HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

RECOGNITION AND ASSESSMENT

Risk factors
- History of non-reassuring cardiotocography (CTG)
- Fetal heart rate abnormalities during labour
- Apgar scores can be low
- Umbilical arterial gas can be acidotic
- Continued resuscitation

SYMPTOMS AND SIGNS

Brain
- Hypo/hyperventilation
- Altered state of consciousness
- Irritability, unresponsiveness to stimulation
- Abnormal posturing, decerebrate rigidity, extensor response to painful stimulus
- Seizures
- Hypo/hypertonia
- Weak (or no) suck

Other signs and symptoms related to effects on other organ systems
- Renal failure
- Respiratory distress syndrome, particularly if preterm
- Pulmonary haemorrhage
- Persistent pulmonary hypertension of the newborn
- Hypoxic cardiomyopathy, hypotension
- Hepatic failure
- Necrotising enterocolitis
- Hypoglycaemia
- Fluid retention
- Disseminated intravascular coagulation (DIC)

INVESTIGATIONS

Bloods
- FBC
- Blood culture
- Clotting screen
- Renal and liver profile, calcium, magnesium
- Glucose
- Blood gas including lactate
- Urine dipsticks

Cranial USS
- Generalised increase in echogenicity, indistinct sulci and narrow ventricles
- After 2-3 days of age, increased echogenicity of thalami and parenchymal echodensities
- After 1 wk, parenchymal cysts, ventriculomegaly and cortical atrophy
- 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

MR scan of brain between days 7-10 of life for grade 2 and 3 HIE
- Hypodense areas in thalamus, basal ganglia and internal capsule indicate poor prognosis

Cerebral function monitoring (aEEG)
- Normal trace upper margin above 10 microvolt and lower margin above 5 microvolt
• Moderately abnormal trace upper margin above 10 microvolt and lower margin below 5 microvolt
• Severely abnormal upper margin below 10 microvolt

**EEG**
• Normal EEG during first 3 days has good prognosis
• Lack of normal background activity associated with a poor outcome

**IMMEDIATE TREATMENT**
• Prompt and effective resuscitation
• Maintain body temperature, avoid hyperthermia
• IV access
• Isotonic glucose-containing IV fluids at 75% of maintenance requirements. See Intravenous fluid therapy guideline

**WHEN TO CONSIDER TREATMENT WITH TOTAL BODY COOLING**

*Treatment criteria*

**Criteria A**
• Infants ≥36 completed weeks gestation admitted to neonatal unit with at least one of the following:
  • Apgar score ≤5 at 10 minutes after birth
  • continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth
  • acidosis within 60 minutes of birth (defined as any occurrence of umbilical cord, arterial or capillary pH <7.00)
  • base deficit >16mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth
• Infants meeting criteria A, assess for whether they meet neurological abnormality entry criteria (B) with at least one of the following:

**Criteria B**
• Seizures or moderate-to-severe encephalopathy comprising:
  • altered state of consciousness (reduced response to stimulation or absent response to stimulation) and
  • abnormal tone (focal or general hypotonia, or flaccid) and
  • abnormal primitive reflexes (weak or absent suck or Moro response)
• Infants meeting criteria A and B can be considered for treatment with cooling

**Criteria for defining moderate and severe encephalopathy**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Moderate encephalopathy</th>
<th>Severe encephalopathy</th>
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<tbody>
<tr>
<td>Level of consciousness</td>
<td>Reduced response to stimulation</td>
<td>Absent response to stimulation</td>
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<tr>
<td>Spontaneous activity</td>
<td>Decreased activity</td>
<td>No activity</td>
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<tr>
<td>Posture</td>
<td>Distal flexion, complete extension</td>
<td>Decerebrate</td>
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<tr>
<td>Tone</td>
<td>Hypotonia (focal or general)</td>
<td>Flaccid</td>
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<tr>
<td>Suck</td>
<td>Weak</td>
<td>Absent</td>
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<tr>
<td>Moro</td>
<td>Incomplete</td>
<td>Absent</td>
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<tr>
<td>Pupils</td>
<td>Constricted</td>
<td>Constricted</td>
</tr>
<tr>
<td>Heart rate</td>
<td>Bradycardia</td>
<td>Variable</td>
</tr>
<tr>
<td>Respiration</td>
<td>Periodic breathing</td>
<td>Apnoea</td>
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SUBSEQUENT MANAGEMENT

*If decision made to treat baby with total body cooling, see Toby register guidelines at http://www.npeu.ox.ac.uk/tobyregister/docs
This should always be a Consultant decision*

- If not using total body cooling, continue with management below

**Oxygen**
- Avoid hypoxaemia. Maintain PaO$_2$ 10-12 kPa and SpO$_2$ >94%
- Episodes of hypoxaemia (possibly associated with convulsions) are indication for IPPV

**Carbon dioxide**
- Maintain PaCO$_2$ 5.0–7.0 kPa
- Hypoventilation leading to hypercapnia (>7 kPa) is indication for IPPV
- Hyperventilation contraindicated but, if baby spontaneously hyperventilating, mechanical ventilation can be necessary to control PaCO$_2$

**Circulatory support**
- Maintain mean arterial blood pressure at 40 mmHg or above for term infants
- If cardiac output poor (e.g. poor perfusion: blood pressure is poor predictor of cardiac output) use inotropes
- Avoid volume replacement unless evidence of hypovolaemia

**Fluid balance and renal function**
- Give 75% of normal maintenance fluid requirement. See Intravenous fluid therapy guideline
- Some infants develop inappropriate ADH secretion at 3-4 days (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

**Acidosis**
- Will normally correct itself once adequate respiratory and circulatory support provided (correction occasionally required during initial resuscitation)
- Repeat blood gas after 30 min and provide base if spontaneous correction not proceeding spontaneously
- Aim to half-correct acidosis using infusion of sodium bicarbonate 4.2% (0.5 mmol/mL over 20 to 30 min)

**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

**Convulsions**
- Prophylactic anticonvulsants not indicated
- In muscle-relaxed infant, abrupt changes in blood pressure, SpO$_2$ and heart rate can indicate convulsions
- Treat persistent (>3/hr) or prolonged convulsions; see Seizures guideline
- Give phenobarbital
If ineffective or contraindicated, give phenytoin. If no response give clonazepam (see Seizures guideline).

Convulsions associated with HIE can be notoriously difficult to control (preventing every little twitch is unrealistic).

Regular fits causing respiratory insufficiency are an indication for IPPV.

Once baby stable for 2-3 days anticonvulsants can usually be withdrawn although phenobarbital can be continued for a little longer (duration can vary depending on individual practise and clinical severity of seizures).

Avoid corticosteroids and mannitol.

**Thermal control**

- Maintain normal body temperature (36.5–37.2°C). Avoid hyperthermia.

**Gastrointestinal system**

- Term infants who suffer a severe asphyxial insult are at risk of developing necrotising enterocolitis (see Necrotising enterocolitis guideline).
- In other infants gastric motility can be reduced: introduce enteral feeds slowly.

**PROGNOSIS**

- Risk of long-term problems increases with the degree of encephalopathy.
- Overall risk of death or significant handicap 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 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.

**DISCONTINUING INTENSIVE CARE**

- When prognosis very poor, discuss withdrawing intensive care support.
- 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.
  - abnormal Doppler cerebral blood flow velocities.
  - persistent burst suppression pattern on cerebral function monitoring and/or EEG.
- Decision to withdraw care requires discussion with parents, and other nursing and medical staff. Such decisions are frequently reached after a series of discussions by infant’s consultant.
- It helps if the same staff speak to parents on each occasion.
- The best interests of the child are paramount.
- Record summary of discussion in notes.

**DISCHARGE AND FOLLOW-UP**

- Arrange clinic follow-up in 4-6 weeks for babies discharged.
- Repeat cranial USS before discharge (see protocol).
- Arrange hearing screen.
- Arrange MR scan for grades 2 and 3 HIE as an outpatient (if not already done as an inpatient), preferably before follow-up.