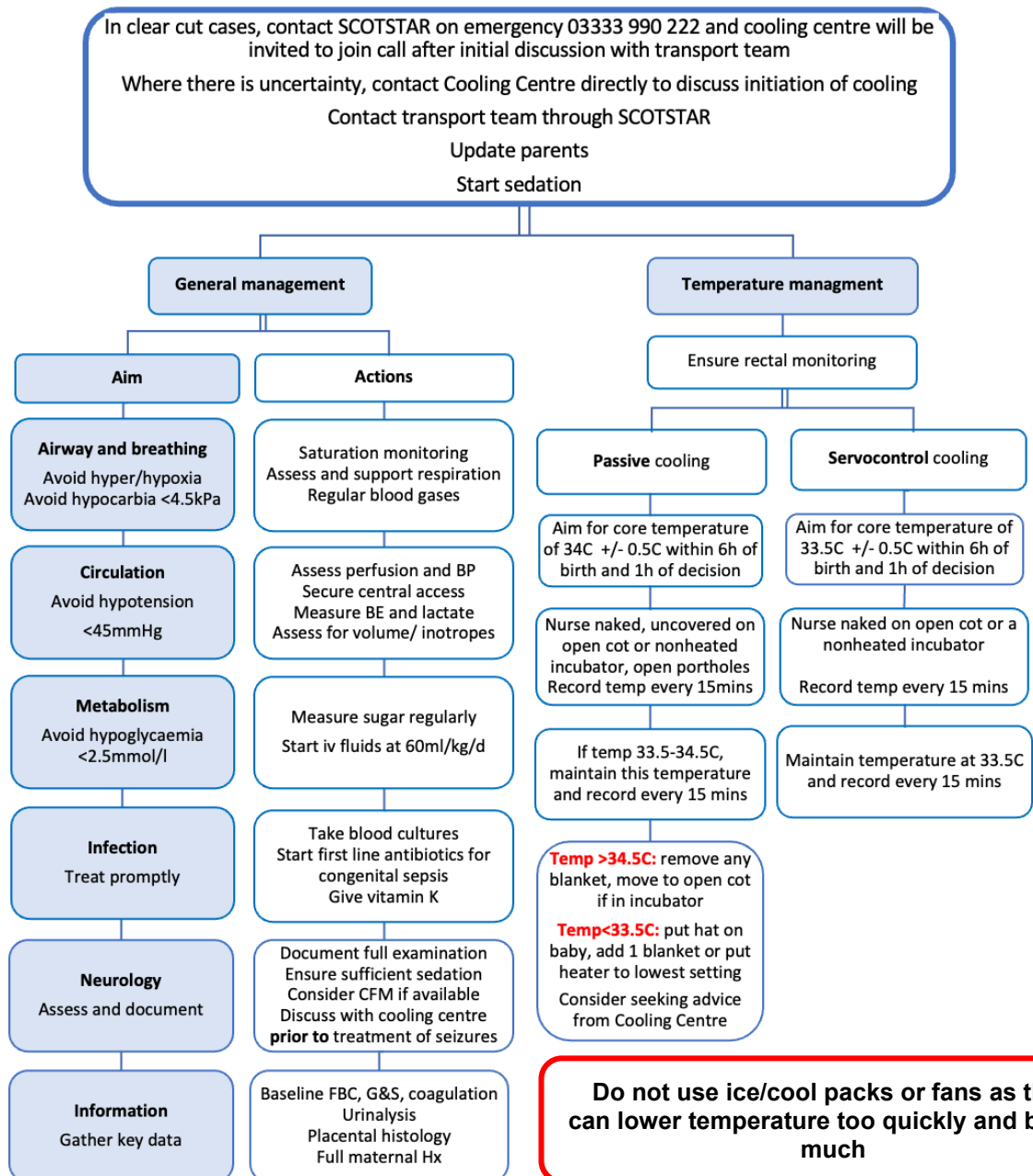
- Ensuring accurate placement of electrodes
- Ensuring correct machine set up, including appropriate scales and speed
- Accurate interpretation of both aEEG and raw EEG
- Ability to identify artefacts
- Ability to identify normal and abnormal patterns, and accurately diagnose seizures

There must be at least one of the following criteria (based on TOBY criteria) present:

- Moderately abnormal activity (upper margin of aEEG $>10\mu\text{V}$ and lower margin $<5\mu\text{V}$)
- Suppressed activity (upper margin of aEEG $<10\mu\text{V}$ and lower margin of aEEG $<5\mu\text{V}$)
- Continuous seizure activity as confirmed on both aEEG and raw EEG (rare before 6 hours of age)

Therapeutic Cooling Management Aid – Referring Centres

Any decision to cool using passive methods is no less significant than a decision involving active methods. Passive cooling should not be seen as a 'halfway house' to be used while the baby is still being assessed.



Prepare the discharge letter:

- ☐ Details of maternal history, labour, delivery, cord pH, resuscitation, time to heart rate >100, first gasp
- ☐ Blood test results and timing of drugs and their dosages
- ☐ Examination of the baby including head circumference, details of neurological examination
- ☐ Time of cooling decision and time to reach target temperature of 33-34C
- ☐ The results of any imaging specifically cranial ultrasound and the position of central lines
- ☐ Details of discussions with parents and whether written parent information has been given

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Therapeutic Cooling Management Aid - Cooling Centres

Parents	• Inform of intention to commence TH and give Parent Information Leaflet • Joint obstetric and neonatal debrief soon after birth • Daily consultant update • Support lactation if intention to breastfeed • Support cooling cuddles where this can be done safely
Temperature	• Site rectal probes • Load with morphine, ensure adequate sedation for optimal neuroprotection • Start servocooling within 6h, and preferably within 4h • Aim to reach 33.5C within 30 min of initiation and to continue cooling for 72h
Monitoring and Investigations	• Continuous HR, O2 saturation and invasive BP monitoring • Regular blood gas and glucose analysis • Fluid balance 6 hourly • Other investigations as indicated (see proforma in full pathway and below) • Monitor for subcutaneous fat necrosis throughout stay
Airway and Respiratory	• Aim for normal blood gas values and saturations- avoid hypocarbia /hyperoxia • Intubation is not always required • Ensure regular repositioning and suction if secretions increase • Watch for stridor in nonventilated patients
Cardiovascular	• Achieve central venous and arterial access • Bradycardia 80-100bpm is normal • Rise in HR may be distress, hypovolaemia, hypotension, seizures or inotropes • Aim for BP >45mmHg and treat hypotension according to local guidelines
Fluids and electrolytes	• Catheterisation recommended in assessing urinary output • Initial maintenance fluids at 40-60ml/kg/d • Avoid hypoglycaemia maintaining glucose ≥ 2.5 • Avoid fluid overload during oliguria and hypovolaemia once diuresis starts • Watch for accumulation of nephrotoxic drugs eg gentamicin
Gastrointestinal and liver	• Consider trophic breast milk if no ongoing organ dysfunction or poor perfusion • Give colostrum as mouthcare where available in all • Beware accumulation of drugs metabolised by liver: morphine, phenobarb • Coagulopathy is physiological in TH but only active bleeding needs treatment
Infection	• Take blood cultures and give antibiotics within one hour of birth for those delivered after spontaneous labour or who have risk factors for infection • Consider lumbar puncture • Physiological drop in white cell count and platelets is normal in TH. Give vit K.
Neurology	• Continuous CFM. Consider EEG where CFM has not normalised by rewarming • Perform neurological examination every 12 hours • Treat seizures with ref to local guidance • MRI at 5-14d, requested and reported according to BAPM standards

Therapeutic Cooling Management Aid – Cooling Centres, continued from previous page:

Rewarming

- Observe for hypotension, apnoea and seizures
- Re-warming can be delayed or slowed where seizures emerge
- Maintain normotheria after re-warming with paracetamol and environmental measures where required

Discharge

- Discharge letter to parents, GP, Obstetrician, HV +/-referring unit including parent expectations and prognosis, and vigilance for subcutaneous fat necrosis
- Ensure plan for 2 year standardised neurodevelopmental follow up
- Signpost parents to support groups where relevant

Appendix 1 – Pre-Cooling Documentation Aid

[See separate attachment on SPN Website](#)

Appendix 2 – Management Aid for Transport Teams

[See separate attachment on SPN Website](#)

Appendix 3 – Cooling in Special Circumstances

Cooling Outside Trial Criteria

Infants <36 weeks gestation

Preterm infants <36 weeks should not be considered for cooling due to the increased risk of poor outcome at these gestations.

Infants >6 hours old

Infants between 6 and 24 hours of age may be considered for cooling; however, beyond 6 hours of age the benefit from hypothermia is likely to be small. The patient should be discussed with the Cooling Centre BEFORE passive or active cooling is started.

Infants presenting with mild encephalopathy

Infants presenting with mild encephalopathy should not currently be considered for cooling outwith clinical trials. It is however important to ensure that an infant with mild HIE does not develop signs of a moderate encephalopathy over the first 6 hours of life. Repeated neurological examination is required during this time to assess potential eligibility for cooling. CFM may be helpful.

Infants with congenital anomalies

Cooling should be considered on a case-by-case basis depending on the underlying anomaly. The following should be considered:

- Is the condition life-limiting? I.e. would cooling improve the long-term outcome?
- Would cooling impact on the anomaly? E.g. cooling may compromise blood flow to the gut in an infant with gastroschisis.
- Would the condition make it harder to assess neurological examination? E.g. a baby with Down's syndrome may be hypotonic as a result of the condition (this does not mean that such a baby should not be cooled, just careful neurological assessment is necessary).

The patient should be discussed with the Cooling Centre BEFORE passive or active cooling is started.

Infants presenting with sudden unexpected postnatal collapse

Infants presenting with in-hospital postnatal collapse can be considered for cooling within 6 hours of collapse. The following should be considered:

- Is there an underlying condition which may be worsened by cooling? E.g. structural cardiac abnormality, intracranial bleeding

The patient should be discussed with the Cooling Centre BEFORE passive or active cooling is started.

The infant whose clinical condition normalises within 6 hours of birth

Careful neurological assessment is essential to demonstrate that such an infant does not meet criteria based on neurological examination.

Babies who improve in the first hour should be cooled if they still meet all 3 criteria A, B and C (rather than awaiting further improvement)

If cooling has been commenced at birth but a baby normalises rapidly in the first hours and no longer meets cooling criteria then it would be reasonable to slowly rewarm the infant. These infants should be carefully observed over the next 24 hours.

The infant whose clinical condition normalises after 6 hours of birth

Infants whose are already being cooled but the clinical condition normalises after 6 hours should continue cooling for 72 hours.

The infant who develops 'rebound' seizures during or following re-warming

Where re-warming is associated with seizures, the process can be slowed or paused until seizure control is achieved. There is no clinical evidence that prolonging cooling to 96 hours improves neurodevelopmental outcome.

Appendix 4 - Ongoing management of the cooled infant with HIE

Monitoring and investigations

1. Double continuous rectal temperature monitoring with alarm limits set within 1°C of the target rectal temperature. Insert rectal probes to 6cm and secure firmly. One rectal probe is to allow the machine to servo-control and the other is connected to monitoring for continuous recording and alarming when out of the target range. Both should be checked for correct placement every hour and placement recorded. If the servocontrol probe is displaced, the cooling machine may start to rewarm the baby to the target temperature, although an alarm will also be activated in the case of a sudden change in temperature.
2. Continuous heart rate, oxygen saturation and invasive BP monitoring.
3. Regular blood gas and glucose analysis to assess metabolic acidosis, adequacy of ventilation and glucose requirements. Temperature-corrected values should be analysed.
4. Fluid balance 6 hourly- measure urine volume by catheter until urine output is normal. Urinalysis in the first 24 hrs following birth.
5. FBC, including Ca and Mg at an appropriate frequency for clinical condition. Daily urea and electrolytes. Initial coagulation screen on day of admission and as clinically indicated thereafter. Anticonvulsant and aminoglycoside levels as required- there may be delayed metabolism during hypothermia and doses may need to be adjusted on the basis of these results (Appendix 7).
6. CFM should be continued throughout cooling and re-warming, particularly as non- clinical seizures may occur on re-warming.
7. Neurological examination and encephalopathy score- every 12-24 hours for the first 4 days of life.
8. Cranial ultrasound scan within 12 hours to exclude other causes of encephalopathy, and as clinically indicated thereafter
9. All infants undergoing TH should have an MRI scan undertaken between 5 and 15 days, preferably between 5 and 7 days of birth.
10. Where possible, Proton (1H) MRS Lactate/N acetyl aspartate (Lac/NAA) of the basal ganglia and thalamus should be performed with the MRI at 5-10 days after birth. This is the most accurate predictor of outcome in babies who have undergone TH.

Ventilation

Cooling does not have any direct effect on respiratory function. Persistent pulmonary hypertension of the newborn or meconium aspiration may coexist with HIE and should be treated with the necessary ventilatory support, including HFOV and nitric oxide if necessary.

- Most babies will require ventilation. A hat should not be used to fixate the ETT.
- Some babies will be able to be extubated halfway through cooling but may require non-invasive support due to sedation and respiratory pathology.
- Ventilator gases should be warmed and humidified in the normal way, according to unit policy.

- Avoid hyperoxaemia and hypocarbia as these are associated with poor outcome. Note that blood gas analysis which does not correct for temperature will overestimate PCO₂ and PO₂. Hypothermia will reduce respiratory rate as metabolism is reduced. If intubated it is easy to over ventilate as CO₂ production is reduced. Hypocarbia may induce seizures.
- More frequent suction and regular re-positioning might be necessary as secretions become more abundant as cooling duration continues. Decisions about whether to use saline during suction should be made on an individual basis.
- Stridor has been reported in the context of hypothermia with or without preceding intubation. Apnoea is more common particularly if sedation has accumulated or if there are seizures. Both are transient although may require temporary escalation of ventilatory support.

Positioning and skin care

- Vary the position 6 hourly during care – flat – slightly uptilted – supine, right or left side to avoid pressure sores
- Do not turn the head only but keep nose in body midline to avoid impairment of cerebral blood flow or return.
- Cyanosis of the hands and feet (but not of the central oral mucous membranes) is common initially but settles with time.
- Subcutaneous fat necrosis is a recognised complication of therapeutic hypothermia in asphyxiated infants. Monitor skin for red painful nodules, and if diagnosed, ensure a plan for regular monitoring of calcium levels over coming weeks.

Cardiovascular Support

Cardiovascular instability is frequent and may manifest as hypotension, metabolic acidosis and pulmonary hypertension. Although some of the pathologic mechanisms associated with asphyxia involve a loss of volume (usually blood), hypovolaemia is not consistently associated with asphyxia initially and in the face of poor myocardial function, volume replacement may worsen cardiac function and inotropic support should be considered early. Cardiovascular support should be directed at improving cardiac contractility and systemic perfusion.

- Use clinical guidelines and assess cardiac function clinically (BP, heart rate) and/or by echocardiogram when choosing volume or drug.
- Electrocardiography and biochemical markers, such as troponin levels, may help in the assessment of myocardial dysfunction.
- Refer to local guidance for management of hypotension.
- Later in cooling infants can become hypovolemic as water is displaced to the interstitial tissue and because hypothermia can induce diuresis. This is particularly common where fluids have been restricted in the prior days and where renal function is not impaired. Volume replacement may be appropriate in this instance.
- During the rewarming process, a rise in body temperature may cause hypotension by inducing peripheral vasodilatation. If hypovolaemia is suspected an initial bolus of 10-20ml/kg of normal saline should be given and repeated if necessary.

- Bradycardia (<100bpm) is normal during cooling as is a prolonged QT interval. It is important to maintain the temperature above 33°C as there is a risk of ventricular fibrillation at lower temperatures. Arrhythmias that may occur during cooling usually resolve with re-warming.
- If there is a rise in heart rate, the infant may be distressed, in pain or it may be a sign of sepsis. Consider increasing sedation if pain or distress are suspected.

Fluid and electrolyte management

Renal function is commonly impaired after asphyxia and weight, creatinine, electrolytes and urine output will guide fluid management. However, be aware that hypothermic patients may need more volume due to redistribution of fluid to the tissue. Although babies may suffer acute renal failure due to the HI insult, cold induces diuresis, and this is often seen after renal function resumes towards the end of cooling. As such babies often need more volume at this stage.

- Babies may require catheterisation to assess urine output accurately.
- Maintenance fluids should start at 40-60 ml/kg/day and fluid balance assessed 6 hourly, with increments in fluids when urine output is adequate.
- Maintain electrolytes in the normal range, including calcium and magnesium levels.
- If there is renal failure, maintenance fluid may be dropped to 30ml/kg/day plus any measured losses
- Ensure blood glucose is kept in the normal range which in the fluid restricted infant may require infusion of higher dextrose concentration (>10%) through central venous access.
- Care must be taken regarding the potential accumulation of nephrotoxic drugs such as aminoglycosides in the event of renal impairment. While aminoglycosides are a common first line choice for antimicrobial therapy, it may be sensible to withhold the dose at the time of level assay until the result is known, or change to a non-nephrotoxic alternative such as a cephalosporin.

Gastrointestinal

Commencing enteral feeds in infants during therapeutic hypothermia should be considered on an individualised basis taking into account the overall clinical status. Enteral feeds should not be given in infants with significant multisystem derangement where gut perfusion may be compromised. Consideration of parenteral nutrition should be given in view of the initial catabolic state, although where there is significant electrolyte, fluid and glucose imbalance this may be complex.

Early minimal feeding may be beneficial and can be started during cooling, but the evidence is limited in this population group. Feed intolerance is common after re-warming as gut circulation may have been compromised and sedation may slow gut motility. There is an increased risk of necrotising enterocolitis in asphyxia and breast milk is preferable to formula milk. Advice and support for mothers regarding expressing breast milk should be provided early in the course of the infant's management appreciating the impact of acute stress on milk production.

Any baby in whom there are concerns with swallow or suck following rewarming should be assessed by a Speech and Language Therapist for suitability for oral

feeding. For other babies with intact gag and suck reflex, oral feeds can be introduced by either breast or bottle.

Impaired synthetic liver function/consumptive coagulopathy

A reduction in the production of clotting factors and platelets is seen with hypothermia resulting in prolonged coagulation, this is physiological. In the absence of bleeding, mild derangement of coagulation can be tolerated without treatment.

Hypothermia may have a significantly adverse effect on clotting if the patient starts out with abnormal coagulation. Be aggressive in checking coagulation and treating deranged clotting when there is a suspicion of bleeding, for example from cord, under scalp or on cranial USS.

Any drug metabolised by the liver has prolonged metabolism in hypothermia especially morphine and phenobarbitone. Avoid continuous infusions of paralytic agents or anticonvulsants where possible, using boluses as an alternative.

Infection

Perinatal infection often co-exists with HIE. All babies should have a septic screen and be commenced on antibiotics (as per local policy) as soon as possible after birth. It is important to consider viral infections such as herpes simplex, and meningitis.

Note that renal impairment may affect aminoglycoside clearance and that careful drug assay monitoring is essential, particularly if urine output is low. Many centres will perform a trough and hold before the giving the second dose.

Note that it is normal to observe a fall in white cell and platelet counts during cooling, as well as a rise in CRP.

Hypothermia is not associated with an increased risk of infection in newborn infants. However ventilated babies do need regular ET suction to clear secretions and regular positioning to avoid skin breakdown. The presence of central venous and arterial lines increases the risk of bloodstream infection.

Neurology

Seizures

Clinical seizures following HIE can be difficult to diagnose and treat. Many seizures are subclinical and only a quarter of suspected seizures have an electrical correlate. On the other hand, two thirds of electrographic seizures do not have overt clinical signs. True seizures secondary to hypoxia-ischaemia are uncommon in the first 6 hours of life and the treatment of presumed seizures within the first 6 hours will alter the neurological examination and may impair robust decision-making about the suitability of a child for therapeutic hypothermia. Other abnormalities of neurological behaviour such as tremulousness, cycling, paddling movements and oromotor dyskinesia are very common and do not require anticonvulsant treatment. As such it is recommended that treatment of seizures only occurs following confirmation on CFM.

All infants undergoing cooling should have continuous CFM monitoring as subclinical seizures are common and may be the only evidence of abnormal electrical activity if the baby is muscle relaxed, or even following anticonvulsant therapy. Symptomatic seizures or where the total electrical seizure (aEEG/EEG) burden within 1 hour is 10 minutes or longer should be treated with anticonvulsants. Seizures may re-emerge on re-warming and CFM monitoring is advised until normothermia is reached. If seizures occur during re-warming, hypothermia to 33.5°C can be re-induced for a further 24 hours and a slower rate of re-warming commenced (<0.5°C/hour).

For choice of treatment of seizures, refer to local guidelines.

Ensure that ventilation and cardiovascular status are stable and monitored before giving anticonvulsant therapy. Anticonvulsant therapy should be given intravenously to achieve a rapid onset of action and predictable blood levels. Drug levels are important when maintenance doses of these drugs are used. Slow elimination rates secondary to cooling, hepatic and/or renal injury may lead to drug accumulation and suppressed neurological activity on examination and background activity on CFM.

Hypothermia may decrease the amplitude of seizures and seizure burden- possibly due to earlier detection and earlier treatment but does not affect background activity.

Note that Lidocaine should not be given if Phenytoin has already been given due to similar arrhythmogenic effects. Other causes of intractable seizures in neonates should be considered, e.g. Pyridoxine deficiency and other inborn errors of metabolism.

Electroencephalography (EEG)

A formal EEG provides information on regional background cerebral activity and can detect some seizures and other abnormalities not seen using aEEG. However, access to neurophysiology services both to perform and interpret the examination can be limited. The most useful prognostic information can be obtained once the infant has been rewarmed and off anticonvulsant medication.

EEG may also be important in the following circumstances:

- If needed clinically to confirm or exclude electrical seizures
- Where aEEG background has not returned to normal at end of cooling
- Continuing clinical concern about encephalopathy after the period of cooling

Cranial ultrasound Scans (CUSS)

Cranial ultrasound scans can provide vital information on infants with HIE. The diagnosis of HIE can be complicated, and other disease processes may present in a similar way such as neonatal stroke. For this reason, a cranial USS should be performed in any infant with suspected HIE, ideally prior to their transfer to a Cooling Centre. Refer to local guidance for image acquisition and interpretation. Scans should be performed on admission and then daily for the first three days of life.

Possible USS Findings in HIE

- Early cerebral oedema – generalised increase in echogenicity, indistinct sulci and narrow ventricles, loss of normal tissue differentiation
- After 2-3 days of age, increased echogenicity of thalami and parenchymal echodensities
- Haemorrhage
- Relative increase of end-diastolic blood flow velocity compared to peak systolic blood flow velocity (Resistive Index <0.55) in anterior cerebral artery predicts poor outcome.

MRI

All infants undergoing TH should have an MRI scan undertaken between 5 and 15 days, preferably between 5 and 7 days of birth. This is best performed in the treating NICU and should be reported by a consultant radiologist with expertise in neonatal brain MRI interpretation. Where possible, Proton (^1H) MRS Lactate/N acetyl aspartate (Lac/NAA) of the basal ganglia and thalamus should be performed with the MRI at 5-10 days after birth. This is the most accurate predictor of outcome in babies who have undergone TH.

Analgesic and sedative therapy

All babies should receive analgesia and sedation as being cold is stressful and unpleasant. Preventing stress can be seen as a component to limit further injury in vulnerable brain. However, it is also important to recognize that medications can have the potential to profoundly alter the developing brain in critically ill encephalopathic neonates.

Infants undergoing therapeutic hypothermia treatment may not be able to display typical behavioural signs of pain and physiological parameters may also be altered. A persistently high heart rate, shivering and facial grimacing may all indicate that a baby is experiencing discomfort and it is not unusual for babies to require an increase in sedation dose. It is important to assess regularly whether the baby is irritable, shivering or has clonus. Shivering has been shown to reduce the neuroprotective effects of cooling and so sedation should be considered to minimise this. Sedation should not be withheld to avoid respiratory depression which can be easily supported with ventilatory adjuncts.

There have not been clinical trials to determine the most appropriate analgesic or sedative or the regimen (repeated boluses or continuous infusion). The type of analgesic or sedative can be guided according to the unit first line choice. Clinicians should be aware of the altered pharmacokinetics and pharmacodynamics of analgesic or sedative during hypothermia and the need for careful titration. Hypothermia decreases the systemic clearance of cytochrome P450 metabolised drugs (opioids and midazolam) during TH.

Common drugs used within the Scottish network include morphine and chloral hydrate. Sedation with morphine should be commenced prior to inducing hypothermia and continued throughout the cooling period. Consider whether infusion rate should be reduced after 24-48 hours to lessen the risk of toxicity due to accumulation as the metabolism of morphine is reduced during hypothermia. At 48 hours, discontinuation

of morphine should be considered. Morphine should be made up in 10% dextrose to avoid hypoglycaemia.

Chloral hydrate may also be given as an adjunct to morphine or as an alternative in non-ventilated babies. There is also a risk of over-sedation due to accumulation. Infants may need ventilatory support following sedation.

Monitoring of pain and distress

Heart rate is a good proxy marker for adequate sedation. At 33.5°C, the average heart rate is around 80-100 bpm. The heart rate changes by 14 beats per minute per 1°C change in temperature over a wide range.

If HR is high (>120bpm) despite hypothermia, the reasons may include distress and/or pain, hypovolaemia, hypotension, inotrope use, seizures.

NB if the heart rate is lower than 80bpm, this suggests the baby may be overcooled, and the position of the temperature probes should be checked immediately. It may also mean that the baby is overly sedated with morphine or anticonvulsants and the doses of these should be reduced.

Appendix 5 – Support for families

Organisation	Description
Birth Trauma Association	Helping people who are finding it hard to cope with their childbirth experience www.birthtraumaassociation.org.uk
Bliss	For babies born too soon, too small, too sick –providing vital support and advice to families of premature and sick babies across the UK. Helpline: 0808 801 0322 www.bliss.org.uk
Child Bereavement Trust	They provide specialised support, information and training to all those affected when a baby or child dies, or when a child is bereaved. www.childbereavementuk.org
Hope for HIE	Connecting families who have experienced HIE worldwide through a comprehensive support network https://www.hopeforhie.org/
PEEPS	Provides dedicated support for those affected by HIE. This includes funded counselling and trauma therapy, peer support, online groups, in person meet-ups and more. http://www.peeps-hie.org
SANDS	A stillbirth and neonatal death charity – supporting anyone affected by the death of a baby and promoting research to reduce the loss of babies' lives www.sands.org.uk

Appendix 6 - Individuals and organisations involved in production and endorsement

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Appendix 7 – References

1. [British Association of Perinatal Medicine \(BAPM\) \(2020\) Therapeutic Hypothermia for Neonatal Encephalopathy: A Framework for Practice](#). London: British Association of Perinatal Medicine. Updated 20 March 2025
2. [British Association of Perinatal Medicine \(BAPM\) \(2023\) Neonatal Brain Magnetic Resonance Imaging: Clinical indications, acquisition and reporting: A Framework for Practice](#). London: British Association of Perinatal Medicine.