

NEONATAL ENCEPHALOPATHY

Definition

- Neonatal Encephalopathy (NE) is a clinical syndrome of disturbed neurological function, caused by failure to make a successful transition to extrauterine gas exchange
- manifests by a difficulty in initiating and maintaining spontaneous respiration, depression of muscle tone and reflexes, depressed consciousness and often seizures
- occurs in approximately 3.5 - 6/1000 live births; usually affects full term infants

Note: The terminology NE is preferred to Hypoxic Ischemic Encephalopathy (HIE) as it is not always possible to document a significant hypoxic-ischemic insult and there are other possible aetiologies such as CNS malformation, infection, metabolic diseases, drug exposure, and neonatal stroke as possible causes of the encephalopathy.

Table 1. Diagnostic criteria for perinatal asphyxia as a cause of Neonatal Encephalopathy

- profound metabolic or mixed acidemia (pH <7.00) in an umbilical cord arterial blood sample, if obtained
- persistence of an Apgar score of 0-3 for longer than 5 minutes
- neonatal neurologic sequelae (e.g. seizures, coma, hypotonia)
- multiple organ involvement (e.g. of the kidney, lungs, liver, heart, intestines)

*From the American Academy of Pediatrics (AAP) and
The American College of Obstetrics and Gynecology (ACOG)*

Hypoxic Ischaemic Encephalopathy (HIE)

- in HIE, the brain injury is caused by a deficit in oxygen supply.
- this can occur by
 - *hypoxaemia* - a decrease in oxygen saturation in the blood supply, or
 - *ischaemia* - a decrease in the amount of blood perfusing the brain
 - or both

Table 2. Staging of neonatal hypoxic ischaemic encephalopathy (HIE)

Variable	Stage I	Stage II	Stage III
<i>Level of consciousness</i>	alert	lethargy	coma
<i>Muscle tone</i>	normal or hypertonia	hypotonia	flaccidity
<i>Tendon reflexes</i>	increased	increased	depressed or absent
<i>Myoclonus</i>	present	present	absent
<i>Seizures</i>	absent	frequent	frequent
<i>Complex reflexes</i>			
<i>Suck</i>	active	weak	absent
<i>Moro</i>	exaggerated	incomplete	absent
<i>Grasp</i>	normal or exaggerated	exaggerated	absent
<i>Doll's eyes</i>	normal	overactive	reduced or absent
<i>Autonomic function</i>			
<i>Pupils</i>	dilated, reactive	constrictive, reactive	variable or fixed
<i>Respirations</i>	regular	variation in rate and depth, periodic	ataxic, apneic
<i>Heart rate</i>	normal or tachycardia	bradycardia	bradycardia
<i>Electroencephalogram</i>	normal	low voltage, paroxysmal	periodic
<i>Outcome</i>	no impairment	25% Impaired	92% Impaired

Note: Only consistent in term infants or > 35 weeks gestation. Not consistent in premature infants adapted from Sarnat and Sarnat (1976)

Management

- adequate and effective resuscitation.
- monitor vital signs, as well as blood gases, urine output, blood sugar and electrolytes
- supportive measures:
 - nurse in thermoneutral environment. Avoid high environmental temperature as fever is associated with adverse outcome
 - maintain normoglycaemia, both hypo- and hyperglycemia can be harmful.
 - review infection risk and cover with antibiotics if necessary
 - maintain adequate hydration (do not dehydrate or over hydrate).
 - if metabolic acidosis is severe or persistent, slow infusion of sodium bicarbonate may be used with caution. (*see chapter on Acid Base Balance*)
- cerebral protection measures
 - maintain BP (Mean Arterial Pressure > 40 mmHg for term infants) with cautious use of inotrope infusion. Volume expansion can be used in case of hypovolaemia.
 - treat seizures promptly. (*see chapter on Neonatal Seizures*)
 - treat/prevent Intracranial Hypertension
 - ventilate to maintain PaCO₂ at 35-45 mmHg. Lowering PaCO₂ less than this may cause cerebral ischaemia. Maintain for 24 - 48 hours only.
 - IV mannitol (0.25g/kg over 20 minutes) may be used where there is raised intracranial pressure. It is contraindicated in oliguria. Maximum 2-3 doses q6 hourly
 - steroids are of no benefit
- treat complications that arise:

Table 3. Complications and management strategies

Organ system	Complication	Treatment
Central nervous system	cerebral oedema, periventricular, subdural / subarachnoid haemorrhage, periventricular leucomalacia, bleeding into choroid plexus, cerebellum, thalamus	treat for cerebral oedema, as described above
Renal	acute tubular necrosis, acute urinary retention	if oliguria (urine output < 1ml/kg/hr) - treat prerenal failure with adequate volume if in established renal failure - fluid restrict; maintain normal electrolyte levels - peritoneal dialysis may be needed
Cardiac	hypoxic damage to myocardium with cardiogenic shock and failure	use of inotropes and careful fluid balance
Lungs	meconium aspiration, Persistent Pulmonary Hypertension (PPHN)	See relevant chapter on PPHN
Gastrointestinal	stress ulcers, feed intolerance, necrotizing enterocolitis (NEC)	enteral feeding preferable to parenteral; avoid rapid increase in volume of feeds to decrease risk of NEC
Others	syndrome of inappropriate anti-diuretic hormone secretion (SIADH), hypomagnesaemia, hypocalcaemia, hypoglycaemia and bleeding disorder	- if SIADH occurs restrict fluids - if DIVC occurs correct haemostasis with FFP, cryoprecipitate, platelet or packed cell as indicated

Investigations

- acute investigations have been described above.
- other investigations as in Table 4.
- a normal cranial imaging study *does not* rule out NE.

Table 4. Investigations

Investigation	Indication
<i>Cranial Ultrasound</i>	To exclude haemorrhage and other intracerebral abnormalities. Doppler studies (done after 24 hours of life) suggest that a resistive index of less than 0.5-0.6 is consistent with the diagnosis of HIE.
<i>Brain CT scan</i>	To exclude haemorrhage, cerebral oedema and other intracerebral abnormalities. May assist with prognosis. Extensive areas of low attenuation with apparent brightness of basal ganglia are associated with very poor prognosis (done after 1st week of life).
<i>Brain MRI</i>	MRI may provide prognostic information. Abnormalities of the thalami and basal ganglia are associated with an increased risk of subsequent abnormal developmental outcome. Superior to CT scans.
<i>Electroencephalogram (EEG)</i>	Severe abnormalities include burst suppression, low voltage or isoelectric EEG. Moderate abnormalities include slow activity The overall risks for death or disability were 95% for severely abnormal EEG, 64% for moderately abnormal EEG and 3 % for normal or mildly abnormal EEG.

Follow up

- all infants with NE should be followed up for to look for development and neurological problems. Full term infants who suffer from Grade 2 or 3 encephalopathy are known to have a high incidence of neurologic damage
- manage epilepsy (see chapter on Epilepsy), developmental delay as appropriate
- remember to evaluate hearing and vision on follow-up and manage appropriately