HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE) INCLUDING PREPARATION FOR ACTIVE COOLING ● 1/6

RECOGNITION AND ASSESSMENT

The following points are useful when making a diagnosis of HIE:

- History of a sentinel event, e.g. abruption or uterine rupture
- History of foetal/intrapartum distress or acidosis
- Low Apgar scores and/or delayed onset of respiration requiring resuscitation
- Symptoms or signs of encephalopathy
- characteristic feature of many cases of HIE is an *evolving* encephalopathy – babies get worse and then get better
- Signs of multi-organ involvement usually occurs in association with a moderate to severe encephalopathy
- Exclusion of other likely causes of encephalopathy

WHEN TO CONSIDER FOR THERAPEUTIC HYPOTHERMIA

Treatment criteria

- **Babies ≥36 weeks' gestation, meeting criteria A, B and C aged ≤6 hr**
- Babies 35^{+0}–35^{+6} weeks' gestation but meeting criteria A, B and C aged ≤6 hr, discuss with cooling centre, as may be suitable for treatment
- there is limited evidence of benefit of TH in babies <35 weeks' gestation and some evidence of an increased risk of complications
- If in doubt about the suitability of any baby for cooling, discuss with cooling centre

Criterion A

At least ONE of the following:

- Apgar score ≤5 at 10 min after birth
- Continued need for resuscitation, including endotracheal or mask ventilation at 10 min after birth (does not include those receiving PEEP or CPAP alone)
- Acidosis within 60 min of birth (defined as umbilical cord, arterial or capillary pH <7.0)
- Base deficit ≥16 mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 min of birth

Criterion 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

Criterion C

- Babies meeting Criteria A and B should be assessed for at least 30 min of amplitude integrated EEG
- There must be one of the following:
- normal background (upper margin >10 μV and lower margin >5 μV) with some seizure activity
- moderately abnormal activity (upper margin >10 μV and lower margin <5 μV)
- suppressed activity (upper margin <10 μV and lower margin <5 μV)
- continuous seizure activity

If aEEG is not available and baby meets criteria A and B commence cooling

Neonatal encephalopathy evolves with time.
Babies who me et Criterion A but are neurologically normal at the time of assessment should be reassessed several times during the first 6 hours of life

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Neurological assessment – repeat and document at regular intervals as babies go through pathway of care:

Parameter	Mild	Moderate	Severe
Level of consciousness	• Normal • Hyper alert	• Lethargic	• Stuperose/comatose
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/without stimulation (all extremities extended)
Tone	• Normal – resists passive motion	• Hypotonic or floppy, either focal or general	• Completely flaccid like a rag doll
Primitive reflexes	• Suck: normal • Moro: normal	• Suck: weak • Moro: incomplete	• Suck: completely absent • Moro: completely absent
Autonomic system	• Pupils: normal size, reactive to light • Heart rate: normal >100 bpm • Respirations: normal	• Pupils: constricted, <3 mm but react to light • Heart rate: bradycardia (<100 bpm variable up to 120 bpm) • Respirations: periodic irregular breathing effort	• Pupils: fixed dilated, not reactive to light • Heart rate: variable inconsistent rate, irregular, may be bradycardic • Respirations: completely apnoeic requiring positive pressure ventilation
Seizures	• None	• Common focal or multifocal seizures	• Uncommon (excluding decerebration) or frequent seizures

REFERRAL

Consent

- Discuss cooling treatment with parents as soon as practically possible. It is not necessary to wait for informed consent before starting cooling
- Document discussions in baby's notes

In addition

Request cord gases (if not already obtained)
Request midwives save placenta for histological examination

Passive cooling

- As soon as decision made for cooling, referring unit to telephone cooling centre and to begin passive cooling
- document this time as 'age when passive cooling commenced'
- document baby's temperature at this time
- begin passive cooling by switching off overhead heater and active heating in a transport incubator
- Nurse baby in an open Babytherm® cot with heater switched off
- If baby nursed in an incubator, open portholes
- Nurse baby naked apart from a nappy

Continuous rectal temperature monitoring

- Insert a rectal probe to 6 cm and commence continuous rectal temperature monitoring
- Target rectal temperature 33–34°C

Regular communication between referring unit and cooling centre is vital

- Once baby accepted by a cooling centre, contact neonatal transport team to arrange transport of baby and complete cooling proforma
- Use servo controlled total body cooling mattress (if available) before arrival of neonatal transport team. Use fans or gloves filled with cold water **only** if continuous rectal temperature monitoring is in place and cooling mattress is not available

Never use ice filled gloves to cool a baby as this can bring the temperature down to dangerously low and uncontrolled levels

STABILISATION PHASE

Passive cooling

- Use referral form from: https://www.networks.nhs.uk/nhs-networks/west-midlands-neonatal-operational-delivery/neonatal-guidelines-2022-2024/
- **Ensure baby's temperature does not fall below 33ºC**. Document every 15 min
- Follow **Passive cooling protocol flowchart**
- Care continues in referring unit with advice from cooling centre as required
- If not already intubated at delivery [most babies will need to be intubated for transfer (see **Intubation** guideline)] discuss with receiving consultant and newborn transfer service
- If possible, insert umbilical arterial and venous catheters and monitor arterial blood pressure (see **Umbilical artery catheter: insertion and removal** and **Umbilical venous catheter: insertion and removal** guidelines). Check position of lines on X-ray
- Aim to maintain arterial $PaCO_2$ of 6–8 kPa
- Document neurology before commencing sedation or anticonvulsants, including size and reactivity of pupils
- Sedate baby using morphine at an infusion rate of 20 microgram/kg/hr. Aim for heart rate of 100 bpm. Faster rates may be a sign of distress, in which case increase sedation
- Maintain mean arterial blood pressure at >45 mmHg (see **Hypotension** guideline)
- Restrict total fluids to 40 mL/kg/day initially
- Keep glucose within normal range – use higher glucose concentration infusion if necessary (see **Hypoglycaemia** guideline)
- Take blood for blood culture, FBC, arterial blood gas, lactate, electrolytes, urea and creatinine, calcium, magnesium, prothrombin time, APTT, glucose and LFT
- Babies ≥37 weeks' gestation with severe brain injury diagnosed in the first 7 days of life meet the Healthcare Safety Investigation Branch criteria for a maternity investigation if baby was:
- actively cooled
- diagnosed with Grade III HIE
- had reduced central tone, was comatose and had seizures of any kind
- notify obstetric team before transfer if baby meets above criteria

SUBSEQUENT MANAGEMENT

Continue with management below if baby not transferred to cooling centre, or in cooling centre without local guideline for active cooling. NOTE that some of the target values are different to those recommended if a baby is being actively cooled

Oxygen

- Avoid hypoxaemia. Maintain PaO_2 10–12 kPa and SpO_2 >94%
- Episodes of hypoxaemia (possibly associated with convulsions) are an indication for IPPV

Carbon dioxide

- Maintain $PaCO_2$ 5.0–7.0 kPa
- Hypoventilation leading to hypercapnia (>7.0 kPa) is an indication for IPPV
- Hyperventilation is contraindicated but, if baby spontaneously hyperventilating, mechanical ventilation, with/without paralysis, may be necessary to control $PaCO_2$

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Circulatory support

- Maintain mean arterial blood pressure at ≥45 mmHg (see **Hypotension** guideline)
- If cardiac output poor (e.g. poor perfusion: blood pressure is a poor predictor of cardiac output) use inotropes
- Avoid volume replacement unless evidence of hypovolaemia

Fluid balance and renal function

- Start fluids at 40 mL/kg/day (see **Intravenous fluid therapy** guideline)
- Observe for SIADH and avoid severe hyponatremia (suggested by hypo-osmolar serum with low serum sodium, associated with an inappropriately high urine sodium and osmolality)
- Further fluid restriction if serum sodium falls and weight gain/failure to lose weight
- If in renal failure, follow **Renal failure** guideline
- Observe for accumulation of nephrotoxic drugs

Acidosis

- Will normally correct itself once adequate respiratory and circulatory support provided (correction occasionally required during initial resuscitation)
- Sodium bicarbonate correction is rarely required post resuscitation and it is better to allow spontaneous correction

Glucose

- Regular blood glucose monitoring
- Target >2.6 mmol/L
- Fluid restriction may require use of higher concentrations of glucose to maintain satisfactory blood glucose
- Avoid hyperglycaemia (>8 mmol/L)

Calcium

- Asphyxiated babies are at increased risk of hypocalcaemia
- Treat with calcium gluconate when serum corrected calcium <1.7 mmol/L or if ionized calcium <0.8 (see **Hypocalcaemia** guideline)
- Maintain serum magnesium (>1 mmol/L)

Seizures

- In muscle-relaxed baby, abrupt changes in blood pressure, SpO_2 and heart rate can indicate seizures
- Consider treating seizures confirmed with aEEG, particularly if associated with physiological disturbance, prolonged (>3 min) or frequent (>3/hr) (see **Seizures** guideline)

Respiratory depression can occur at high doses of anticonvulsants in babies who are not ventilated

- While seizures are common in HIE, unremitting seizure activity should lead to urgent consideration of other causes of epileptic encephalopathy, including consideration of a trial of pyridoxine

Gastrointestinal system

- Give buccal colostrum unless maternal breast milk contraindicated (see **Nutrition** guideline)
- If no ongoing organ dysfunction or poor perfusion, offer trophic breast milk
- Term babies who suffer a severe asphyxial insult are at risk of developing NEC [see **Necrotising enterocolitis (NEC)** guideline]

Sedation

- Assess for pain and distress and treat with opiate medication (evidence that distress increases brain injury in neonatal encephalopathy)
- Use analgesia for procedures likely to cause pain and distress (see **Pain assessment and management** guideline)

Rewarming

- Monitor for hypotension, apnoea and seizures, including continuing aEEG
- Can be delayed or slowed if seizures emerge
- After rewarming maintain normothermia using paracetamol and environmental measures if required

Cranial ultrasound

- Within 12 hr to rule out other causes of encephalopathy
- Generalised increase in echogenicity, indistinct sulci and narrow ventricles
- After aged 2–3 days, increased echogenicity of thalami and parenchymal echodensities
- After 1 week, parenchymal cysts, ventriculomegaly and cortical atrophy may develop
- Cerebral Doppler used early, but does not affect management
- 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 (repeat after 24 hr)

MRI

- **Between days 5–15 of life (preferably day 5–7)**

PROGNOSIS

- Risk of long-term problems increases with the degree of encephalopathy
- Normal EEG during first 3 days has good prognosis
- Overall risk of death or significant handicap is negligible for mild HIE, 26% for moderate and almost 100% for severe HIE
- Prolonged encephalopathy (e.g. moderate HIE lasting >6 days) also associated with poor outcome
- Persistent oliguria is associated with poor outcome in 90%
- Prognostic factors indicative of worse outcome:
- prolonged duration of ventilation
- prolonged need for anticonvulsants
- time taken to establish oral feeding
- lack of normal background activity on EEG
- areas of altered signal in thalamus, basal ganglia and posterior limb of the internal capsule
- Discuss prognosis with parents before discharge from NICU, document and relay to referring unit

REORIENTATION OF CARE

- When prognosis very poor, discuss withdrawing intensive care support and palliative care
- Very poor prognostic factors include:
- need for prolonged resuscitation at birth
- evidence of severe asphyxia
- multi-organ failure
- intractable seizures
- coma
- very abnormal cranial ultrasound scan and/or MRI
- persistent burst suppression pattern on cerebral function monitoring and/or EEG
- If baby physiologically stable during TH delay consideration of reorientation of care for 48 hr to allow for any recovery before discussions
- Decision to withdraw care requires discussion with parents, and other nursing and medical staff. Such decisions are frequently reached by baby's consultant after a series of discussions
- It helps if the same staff speak to parents on each occasion
- The best interests of the child are paramount
- Record a summary of discussion in notes

DISCHARGE AND FOLLOW-UP

- Arrange clinic follow-up in 4–6 weeks for babies discharged
- Arrange hearing screen (see **Hearing screening** guideline)
- All babies who have been cooled need a standardised neurodevelopmental assessment at aged 2 yr (see **Follow-up of babies discharged from neonatal unit** guideline)

INFORMATION FOR PARENTS

Offer parents information on HIE, available from:
https://www.bliss.org.uk/parents/about-your-baby/medical-conditions/hypoxic-ischaemic-encephalopathy-hie

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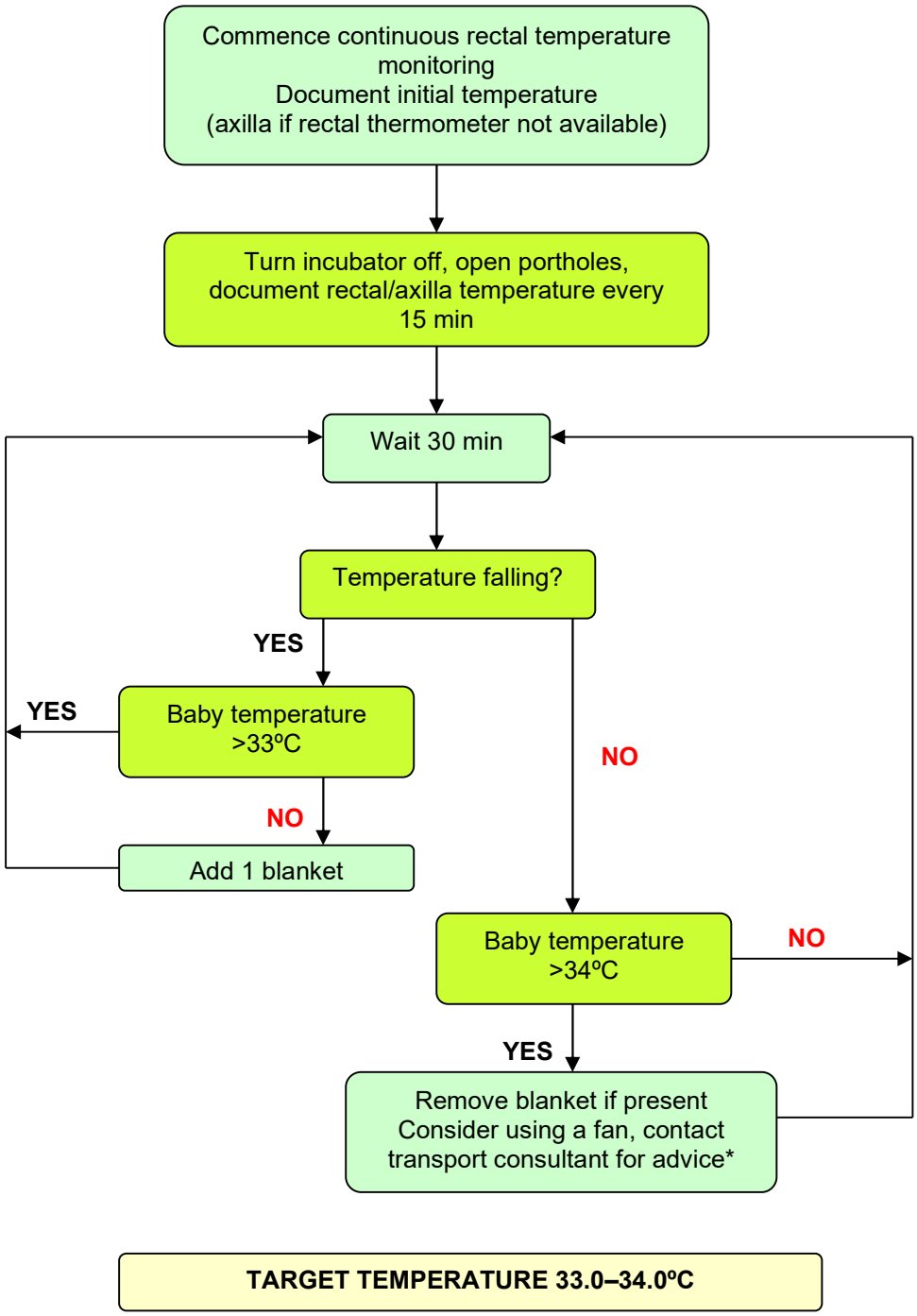
Flowchart: Passive cooling protocol



**Do not use ice packs for cooling as severe hypothermia can result*