Yorkshire and Humber ODN Pan Network Clinical Guideline

Title: Management of Hypoxic Ischaemic Encephalopathy Including Therapeutic Hypothermia

Authors: Adapted from the NTNN and YNN guidelines by Y&H ODN HIE group

Date written: February 2021

Review date: June 2026

This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire and Humber Neonatal ODN. It has subsequently been updated following publication of BAPM framework on Therapeutic Hypothermia. The Yorkshire and Humber Neonatal ODN recognise the recommendations of the BAPM framework and support the use of aEEG within our LNUs where the equipment and skills are available. At this time, our consensus opinion promotes excellence in passive cooling but does not support absolute use of cooling mattresses outside the NICU, having reviewed our geography and patient transport arrangements. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

Aim of Guideline

- To ensure that babies with suspected hypoxic ischaemic encephalopathy (HIE) are appropriately assessed and managed clinically.
- To ensure therapeutic hypothermia is considered and initiated appropriately
- To ensure that therapeutic hypothermia is managed in a safe and timely manner
- To outline the care pathway for the care of infants with HIE

Therapeutic hypothermia should be offered to all babies who achieve at least one criteria A , fulfil criteria B, and at least one criteria C. *See full guideline for units where aEEG not available or "special cases".*

Criteria A
Infants ≥ 36/40 with at least one of:

- Apgar ≤ 5 @ 10 mins after birth
- Continued need for resuscitation, including endotracheal or mask ventilation (not PEEP/CPAP alone) @ 10 mins after birth
- Acidosis defined as any occurrence of:
  - pH≤7.00
  - Base deficit ≥ 16

  in any cord or baby gas sample within 60 mins of birth

Criteria B
Moderate to severe encephalopathy

- Altered state of consciousness (lethargy/stupor/coma)

***AND* at least one of the following:**

- Hypotonia
- Abnormal reflexes including oculomotor or pupillary abnormalities
- Absent or weak suck
- Clinical seizures

Criteria C – aEEG to be assessed in infants that meet criteria A & B. This should NOT delay decision making or transfer if not available.
At least 30 minutes of amplitude integrated EEG recording that shows abnormal background aEEG activity or seizures. There must be one of the following:

- Normal background with some seizure activity
- Moderately abnormal activity
- Suppressed activity
- Continuous seizure activity

Index:

1. Indications for therapeutic hypothermia[1,2,3]

Therapeutic hypothermia (cooling) is an effective therapy for the treatment of newborn encephalopathy. Active cooling should only be conducted in centres that regularly cool infants and have the appropriate equipment and monitoring. Passive cooling should be considered as soon as possible after delivery, once cardiorespiratory stability has been achieved, and can occur in the hospital of birth, using these guidelines. Hyperthermia is associated with increased brain injury in animal models of hypoxic-ischaemia[4] and in infants who were not cooled for HIE[5]. It therefore must be avoided in all infants while they are being assessed for therapeutic hypothermia.

Therapeutic hypothermia should be offered to all babies who achieve at least one criteria A, fufil criteria B, and at least one criteria C (if available).

Criteria A
Infants ≥ 36/40 with at least one of:

- Apgar ≤ 5 @ 10 mins after birth
- Continued need for resuscitation, including endotracheal or mask ventilation (not PEEP/CPAP alone) @ 10 mins after birth
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At least 30 minutes of amplitude integrated EEG recording that shows abnormal background aEEG activity or seizures. There must be one of the following:

- Normal background with some seizure activity
- Moderately abnormal activity
- Suppressed activity
- Continuous seizure activity

Do not start cooling if infant:

- Is likely to require surgery during first three days after birth
- Has other major congenital abnormalities indicative of poor long term outcome
- Is felt to be dying
- Has a significant intracranial bleed

Special cases (see guidelines below):

- Infants 33-35+6 weeks
- Sudden unexpected postnatal Collapse
- Mild neonatal encephalopathy

Document time cooling (passive and active) commenced and time therapeutic range reached in the notes.

HIE often co-exists with persistent pulmonary hypertension (PPHN). Therapeutic hypothermia may worsen PPHN and risks may outweigh benefits if PPHN is severe. Initiate cooling with caution and consider rewarming if oxygenation is poor.

Neonatal encephalopathy can evolve with time. Therefore infants who meet criteria A but are neurologically normal on initial examination should be reviewed at least 3 times in the first 6 hours of life (1st hour, 2 hours and between 4-6 hours of age) by a trained practitioner who is competent in neurological examination.

Therapeutic hypothermia incurs most benefit if initiated within 6 hours of the insult therefore every effort should be made to diagnose infants as soon as possible. There is only modest evidence that initiating cooling between 6 and 24 hours might be of benefit[6], however, in the absence of evidence of harm or other treatments, clinicians may decide to initiate therapeutic hypothermia in this context.

It is important to note that there is a tension between the evidence of increased benefit the earlier that therapeutic hypothermia is initiated, and the concept that it would be better not to cool infants whose later review would suggest that therapeutic hypothermia was not indicated, or that the initiation of cooling might distract attention from the important task of stabilisation. This uncertainty, combined with variation in skill-mix and staffing between units might lead to a small variation in local practice based on this guideline.

If possible, confirm severity of encephalopathy with amplitude integrated electroencephalography (aEEG)) before commencing therapeutic hypothermia. aEEG is a very helpful tool in obtaining evidence of cerebral depression as well as in ongoing management of these infants, including prognostication and recognition of seizures[7]. Using aEEG as part of eligibility may reduce the number of babies cooled unnecessarily. Normal initial aEEG indicates a high probability of normal outcome. In this case therapeutic hypothermia is unlikely to be beneficial, and if treatment has been commenced the neonatal consultant may consider discontinuing. **However, initiation of cooling in infants who are clearly neurologically abnormal, or transfer to an NICU, should not be prevented or delayed whilst awaiting aEEG data.**

Special cases:

Therapeutic hypothermia can be commenced in the following special circumstances after thorough discussion with a neonatal intensive care consultant (with ideally a second neonatal intensive care opinion sought) & parents

Infants 33-35+6 weeks

There is currently no randomised controlled trial evidence to support the use of therapeutic hypothermia in infants less than 36 weeks. Many cooling centres have offered therapeutic hypothermia to selected infants from 33-35 weeks and have published non controlled case series[8] in which the possibility of higher risk of complications including hyperglycaemia, death and brain injury exists[9]. Therapeutic hypothermia for these infants should only be undertaken after careful consideration including a detailed discussion with the parents including explaining the risks of therapeutic hypothermia which may be increased in such late preterm infants, and the limitations of the evidence suggesting benefit. A second opinion from a consultant would be good practice and this should always occur for infants born outside a neonatal intensive care. The basis and outcome of these discussions should be clearly documented.

Sudden Unexpected Postnatal Collapse

There is currently no randomised controlled trial evidence to support the use of therapeutic hypothermia in infants who have signs of moderate or severe encephalopathy following a postnatal collapse, and given the rarity of this condition high-quality trial data is unlikely to become available. However, many animal models of neonatal hypoxic-ischaemic encephalopathy that demonstrate the effectiveness of therapeutic hypothermia involve a postnatal insult.

Moreover a cohort study indicated that the outcomes of infants cooled following postnatal collapse are similar to that of infants cooled for presumed HIE, providing circumstantial evidence that therapeutic hypothermia might be of benefit[8]. As the underlying conditions leading to sudden unexpected postnatal collapse are varied, including conditions in which therapeutic hypothermia may carry adverse risks, it is recommended that every effort is taken to understand any underlying reasons for collapse preferably before therapeutic hypothermia is initiated. It is recommended that decision-making involves a second senior person, and that the decision is taken in conjunction with the parents with an explanation of the potential risks and benefits.

Mild neonatal encephalopathy

There is no clear agreed definition of mild neonatal encephalopathy but it is commonly based on one or two identified features in a standard neurological examination in the context of features suggesting perinatal hypoxia. There is some evidence of increased neurological morbidity in this group[10]. However, in the absence of any evidence of benefit, therapeutic hypothermia for mild HIE is not recommended outside of clinical trials[11].

2. Criteria for defining encephalopathy:

BAPM framework[3] suggests that repeated neonatal neurological examination is based on a modified Sarnat scoring system. The presence of stage 2 or 3 encephalopathy is defined by seizures or the presence of signs in at least 3 of the remaining 6 categories below. If repeated examination within the 6 hours after birth suggests deterioration to stage 2 or 3, apply aEEG if not already in place and commence therapeutic hypothermia if meets criteria C.

Domain	Stage 1 (mild)	Stage 2 (moderate)	Stage 3 (severe)
Seizures	None	Focal or multifocal seizures	Uncommon (excluding decerebration) Or frequent seizures
Level of consciousness	Normal Hyperalert	Lethargic Decreased activity in an infant who is aroused and responsive Can be irritable to external stimuli	Stuperose/ comatose Not able to rouse and unresponsive to external stimuli
Spontaneous activity when awake or aroused	Active Vigorous, does not stay in one position	Less than active Not vigorous	No activity whatsoever
Posture	Moving around and does not maintain only one position	Distal flexion, complete extension or frog – legged position	Decerebrate with or without stimulation (all extremities extended)
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 extension of limbs followed by flexion	Suck: weak Moro: incomplete	Suck: completely absent Moro: completely absent
Autonomic system	Pupil – normal size Reactive to light Heart rate normal >100 Respirations - normal	Pupils – constricted <3mm but react to light Heart rate: bradycardia (<100 variable up to 120) Respirations: periodic irregular breathing effort	Pupils: fixed dilated, skew gaze not reactive to light Heart rate: variable inconsistent rate, irregular, may be bradycardic Respirations: completely apnoeic requiring positive pressure ventilation

3. Passive Cooling Guideline

- Stop active warming by turning off heat sources.
- Continuous rectal temperature monitoring is essential with documentation every 15 minutes
- Maintain the rectal temperature between 33.0–34.0°C by passive cooling only (heater off and removal of clothing).
- Turn the heater on if the rectal temperature is less than 33.5 °C and continue to closely monitor the rectal temperature.
- When continuous rectal temperature monitoring is used, insert rectal thermostat/probe into the anus to at least 2cm (acceptable ranges between 2-5cm) and fix it to the thigh. It is very important that the probe is inserted to this depth to accurately measure the core temperature but there is also risk of perforation so the probe should not be advanced beyond this point and should not be advanced if resistance is felt.
- It is preferable to use a platform or resuscitaire in the neonatal unit for passive cooling. However, if not possible due to local constraints, the unit should have available a cold incubator (i.e. not pre-warmed) for this purpose which can be used with the portholes open.

Do not delay passive cooling to await the arrival of the transport/retrieval team.

Risks and Precautions

- Continuous rectal temperature monitoring is essential.
- Ensure low reading thermometer is used to check axilla temperatures- some will have a lower limit with leads to false readings.
- Do not allow the temperature to fall below 33°C
- Active cooling with the use of a fan, or using cool bags of fluids can cause overcooling and is discouraged. These methods should only be used with rectal monitoring.
- **Ice packs must not be used to reduce the infant's temperature as they can result in severe hypothermia**

4. General care for infants with Hypoxic Ischaemic Encephalopathy

The main principle of the management of these infants is to maintain normal homeostasis. Good documentation is essential.

At delivery

- Adequate resuscitation, as per the Newborn Life Support (NLS) guidelines
- Ask for arterial and venous umbilical cord gases and document in baby's notes
- If encephalopathy is clearly apparent, the baby is ≥36wks gestation and resuscitation is complete with cardiorespiratory stability achieved (including heart rate and oxygen saturation), consider commencing passive cooling by switching off the overhead heater. We note again the balance discussed above between earliest initiation of cooling and completion of a full assessment and, unless the case is very clear-cut, we advise maintaining normothermia (in particular avoiding hyperthermia) in delivery suite pending full assessment on arrival to the neonatal unit.
- If initiating passive cooling, monitor temperature continuously and avoid overcooling.
- Ask for placenta to be sent to histopathology

Postnatal collapses – It is important to consider other diagnoses, such as sepsis and metabolic disorders. Refer to BAPM guideline for recommended investigations.[12]

Ongoing care

Ventilation

- Consider artificial ventilation to maintain gaseous exchange or if respiratory effort insufficient.
- Maintain PaO2 6-10 kPa, PaCO2 5-7 kPa.

- Hypocapnia should be avoided as independently associated with unfavourable outcomes. Some babies spontaneously hyperventilate and this cannot easily be prevented, but consider ventilation and sedation if extreme and persistent.
- Low dose morphine (10micrograms/kg/hr) may be used as sedation acutely, but may require to be discontinued later to allow adequate assessment of the baby's neurological status, especially if considering withdrawal of intensive care.
- Avoid paralysis unless essential for effective ventilation.

Cardiovascular system

- Obtain central vascular access, both venous and arterial (UAC/UVC).
- Collect samples for FBC, CRP, U&Es, Ca, Mg, LFTs, group & save, cultures & baseline clotting.
- Bradycardia at 80-100 is normal.
- Rise in heart rate may be due to distress, hypovolaemia, hypotension, seizures or inotropes.
- In term infants the mean arterial blood pressure (MAP) should be > 45mmHg
- If MAP <45mmHg consider the following:
    - Single 10ml/kg 0.9% saline bolus, taking into account any fluid given during resuscitation.
    - Further 0.9% saline bolus or blood product replacement **only** if evidence of hypovolemia e.g. feto-maternal haemorrhage.
    - Only use bicarbonate boluses if prolonged acidosis is causing compromise- the acidosis is usually due to anaerobic metabolism during the hypoxic ischaemic insult and will usually correct without intervention
    - If MAP remains low there may be depressed myocardial function and large volumes of colloid or crystalloid may be harmful, causing worsening hypotension and increasing risk of cerebral oedema.
    - As hypotension likely to be related to myocardial dysfunction suggest start with 5-10 micrograms/kg/min dobutamine, titrated up to a maximum 20 micrograms/kg/min. Add dopamine or noradrenaline if insufficient response
    - Consider performing echo and ECG.

Fluids & Metabolic

- Start 10% dextrose at 40ml/kg/day, but review carefully in the light of progress at least 3 times in the first 24 hours.
- Maintain normoglycaemia, particularly avoiding hypoglycaemia (<2.6mmol/L) – increasing glucose concentration rather than volume will avoid fluid overload. If a bolus is required concentration should be increased to avoid the need for multiple boluses.
- Watch for SIADH and avoid severe hyponatraemia.
- Monitor and treat hypocalcaemia (due to transient hypoparathyroidism and sick cell syndrome) and hypomagnesaemia.
- Check the lactate soon after admission, but remember the acidosis is usually metabolic due to anaerobic metabolism and will usually correct without volume or bicarbonate.
- Check LFTs and consider full metabolic screen
- Monitor the urine output and have a low threshold for catheterisation.
- Test the urine for blood and protein.
- If urine output is poor treat as renal failure with fluid restriction, but remember that prolonged fluid restriction may exacerbate or even cause renal failure.
- Avoid hypovolaemia once diuresis starts, may need to liberalise to 60ml/kg/day.

CNS & Seizures

- Use aEEG early, if available, to establish severity of encephalopathy. It may also be used to monitor seizures.
- Perform a neurological examination, including assessment of pupils, and document the clinical stage of encephalopathy (see appendices C and D).
- If need for therapeutic hypothermia is unclear, full neurological examination should be repeated at least 3 times in the first 6 hours of life (1st hour, 2 hours and between 4-6 hours of age) as encephalopathy can evolve. See Appendix D

- Consider requesting a formal EEG.
- Consider treating seizures which are confirmed with aEEG, particularly if they are associated with physiological disturbance, are prolonged (>3 minutes) or frequent (>3 per hour).
- If aEEG is not available, only treat seizures after discussion with neonatal intensive care consultant as treatment may affect clinical assessment and subsequent aEEG interpretation.
- There is no evidence that prophylactic anticonvulsants are of benefit and they should not be given.
- Detection of seizures is an indication for urgent review of blood sodium, glucose, calcium and magnesium.
- Use intravenous phenobarbital as first line treatment in babies undergoing therapeutic hypothermia, with a dose of 20 mg/kg given over 20 minutes. Repeat in a dose of 10-20 mg/kg to a maximum of 40 mg/kg if seizures continue. Note that in babies who are not ventilated respiratory depression can occur at these high doses.
- In babies who do not respond to phenobarbital consider phenytoin IV 20 mg/kg over 30 minutes. Levetiracetam 20mg/kg IV over 15 minutes with repeat doses to a maximum of 40 mg/kg, or midazolam 150 micrograms/kg over 5 minutes followed by a continuous infusion of 60 micrograms/kg/hour (max 300 microgram/kg/h) being aware that midazolam levels will accumulate. Lidocaine has also been shown to be effective but dosing should be modified in therapeutic hypothermia and avoided if phenytoin has already been given[13].
- Opisthotonic and tonic generalised seizures after profound asphyxia may have no EEG correlates and may not benefit from anticonvulsants.
- While seizures are common in HIE, unremitting seizure activity should lead to consideration of other causes of epileptic encephalopathy, including consideration of a trial of pyridoxine
- Morphine sedation for comfort during therapeutic hypothermia (10mcg/kg/hr is usually sufficient for comfort).

Imaging:

- All infants undergoing therapeutic hypothermia should have an early cranial ultrasound, ideally within 12 hours, to exclude other causes of encephalopathy, anatomical abnormalities and intracranial haemorrhage. Particularly if unusual features suggestive of other intracranial pathology e.g. asymmetrical neurology, unusual perinatal history.
- Cranial ultrasound is less sensitive than MRI for the detection of small or subtle problems (e.g. focal arterial infarction).
- All infants undergoing therapeutic hypothermia should have an MRI performed between 5 and 15 days, preferably between 5 to 7 days after birth. This would be best performed in the treating NICU and should be reported by a consultant radiologist with expertise in neonatal brain 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 5-15 days after birth. This is the most accurate predictor of outcome in babies who have undergone therapeutic hypothermia. There is much more detailed guidance regarding MRI and spectroscopy in appendix 1 of the BAPM framework[3].

Sepsis

- Start antibiotics after taking cultures if clinically indicated.
- If using gentamicin, do pre dose level and wait for result before giving second dose, because of risk of acute renal injury.
- Physiological drop in white cell count and platelets is common in therapeutic hypothermia
- C-reactive protein rise with therapeutic hypothermia and may not be a sensitive marker of infection

Feeding:

- Consider trophic breast milk if there is no ongoing organ dysfunction or poor perfusion.
- Give colostrum as mouth care where available in all.

- Feed intolerance is common as gut circulation may have been compromised, this may increase the risk for necrotising enterocolitis (NEC) [14], therefore breast milk is preferable and feeds should be introduced gradually

Monitoring:
Monitoring throughout the therapeutic hypothermia and rewarming period should include:

- Continuous blood pressure monitoring (ideally invasive)
- Continuous oxygen saturation
- Continuous respiratory monitoring
- Continuous electrocardiograph (ECG)
- Continuous amplitude integrated electroencephalography (aEEG) commenced as soon as possible, if available. This is prognostic and may assist in guiding therapy (treatment of significant electrical seizures may lessen excitotoxic damage)
- Continuous rectal temperature monitoring
- Documented observations including:
    - Urine output

    And hourly:
    - oxygen saturation
    - heart rate and blood pressure
    - respiration rate
    - Temperature (for continuous rectal temp document every 15 minutes and hourly for Axilla)

Daily investigations (and more frequently if abnormal):

- Blood gases, electrolytes, glucose and lactate (may all be obtained from the blood gas sample)
- Full blood count including platelets, liver function tests, clotting (which may be sampled from an arterial line)
- Coagulopathy is physiological in therapeutic hypothermia but only active bleeding needs treatment. Be alert for any evidence of intracranial bleeding and consider correcting coagulation accordingly.

Parents
Senior member of medical team should speak to family as soon as possible to explain level of concerns mentioning risk of death & disability. Discuss use of aEEG and therapeutic hypothermia if appropriate (see section 5).

Transfer
Infants who may require transfer for therapeutic hypothermia/intensive care should be referred as early as possible to enable the team to mobilise quickly. These infants will require:

- Full documentation (Badger)
- X-rays made available to receiving centre
- 2 points of IV access
- Labelled maternal blood sample for cross match

There should be timely transfer of mothers after delivery to ensure there are no barriers to parents being with and caring for their baby and to minimise separation.

Active cooling
Active cooling in tertiary centres is not covered in the guidance and management of equipment should be supported by local/manufacturer guidance.

Rewarming
Rewarming is also not covered in this guidance and should be addressed in the local guidance as outlined above but as a rule when rewarming the rectal temperature should be allowed to rise by no more than 0.5°C per hour, to 37±0.2°C.

The infant's temperature must be carefully monitored for 24 hours after normothermia has been achieved to prevent rebound hyperthermia, as this might be detrimental.

Developmental Care
Aim to ensure the wellbeing and optimal development of the infants throughout care for HIE, acknowledging the potential long-term consequences of adverse experiences during the neonatal unit and strives to mitigate their impact.

Developmental care practice includes:

- Ensuring infants receive individualised and responsive care
- Implementing developmentally supportive techniques
- Engaging in family centred care
- Optimising infant's sensory experience (adapt the environment when possible)
- Reducing the infant's pain and stress

Please refer to the Yorkshire and Humber Family Care Training package (include link).

Governance
Ensure there is a timely multidisciplinary and multispecialty review, following standardised Trust risk management procedures, of the perinatal care of any infant who undergoes therapeutic hypothermia with a particular focus on avoidable factors. These cases will also undergo Healthcare Safety Investigation Branch (HSIB) review. This should be discussed with parents in a timely open and honest way, meeting standards of GMC/NMC duty of candour.

There should be annual review and benchmarking, using consistent criteria and definitions, of therapeutic hypothermia and neonatal encephalopathy cases across network units.

There should be formal logs of training and competence in the key skills of standardised neurological examination and its interpretation, and in aEEG interpretation at trust level.

There should be clear, contemporaneous and complete documentation of decision making and management of cases where therapeutic hypothermia has been considered and initiated or not initiated including regular review of neurology and aEEG in the patient record. This should include documentation of discussions with parents.

5. Parental advice regarding therapeutic hypothermia

Criteria	Advice to parent(s)
Resuscitation	Your baby needed significant resuscitation at birth to help him/her breathe. He/she appears to have suffered from the effects of lack of oxygen and blood supply to the brain
Consequences	This can result in brain damage from direct injury and also from ongoing changes that begin around six hours after the injury
Prognosis	Babies who survive after this degree of damage to their brain may develop long-term disabilities. These disabilities include cerebral palsy and severe learning difficulties.
Treatment	Cooling babies following a period of reduced oxygen and blood supply reduces the secondary brain injury, increases the chances of survival by one fifth and reduces the risk of severe long-term disability by one third.
What does the treatment entail	Your baby will receive cooling therapy (therapeutic hypothermia) in addition to standard intensive care support Your baby's temperature will be slowly lowered and kept between 33 to 34°C for 72 hours. Your baby's temperature and other vital signs will be closely monitored throughout the process. If your baby shows any signs of discomfort during cooling he/she will be prescribed medication to reduce this. After 72 hours of cooling therapy, your baby will be gradually rewarmed to a temperature of 37°C

There is a Bliss parent information leaflet available at https://shop.bliss.org.uk/en/products/parent-resources/hie-a-guide-for-parents

PEEPS HIE are the only UK charity dedicated to supporting those affected by HIE (Hypoxic-Ischaemic Encephalopathy). They offer free emotional, practical and financial support, for any family regardless of cause or outcome. They also provide free parent packs to neonatal units across the UK to offer families support and advice as and when they are ready. The website is found at www.peeps-hie.org.

Parent information leaflets from PEEPS:

Alongside, specific information about HIE ensuring that all neonatal care is psychologically informed will protect the baby and their family from the potentially damaging impact of the neonatal experience and create neonatal environments in which the best care can be provided. Please see appendix 5 for more information and link to e-learning.

6. Amplitude-integrated EGG (aEEG)

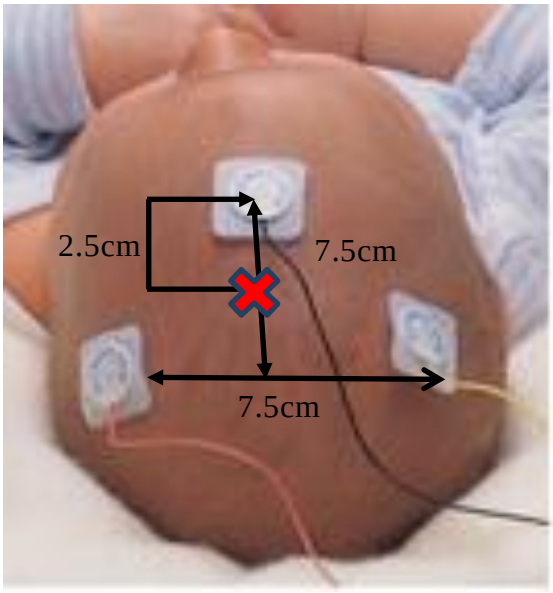
An amplitude-integrated EEG (aEEG), or Cerebral Function Monitor (CFM), is a device used to measure electrocortical activity in the brain. An abnormal aEEG trace in the first six hours of life, after an asphyxial insult, is predictive of abnormalities on acute neurological testing and long term neurodevelopmental outcome.

Either single channel or dual aEEG can be used. The site of electrode placement is as described below for both types but please refer to local guidelines for your monitor. Needle EEG electrodes are commonly used and the use of collodion may be considered to hold the electrodes in place.

Note that interpretation requires some degree of expertise and therefore aEEG may not be appropriate in all settings. The indications for the use of therapeutic hypothermia are clinical and aEEG only acts as an adjuvant to this.

Trusts with aEEG should ensure there is suitable storage of electronic aEEG files in compliance with the Data Protection Act, in ways that can be easily retrieved if later case review is required.

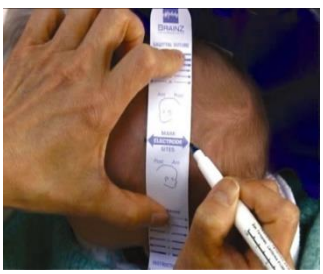
Single channel

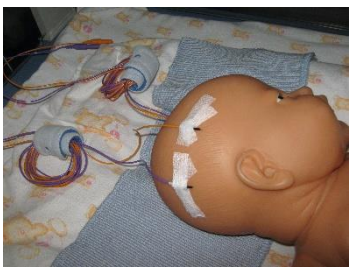


✖ fontanelle

Dual channel

2 leads each side and a central reference electrode as with single channel above or a gel reference electrode placed on the shoulder.

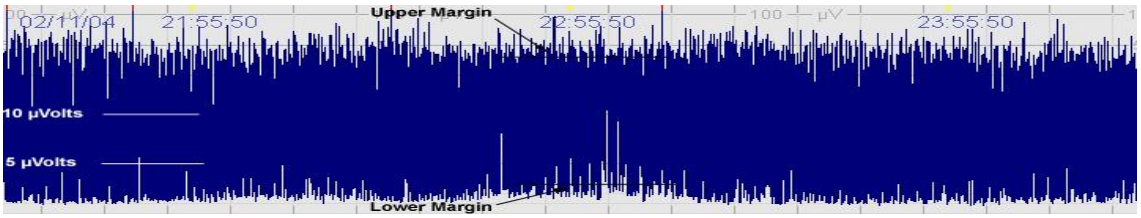




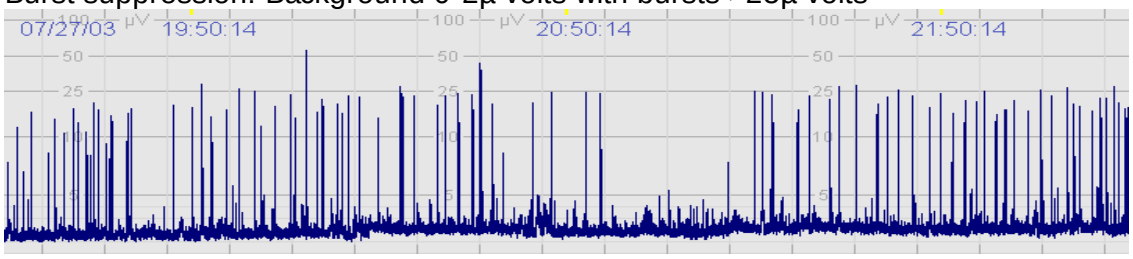
Position the strip vertical and parallel to the baby's face. Align strip so that the letter (A-H) at the saggital suture is the same as the letter at the tragus	Using a marker pen, mark the two sensor sites at the ends of the arrows.	Insert a needle electrode subdermally at insertion sites. Leads are directed to the top of the head Ensure all metal is under the dermal layer

Normal aEEG:
Sleep/wake cycle, upper margin >10µ volts, lower margin > 5µ volts, limited variability

Moderately abnormal aEEG:
Discontinuous normal voltage: No sleep/wake cycle, upper margin >10 µ volts, lower margin < 5µ volts



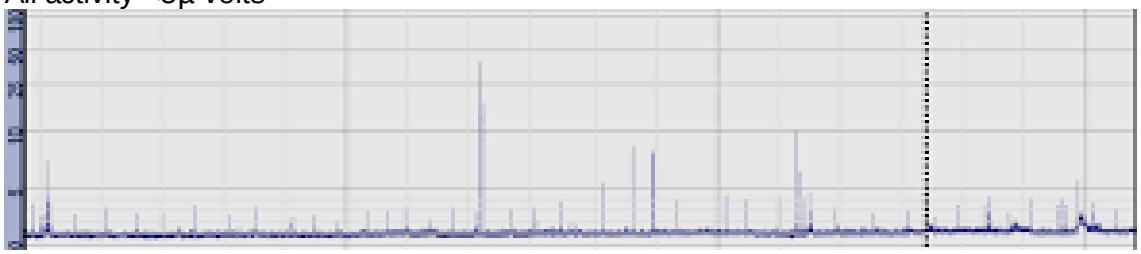
Severely abnormal aEEG:
Burst suppression: Background 0-2µ volts with bursts >25µ volts



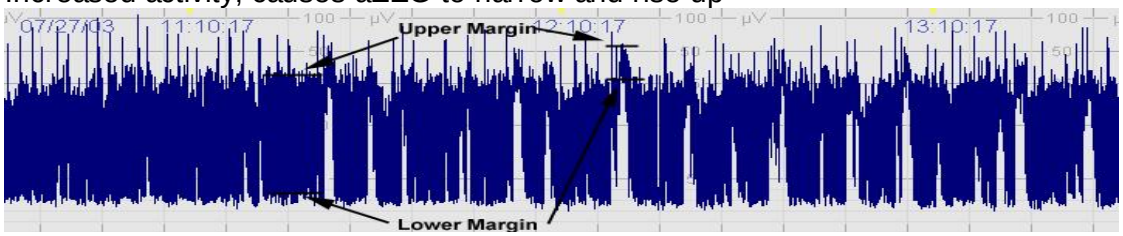
Low voltage:
Upper margin < 10µ volts, lower margin < 5µ volts, greatly reduced variability

Isoelectric:

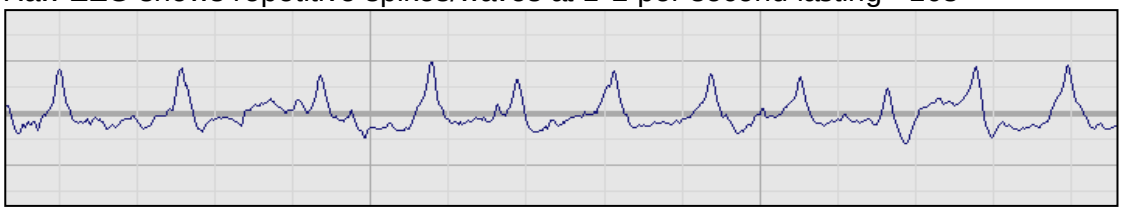
All activity <5µ volts



Seizures:
Increased activity, causes aEEG to narrow and rise up



Raw EEG shows repetitive spikes/waves at 1-2 per second lasting >10s



7. Complications of therapeutic hypothermia

Complications of therapeutic hypothermia are infrequent and symptoms may also be related to the effects of the original asphyxial insult on all systems.

Adverse effects which are transient and reversible with warming include[15]

- sinus bradycardia
- hypotension requiring inotropic treatment
- increased oxygen requirement
- thrombocytopenia and coagulopathy
- fat necrosis

However, no clinically significant complications related to treatment with therapeutic hypothermia in asphyxiated infants have been reported to date.[16-18]

8. Prognosis

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

Good prognostic features
Stage 1 encephalopathy
Absence of fits in first 24 hours
Resolution of fits, off anticonvulsants, by 7 days
Ability to suck and feed by 7 days

Poor prognostic features
Stage 2/3 encephalopathy

Encephalopathy >5 days
Unreactive or discontinuous EEG
Ultrasound evidence of thalamic or extensive parenchymal involvement

Prognosis by stage of encephalopathy
Early onset neonatal encephalopathy is the best single predictor of long-term outcome
Quick recovery is associated with a better outcome

Stage 1 (Mild)
Wide-eyed, hyper-alert, irritable, weak suck, normal tone. No seizures, normal EEG. Resolves in 24 - 48 hrs. Normal neurologic outcome in greater than 90% of cases.[19]

Stage 2 (Moderate)
Lethargy, little spontaneous movement, hypotonia. Brisk reflexes, sustained clonus, weak or absent suck. Small pupils, doll's eye movements present, apnoeas. Clinical or electrophysiological seizures. Should resolve within 5 days. Majority normal on follow-up. Risk of abnormality higher if prolonged encephalopathy. Incidence of poor outcomes ranges from 30 - 60%.[19]

Stage 3 (Severe)
Coma, flaccidity, diminished or absent reflexes, usually require assisted ventilation. Absent doll's eye movements, absent gag reflex. Poorly reactive or absent pupillary light reflex. Most die. Severe neurological abnormality in survivors.[19]

Prognosis by electroencephalogram abnormality
Background EEG abnormalities, detected in the first few days of life after HIE can provide prognostic information even in babies treated with hypothermia. Grade of abnormality predicts the rate of death or severe handicap.[7,20]

At 6 hours of age a moderately abnormal aEEG gives a PPV for disability of 0.23, and a severely abnormal aEEG a PPV of 0.55.[21]

Failure of improvement of the aEEG to moderately abnormal/normal by 48 hours of age suggests a 90% chance of death or severe disability.[22]

Prognosis by MRI findings
MRI is an established investigation in the evaluation of neonates with suspected hypoxic-ischaemic encephalopathy (HIE). However, its role as a predictor of neurodevelopmental outcome remains complex.

Grade 1 (mild) MR changes	Normal outcome [23]
Grade 3 (severe) changes	Death or severe disability

There is further information regarding MRI following therapeutic hypothermia in appendix 1 of the BAPM framework.[3]

Given the nature of severe neonatal encephalopathy and associated multi-organ pathology there will be some infants for whom the reorientation of care to a palliative pathway is appropriate.

In infants in whom it is possible to deliver therapeutic hypothermia with physiological stability, it is recommended that such consideration be delayed for 48 hours to assess any recovery before considering reorientation of care.

Consideration should be given to the drugs that have been administered and appropriate tests should be undertaken to ensure that the assessment of prognosis has not been confused by drug effects.

If a baby is in a poor prognostic group consider early (<5days) MRI to aid decision making. Palliative care and referral to local hospice should be offered to babies who are dying or where life sustaining treatments are being withdrawn due to poor prognosis.

9. Follow up

All infants undergoing therapeutic hypothermia should have an MRI should be performed between 5 and 15 days, preferably between 5 to 7 days after birth.

Ensure regular neurodevelopmental follow up after discharge. It is a National Neonatal Audit Programme (NNAP) requirement that all babies who have received therapeutic hypothermia as treatment for HIE, should be followed up for long term neurodevelopmental assessment at 2 years. BAPM guidance is that this 2 years assessment should ideally be a standardised neurodevelopmental assessment such as the Griffiths, Mullen or Bayley.

Referral for therapy input: Babies in high and medium risk groups should have early and sequential assessments with experienced medical and/or Paediatric Allied Health Practitioners. This should be aimed at early detection of developmental problems with early intervention, in order to optimise outcomes.(3)

All parents whose child has died following intrapartum hypoxic-ischaemia should be offered a post mortem examination. Organ and heart valve donation should also be considered in these cases. The family should be offered bereavement support and referral to the local children's hospice.

10. Theory and Evidence for Therapeutic Hypothermia

Neonatal encephalopathy has an incidence of approximately 3/1000 births, with hypoxic-ischaemic encephalopathy (HIE) occurring in approximately 1.5-2/1000.[24]

A word to use with caution: asphyxia is a term which is often used in the wrong context, and when used incorrectly may have serious medico-legal consequences. Be careful not to mislabel an infant with low Apgar scores at birth and who requires resuscitation, but has no other problems, as 'asphyxiated'. It is recommended that the terms 'perinatal asphyxia', 'birth asphyxia' and 'HIE' not be used until or unless there is some available evidence specific to the asphyxial origin for the neurological illness in the baby. "Poor condition at birth" can be used

Hypoxic-ischaemic insult occurring around the time of birth may result in neonatal encephalopathy. Affected infants may present with a need for resuscitation at birth, neurological depression, seizures and cerebral function monitoring abnormalities. The risk of death or neurodevelopmental abnormalities increases with the severity of the encephalopathy.

Evidence:

Results of 11 randomised controlled trials, including the UK total body cooling trial (TOBY) confirm that 72 hours of therapeutic hypothermia to a core temperature of 33-34 °C started within six hours of birth reduces death and disability at 18 months of age and improves a range of neurodevelopmental outcomes in survivors. [25-28]

A Cochrane review concluded "Therapeutic hypothermia resulted in a statistically significant and clinically important reduction in the combined outcome of mortality or major neurodevelopmental disability to 18 months of age (typical RR 0.75 (95% CI 0.68 to 0.83); typical RD -0.15, 95% CI -0.20 to -0.10); number needed to treat for an additional beneficial outcome (NNTB) 7 (95% CI 5 to 10) (8 studies, 1344 infants). Therapeutic hypothermia also resulted in statistically significant reductions in mortality (typical RR 0.75 (95% CI 0.64 to 0.88), typical RD -0.09 (95% CI -0.13 to -0.04); NNTB 11 (95% CI 8 to 25) (11 studies, 1468 infants) and a reduction in neurodevelopmental disability in survivors (typical RR 0.77 (95% CI 0.63 to 0.94), typical RD -0.13 (95% CI -0.19 to -0.07); NNTB 8 (95% CI 5 to 14) (8 studies, 917 infants)." [27]

With current practice of therapeutic hypothermia, mortality due to HIE has reduced from 25% in the clinical trials to 9% and disability from 20% to around 16% with a reduction in the rate of cerebral palsy, although some of this improvement may be due to the use of hypothermic therapy in some

infants with less severe brain injury.[29,30] However, not all children benefit from treatment and some level of intellectual impairment may remain even in the absence of cerebral palsy.[31]

NICE and BAPM support the use of this treatment in selected neonates with HIE.[1, 3]

No single factor predicts outcome (death or disability) with absolute certainty. Apgar score alone is a poor predictor of outcome. Apgar scores at 10 minutes provide useful prognostic data before other evaluations are available for infants with HIE. Death or moderate/severe disability is common but not uniform with Apgar scores < 3; caution is needed before adopting a specific time interval to guide duration of resuscitation.[32]

In a large series of infants, an Apgar score of 0-3 at 20 minutes was associated with death within one year in 59% of infants and cerebral palsy in 57% of the survivors.

Actions of therapeutic hypothermia

Hypothermia appears to have multiple effects at a cellular level following cerebral injury. Hypothermia reduces vasogenic oedema, haemorrhage and neutrophil infiltration after trauma. In addition mild hypothermia may reduce the activation of the cytokine and coagulation cascades through increased activation of suppressor signalling pathways, and by inhibiting release of platelet activating factor. Experimental studies show that following hypoxic-ischaemic injury, mild induced hypothermia – a reduction of body temperature by 3-4°C – preserves cerebral energy metabolism, reduces cerebral tissue injury and improves neurological function. Randomised trials in full term and near full term newborns suggest that treatment with mild hypothermia is safe and may improve survival without disabilities up to 18 months of age, but long term efficacy and safety are yet to be established.

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12. Appendices

Appendix A - Bliss parent information leaflet: https://shop.bliss.org.uk/en/products/parent-resources/hie-a-guide-for-parents

Appendix B - PEEPS leaflet:
Info-after-NICU.pdf (peeps-hie.org)
Peeps-Leaflet-V5.pdf (peeps-hie.org)

Appendix C Psychologically informed care
Ensuring that all neonatal care is psychologically informed will protect the baby and their family from the potentially damaging impact of the neonatal experience and create neonatal environments in which the best care can be provided.

In the implementation of this guideline consider the following:

- Infant and parent focus:
    - How can we ensure that parents are truly partners in care and what would enable them to support their baby?
    - What are the parent's/ family's understanding, feelings and opinions regarding this element of care? How can this be explored further if needed and appropriately supported.
    - Are there any additional support needs arising for the family, either in communication about this practice / procedure, during the procedure, or following it?
- Staff focus:
    - Is this element of care particularly challenging for the staff involved, for instance, in delivery of the procedure itself, complex team working, supporting babies in distress, or in communication and support of the parents and family?
    - Have you checked this with your team and considered how you can support each other in the preparation, throughout and following the procedure?

For more information see: Psychologically Informed Neonatal Care elearning
Psychologically-Informed Neonatal Care - elearning for healthcare (e-lfh.org.uk)

Appendix D – Assessment prior to Therapeutic hypothermia

Appendix E – Therapeutic hypothermia Daily Assessment 1, Daily Assessment 2, Daily Assessment 3

Appendix D

Assessment prior to therapeutic hypothermia

Date of Birth: Time of Birth:

Gestation: Weight: OFC:

Apgar score at 10 minutes:

Continued need for resuscitation at 10 minutes of age: Yes/No

Gases: Cord arterial Cord venous Admission gas

pH:

BE:

Lactate:

Name:
DOB:
Hosp number:
NHS number:

Does the infant meet any exclusion criteria (see reverse page): Yes/No

		Documentation of Review			Sarnat scoring system		
		1st hour	2 hours age	4-6 hours age			
		Date: Time: Age:	Date: Time: Age:	Date: Time: Age:	1	2	3
Sarnat scoring system (grade 1-3)	Seizures	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	None	Focal or multifocal seizures	Uncommon (excl. decerebration) Or frequent seizures
	Conscious level	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	Normal Hyperalert	Lethargic Decreased activity Can be irritable	Stuperose/ comatose Unresponsive to external stimuli
	Activity	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	Active Vigorous	Less than active Not vigorous	No activity
	Posture	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	Moving, does not maintain only one position	Distal flexion, complete extension or frog-leg position	Decerebrate with/without stimulation
	Tone	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	Normal, hypertonic, or jittery	Hypotonic, focal or general	Flaccid/rag doll
	Primitive reflexes	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	Suck: vigorous Moro: normal	Suck: weak Moro: incomplete	Suck: absent Moro: absent
	Autonomic system	1 / 2 / 3	1 / 2 / 3	1 / 2 / 3	Pupils: normal size, reactive to light HR: normal >100 Resp - normal	Pupils: constricted <3mm but reactive HR: bradycardia (<100 up to 120) Resp: irregular	Pupils: fixed dilated, skew gaze, not reactive to light HR: variable, inconsistent Resp: apnoeic
	Agreed sarnat grade				Stage 2 or 3 encephalopathy is defined by seizures or the presence of signs in at least 3 of the remaining 6 categories		
aEEG (if available)		+ seizures? Y/N	+ seizures? Y/N	+ seizures? Y/N	**Normal:** Baseline>5µv, upper>10µv,sleep/wake cycle **Discontinuous:** Baseline <5µv, upper >10µv **Burst suppression:** Background 0-2µv with bursts >25µv **Low Voltage:** Baseline <5µv, upper <10µv **Flat trace:** All activity <5µv		
Decision to cool?		Y / N	Y / N	Y / N	For treatment criteria, see overleaf		
Reason for decision							
Name Signature Grade							

If cooled, date and time target temperature (33.5) reached:

Therapeutic hypothermia treatment criteria

A. Infants ≥ 36 completed weeks gestation admitted to the neonatal unit with at least one of the following:

- Apgar score of ≤5 at 10 minutes after birth
- Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth
- Acidosis defined as occurrence of any:
    - pH ≤7.00
    - Base Deficit ≥ 16 mmol/L

  in any cord or baby gas sample (venous, capillary or arterial) within 60 minutes of birth

Infants that meet criteria A should be assessed for whether they meet the neurological abnormality entry criteria (B):

B. Moderate to severe encephalopathy, consisting of:

- Altered state of consciousness (lethargy, stupor or coma)

  AND at least one of the following:
- Hypotonia
- Abnormal reflexes including oculomotor or pupillary abnormalities
- Absent or weak suck
- Clinical seizures

Infants that meet criteria A & B will be ideally assessed by aEEG:

C. At least 30 minutes of amplitude integrated EEG recording that shows abnormal background aEEG activity or seizures. There must be one of the following:

- Normal background with some seizure activity
- Moderately abnormal activity
- Suppressed activity
- Continuous seizure activity

However, initiation of therapeutic hypothermia in infants who are clearly neurologically abnormal should not be prevented or delayed whilst awaiting aEEG data.

Exclusions for therapeutic hypothermia

Do not start therapeutic hypothermia infants if:

- Is likely to require surgery during first three days after birth
- Has other major congenital abnormalities indicative of poor long term outcome
- Is felt to be dying
- Has a significant intracranial bleed

Decision to cool infants of 33-35+6 weeks should be made by 2 NICU consultants.

Appendix E

Therapeutic hypothermia: daily assessment 1

Up to 24 hours of age

Name:
DOB:
Hosp number:
NHS number:

Date and time: Age (hours):

Gestation: Weight: OFC:

Neurological Assessment – Sarnat Score

Domain	Stage 1 (mild)	Stage 2 (moderate)	Stage 3 (severe)
Seizures	None	Focal or multifocal seizures	Uncommon (excl. decerebration) Or frequent seizures
Level of consciousness	Normal Hyperalert	Lethargic Decreased activity in an infant who is aroused and responsive Can be irritable to external stimuli	Stuperose/ comatose Not able to rouse and unresponsive to external stimuli
Spontaneous activity when awake or aroused	Active Vigorous, does not stay in one position	Less than active Not vigorous	No activity whatsoever
Posture	Moving around and does not maintain only one position	Distal flexion, complete extension or frog-legged position	Decerebrate with or without stimulation (all extremities extended)
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 extension of limbs followed by flexion	Suck: weak Moro: incomplete	Suck: completely absent Moro: completely absent
Autonomic system	Pupil – normal size, reactive to light Heart rate normal >100 Respirations - normal	Pupils – constricted <3mm but react to light Heart rate: bradycardia (<100 variable up to 120) Respirations: periodic irregular breathing effort	Pupils: fixed dilated, skew gaze, not reactive to light Heart rate: variable inconsistent rate, irregular, may be bradycardic Respirations: completely apnoeic requiring positive pressure ventilation
Agreed Sarnat Score		Stage 2 or 3 encephalopathy is defined by seizures or the presence of signs in at least 3 of the remaining 6 categories	

aEEG/EEG	**Normal** Baseline>5µv, Upper>10µv Sleep/wake cycle	**Discontinuous normal voltage** Baseline <5µv Upper >10µv	**Burst suppression** Background 0-2µv with bursts >25µv	**Low voltage** Baseline <5µv Upper <10µv	**Flat trace** All activity <5µv
Seizures?	Yes / No				
Comments					

Anticonvulsants and sedatives given

Name	Date and time given

Signature: Name: Grade:

Appendix E

Therapeutic hypothermia: daily assessment 2

24 to 48 hours of age

Name:
DOB:
Hosp number:
NHS number:

Date and time: Age (hours):

Neurological Assessment – Sarnat Score

Domain	Stage 1 (mild)	Stage 2 (moderate)	Stage 3 (severe)
Seizures	None	Focal or multifocal seizures	Uncommon (excl. decerebration) Or frequent seizures
Level of consciousness	Normal Hyperalert	Lethargic Decreased activity in an infant who is aroused and responsive Can be irritable to external stimuli	Stuperose/ comatose Not able to rouse and unresponsive to external stimuli
Spontaneous activity when awake or aroused	Active Vigorous, does not stay in one position	Less than active Not vigorous	No activity whatsoever
Posture	Moving around and does not maintain only one position	Distal flexion, complete extension or frog-legged position	Decerebrate with or without stimulation (all extremities extended)
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 extension of limbs followed by flexion	Suck: weak Moro: incomplete	Suck: completely absent Moro: completely absent
Autonomic system	Pupil – normal size, reactive to light Heart rate normal >100 Respirations - normal	Pupils – constricted <3mm but react to light Heart rate: bradycardia (<100 variable up to 120) Respirations: periodic irregular breathing effort	Pupils: fixed dilated, skew gaze, not reactive to light Heart rate: variable inconsistent rate, irregular, may be bradycardic Respirations: completely apnoeic requiring positive pressure ventilation
Agreed Sarnat Score		Stage 2 or 3 encephalopathy is defined by seizures or the presence of signs in at least 3 of the remaining 6 categories	

aEEG/EEG	**Normal** Baseline>5µv, Upper>10µv Sleep/wake cycle	**Discontinuous normal voltage** Baseline <5µv Upper >10µv	**Burst suppression** Background 0-2µv with bursts >25µv	**Low voltage** Baseline <5µv Upper <10µv	**Flat trace** All activity <5µv
Seizures?	Yes / No				
Comments					

Anticonvulsants and sedatives given

Name	Date and time given

Signature: Name: Grade:

Therapeutic hypothermia: daily assessment 3

48 to 72 hours of age

Date and time: Age (hours):

Name:
DOB:
Hosp number:
NHS number:

Neurological Assessment – Sarnat Score

Domain	Stage 1 (mild)	Stage 2 (moderate)	Stage 3 (severe)
Seizures	None	Focal or multifocal seizures	Uncommon (excl. decerebration) Or frequent seizures
Level of consciousness	Normal Hyperalert	Lethargic Decreased activity in an infant who is aroused and responsive Can be irritable to external stimuli	Stuperose/ comatose Not able to rouse and unresponsive to external stimuli
Spontaneous activity when awake or aroused	Active Vigorous, does not stay in one position	Less than active Not vigorous	No activity whatsoever
Posture	Moving around and does not maintain only one position	Distal flexion, complete extension or frog-legged position	Decerebrate with or without stimulation (all extremities extended)
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 extension of limbs followed by flexion	Suck: weak Moro: incomplete	Suck: completely absent Moro: completely absent
Autonomic system	Pupil – normal size, reactive to light Heart rate normal >100 Respirations - normal	Pupils – constricted <3mm but react to light Heart rate: bradycardia (<100 variable up to 120) Respirations: periodic irregular breathing effort	Pupils: fixed dilated, skew gaze, not reactive to light Heart rate: variable inconsistent rate, irregular, may be bradycardic Respirations: completely apnoeic requiring positive pressure ventilation
Agreed Sarnat Score		Stage 2 or 3 encephalopathy is defined by seizures or the presence of signs in at least 3 of the remaining 6 categories	

aEEG/EEG	**Normal** Baseline>5µv, Upper>10µv Sleep/wake cycle	**Discontinuous normal voltage** Baseline <5µv Upper >10µv	**Burst suppression** Background 0-2µv with bursts >25µv	**Low voltage** Baseline <5µv Upper <10µv	**Flat trace** All activity <5µv
Seizures?	Yes / No				
Comments					

Anticonvulsants and sedatives given

Name	Date and time given

Signature: Name: Grade:

Version Control Table - Document History			
Date *(of amendment/ review)*	**Issue No**.*(e.g V1)*	**Author** *(Person/s making the amendment or reviewing the Guideline)*	**Detail** *(of amendment/misc notes)*
Feb 2024		Marie-Anne Kelly	Additions: -active cooling practicalities -links to resources – PEEPS/psychologically informed care