NEONATAL HYPOXIC-ISCHAEMIC ENCEPHALOPATHY (HIE) & COOLING THERAPY

Background

- A perinatal hypoxic-ischaemic insult may present with varying degrees of neonatal encephalopathy, neurological disorder and seizures. It is crucial to intervene appropriately as the risk of death or poor neurodevelopmental outcome increases with the severity of the encephalopathy.

Management of Hypoxic-Ischaemic Encephalopathy

Process for cooling

1. Confirm indications for cooling
   - Cooling should be offered to all babies who meet both criteria A **and** B:

CRITERIA A INFANTS **≥ 35+0** WEEKS GESTATION **AND ≥ 2000 g** **AND** AT LEAST ONE OF:	**CRITERIA B** INFANTS WITH **SEIZURES** **OR** MODERATE TO SEVERE ENCEPHALOPATHY:
Apgar ≤ 5 at 10 min after birth	Altered state of consciousness (lethargy, stupor, coma)
Assisted ventilation needed after birth	Abnormal tone (focal/generalised hypotonia, flaccid)
Acidosis pH < 7.1 within 60 min of birth	
Base deficit ≥ 12 within 60 min of birth	

2. Confirm severity of encephalopathy with CFM
   - Before cooling if possible, but do not delay cooling for CFM
3. Rule out any contraindications to cooling
   - Newborn likely to require surgery within 3 days of birth
   - Abnormalities indicative of poor long term outcome
   - Moribund
4. Start cooling as soon as possible
   - Cool to rectal temperature of 33.5^{o}C (using Tecotherm® instructions)
5. Cool for 72 hours
6. Re-warm after 72 hours
   - Rectal temperature must rise by no more than 0.5 ^{o}C/h to 37 +/- 0.2 ^{o}C
   - Monitor temperature for 24 hours after return to normothermia to prevent rebound hyperthermia

General clinical management

1. Delivery room management
   - Follow NLS guidelines, resuscitation with high oxygen levels is discouraged.
   - Take arterial and venous umbilical cord blood for gases and request for the placenta to be kept.

- If encephalopathic secondary to suspected HIE & > 36 weeks gestation commence passive cooling by switching off the overhead heater.

2. Ventilation
   - Most babies will be ventilated and this should be continued for transfer.
   - Monitor blood gases and aim to maintain PaO_2 6-10 kPa, $PaCO_2$ 5-7 kPa. Most infants with HIE are easily ventilated as their lungs are usually in good condition. Initially the main problem is often with reduced respiratory drive whilst recovering from lactic acidosis.
   - Initially try to avoid paralysis & morphine sedation as these will interfere with assessment of neurological status. If sedation is necessary start the CFM first, make a formal neurological assessment and record the findings.
   - Hyperventilation may occur due to brain injury. Hypocapnia should be avoided as the resultant reduction in cerebral blood flow will exacerbate any cerebral damage. Weaning ventilation alone will rarely resolve hypocapnia. Sedation and paralysis will be needed to suppress overbreathing and keep PaCO2 levels between 5 and 7 kPa. Do not be tempted to extubate at this stage. The baby will continue to overbreath or worse still become apnoeic and collapse.
   - More complicated ventilation strategies may be needed for meconium aspiration syndrome and NO therapy for pulmonary hypertension.
   - Consider timely elective ventilation with worsening seizures. Increasing anticonvulsant therapy will eventually result in reduced respiratory drive and apnoea.
3. CVS
   - Monitor for dysrhythmias and hypotension.
   - HR ~100bpm and mean BP > 40 mmHg = adequate cooling
   - HR > 110 bpm may indicate distress and the need for sedation.
   - If MAP < 40 mmHg consider need for intra-arterial monitoring and a central venous line for inotrope therapy; give 10 ml/kg 0.9% sodium chloride bolus +/- an additional 10 ml/kg 0.9% sodium chloride bolus
   - If the BP remains suboptimal commence Dopamine and consider adding Dobutamine (see prescribing guideline).
   - Consider steroids in refractory hypotension
   - Lactic acidosis usually corrects over a period of hours with adequate ventilation and re-establishment of circulation. Rapid correction of metabolic acidosis with bicarbonate may worsen cerebral acidosis and should be avoided unless contributing significantly to cardiac dysfunction.
4. Fluids and feeding
   - Keep nil by mouth during cooling therapy.
   - Commence a 10% glucose intravenous infusion at 40 ml/kg/day.
   - If in anuric renal failure reduce fluid intake to 30 ml/kg/day + measured losses.
   - Avoid hypoglycaemia and aim for blood glucose levels in the 3 - 5 mmol/l range. If hypoglycaemia persists insert a central line and increase the infused glucose concentration rather than increasing the fluid intake.
5. CNS
   - Undertake and record a base line neurological examination following admission and then daily during cooling therapy and again at 7 days or before discharge.
   - Do not use steroids or hyperventilation in an attempt to reduce brain oedema.
   - Record CFM findings daily during cooling therapy (see CFM guideline). A normal initial CFM indicates a high probability of normal outcome.
   - Prolonged seizures will exacerbate any cerebral damage due to HIE. The aim should be to eliminate all or nearly all clinical and electrographic seizures (see

seizure guideline).

6. Sepsis and haematology
   - Take blood cultures, start antibiotics and continue until cultures are negative.
   - Monitor clotting and LFTs and treat with vitamin K and FFP as needed.
7. Monitoring and further investigations
   - Insert rectal probe (3 - 5 cm) and start continuous rectal temperature monitoring. Ensure at least one other form of temperature monitoring plus axillary temperature 6 hourly or if rectal temperature deviates from target
   - Monitor continuously/regularly – HR, RR, Saturations and BP
   - Monitor weight
   - Group and save on admission, daily – twice daily FBC, U&Es, LFTs (incl. AST), glucose, lactate, troponin and clotting. Hourly urine output.
   - Cranial USS and Doppler examination (see appendix) following admission and daily during cooling therapy. Repeat cranial USS at 7 days or before discharge.
   - Aim for an EEG at 24 - 48 hours of age.
   - MRI brain at 10-14 days – gives best information for prognosis
   - Early Diffusion Weighted Imaging at < 48 h may be useful if considering palliative care.
   - Check hearing prior to discharge
   - Routine investigations may be extended to exclude genetic, metabolic, infective or neuromuscular conditions that may have put the baby at risk of HIE (or as differential diagnosis).
8. Prognosis and relatives
   - A member of the senior medical team should speak to the family as soon as possible to explain severity of the condition and the role of CFM and cooling. It is often very difficult to predict outcome within the first few hours of life and it is usually best to remain guarded. Keep parents updated as more information becomes available.
   - Risk of death or severe neurodevelopmental problems according to HIE grade

HIE grade	**Risk of death or severe neurodevelopmental problem**		
	Percentage (%)	Likelihood ratio	(95% CI)
Mild (I)	1.6	0.05	0.02-0.15
Moderate (II)	24	0.94	0.71-1.23
Severe (III)	78	10.71	6.71-17.1

9. Documentation and follow-up
   - A detailed antenatal, labour, delivery and resuscitation history is vital
   - Document neurological, CFM and cranial US findings daily during cooling therapy
   - Record all conversations with parents
   - Complete the Badger HIE Data Form in the Audit/Research section. Include MRI findings and CFM tracings.
   - Arrange neurodevelopmental follow-up – including at 2 years

Appendix

Clinical neurological evaluation

	Moderate Encephalopathy	Severe Encephalopathy
Level of consciousness	Reduced response to stimulation	Absent response to stimulation
Spontaneous activity	Decreased activity	No activity
Posture	Distal flexion, complete extension	Decerebrate
Tone	Hypotonia (focal or general)	Flaccid
Suck	Weak	Absent
Moro	Incomplete	Absent
Pupils	Constricted	Constricted
Heart rate	Bradycardia	Variable
Respiration	Periodic breathing	Apnoea

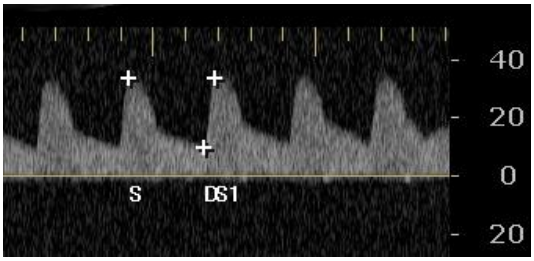
Values for Resistance Index (RI = PSV – EDV / PSV) in term newborn infants

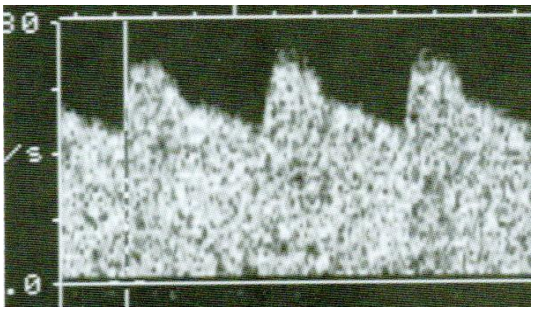
Postnatal Age	**6h**	**12h**	**24h**	**48h**
RI	0.70 ± 0.12	0.63 ±0.06	0.64 ± 0.10	0.66 ± 0.07

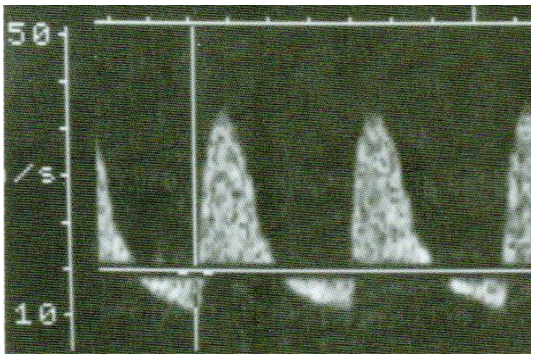
RI is assessed in the anterior or middle cerebral artery using Pulsed Doppler flow.

- A high RI correlates with an increased cerebral vascular resistance and a decreased blood flow velocity, and a low RI with a decreased resistance and an increased blood flow velocity. Abnormally low RI values of the anterior cerebral artery may predict adverse neurodevelopmental outcome.
- Positive predictive value of low RI (≤ 0.55) 60% (95% CI: 45 - 74%), negative predictive value 78% (95% CI: 67%, 86%). The PPV during hypothermia is significantly lower than the pooled PPV of 84% (95% CI 73%, 91%) from published studies of RI at normothermia. NPV during hypothermia and normothermia was 76% (95% CI 69 - 82%).

Flow pattern of anterior cerebral artery at > 12 hours of life in relation to outcome







Stage I

- Normal flow pattern with normal RI = likelihood high for good outcome

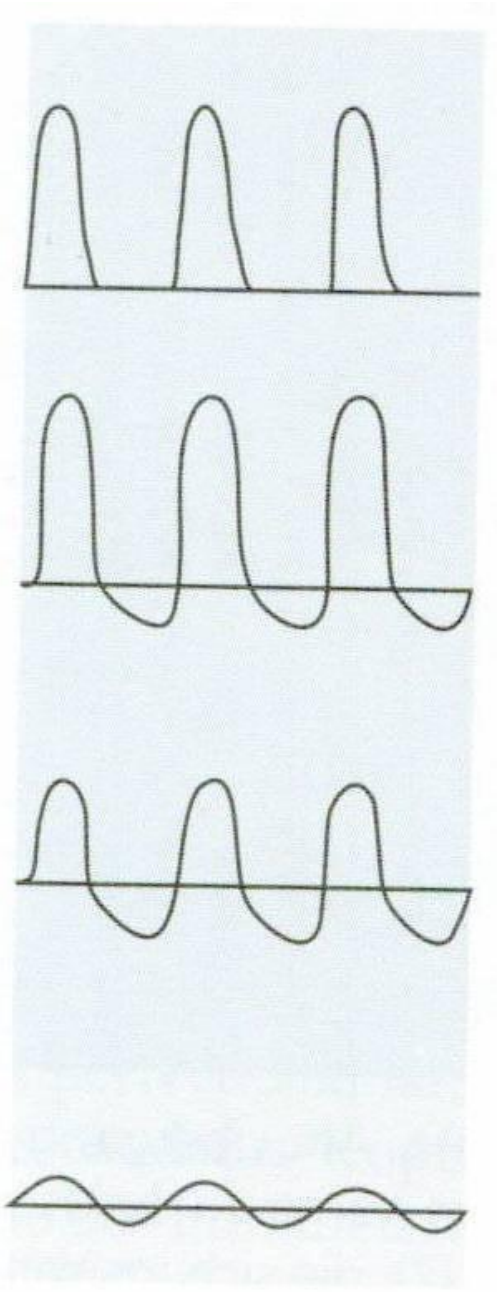
Stage II

- Increased diastolic flow with increased end-systolic and end-diastolic flow velocity pattern with low RI = likelihood high for some neurodevelopmental abnormalities

Stage III

- Decreased endsystolic and enddiastolic flow velocity pattern with normal to high RI = likelihood high for death or severe neurodevelopmental abnormalities

Stages of evolving brain death based on anterior cerebral artery Doppler findings



Stage I

Absent enddiastolic flow

Stage II

Reversed enddiastolic flow (see stage three above)

Stage III

Reversed enddiastolic flow plus decreased systolic flow (see stage three above)

Stage IV

Undulating flow around baseline