Asphyxia Neonatorum (Hypoxia-Ischemia) (Hypoxic Ischemic Encephalopathy)

- Anoxia: the consequences of complete lack of O2
- Hypoxemia: ↓ of arterial concentration of O2
- Hypoxia: decreased oxygenation to cells or organs
- Ischemia: blood flow to cells or organs that is insufficient to maintain their normal function
- Hypoxic ischemic encephalopathy is an important cause of permanent damage to CNS tissue that may result in neonatal death or manifest later as CP or developmental delay
- 15-20% of infants with HIE die in the neonatal period, 25-30% of survivors are left with permanent neurodevelopmental abnormalities (CP, MR)
• Failure of the newborn baby to establish an effective respiration immediately after birth

• After an episode of hypoxia and ischemia, anaerobic metabolism occur, this generate increased amount of lactate, inorganic phosphate, toxic amino acids (glutamate) and these accumulate in the damaged tissues

• Increased amounts of intracellular Sodium and Calcium may result in tissue swelling and cerebral edema

• There is also increased production of free radicals and nitric oxides in these tissues
Early congestion, fluid leak from increased capillary permeability, and endothelial cell swelling may then lead to signs of coagulation necrosis and cell death. Prolonged intrauterine hypoxia may result in inadequate perfusion of the periventricular white matter, resulting, in turn, in PVL particularly in preterm infants. Term infants demonstrate neuronal necrosis of the cortex (later, cortical atrophy)
• Etiology:
  1. Fetal hypoxia:
     a. maternal hypoxia: hypoventilation during anesthesia, chronic pulmonary or cardiac diseases, resp failure
     b. maternal hypotension: acute blood loss, spinal anesthesia, compression of the vena cava by the gravid uterus
     c. uterine tetany caused by excess oxytocin( inadequate relaxation of uterus to permit placental filling
     d. premature separation of the placenta
     e. cord compression or knotting
     f. placental insufficiency from toxemia or postmaturity
2. After birth:
   a. failure of oxygenation as a result of severe forms cyanotic CHD, severe pulmonary disease
   b. severe anemia( hemorrhage, hemolytic disease)
   c. shock: interfere with the transport of O2 to vital organs; overwhelming sepsis, massive blood loss, I C or adrenal hemorrhage
Fig. 12.7 The effects of asphyxia on a newborn animal showing primary and secondary apnea. (Redrawn from Dawes 1968 with permission of Blackwell Scientific Publications.)
The effects of Asphyxia:
1. CNS: HIE, infarction, hemorrhage, cerebral edema, seizures, hypotonia, hypertonia
2. CVS: myocardial ischemia, poor contractility, hypotension, tricuspid insufficiency
3. pulmonary: P. HTN, hemorrhage, RDS
4. renal: acute cortical or tubular necrosis
5. adrenal: hemorrhage
6. GI: perforation, ulceration with HGE, necrosis
7. metabolic: ISADH, hypo Na, hypoglycemia, hypo Ca, myoglobinuria
8. Integument: subcutaneous fat necrosis
9. hematology: DIC

Management

1. Identification of at risk infants:
   a. prenatal:
      - Intrauterine growth restriction may develop in chronically hypoxic fetuses without the traditional signs of fetal distress
      - fetal acidosis (PH less than 7.0)
      - Doppler umbilical waveform velocimetry
        (demonstrating increased fetal vascul R)
      - cordocentesis: hypoxia, lactic acidosis
      - a variable or late deceleration pattern

Particularly in infants near term, these signs should lead to the administration of high concentrations of oxygen to the mother and consideration of immediate delivery to avoid fetal death and CNS damage.
b. at birth: yellow meconium stained amniotic fluid (fetal distress)
   - pallor, cyanosis, apnea, bradycardia, unresponsiveness to stimulation

2. Assessment:
   a. APGAR score
   b. Amplitude Integrated EEG: help to determine which infants are at highest risk for long-term brain injury
<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>0</th>
<th>1</th>
<th>2</th>
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</thead>
<tbody>
<tr>
<td>Color</td>
<td>Pale or blue</td>
<td>Pink body, blue extremities</td>
<td>Pink body and extremities</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>Absent</td>
<td>Less than 100 beats per minute</td>
<td>Greater than 100 beats per minute</td>
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<tr>
<td>Respiration</td>
<td>Absent</td>
<td>Slow and irregular</td>
<td>Good breathing with crying</td>
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<tr>
<td>Reflex Response</td>
<td>Absent</td>
<td>Grimace or noticeable facial movement</td>
<td>Coughs, sneezes or pulls away</td>
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<tr>
<td>Muscle Tone</td>
<td>Absent</td>
<td>Some flexion of extremities.</td>
<td>Active and spontaneous movement of limbs</td>
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c. MRI: Diffusion-weighted MRI is the preferred imaging modality in neonates with HIE because of its increased sensitivity and specificity early in the process and its ability to outline the topography of the lesion

3. Treatment:
   a. resuscitation
The goals of neonatal resuscitation are to prevent the morbidity and mortality associated with hypoxic-ischemic tissue (brain, heart, kidney) injury and to reestablish adequate spontaneous respiration and cardiac output. High-risk situations should be anticipated from the history of the pregnancy, labor, and delivery and identification of signs of fetal distress. Infants who are born limp, cyanotic, apneic, or pulseless require immediate resuscitation before assignment of the 1-min Apgar score. Rapid and appropriate resuscitative efforts improve the likelihood of preventing brain damage and achieving a successful outcome.
Birth

Term gestation? Breathing or crying? Good muscle tone?

- Yes, stay with mother
- No
  - Warm, open airway, dry, stimulate

HR below 100, gasping, or apnea?

- Yes
  - PPV, consider SPO₂ monitoring

- No
  - Labored breathing or persistent cyanosis?
    - No
    - Consider SPO₂ monitoring, Consider CPAP
    - Yes
    - Ensure adequate ventilation
      - Consider ET intubation!
  
HR below 100?

- Yes
  - Post-resuscitation care

- No
  - HR below 60?
    - Yes
      - Chest compressions, Coordinate with PPV

HR below 60?

- Yes
  - IV epinephrine

- No
b. systemic or selective cerebral hypothermia: suppress the production of neurotoxic mediators as glutamate, free radicals, NO, and lactate. Systemic hypothermia may result in more uniform cooling of the brain and deeper CNS structures. Infants treated with systemic hypothermia have a lower incidence of cortical neuronal injury on MRI.

c. Careful attention to ventilatory status and adequate oxygenation, blood pressure, hemodynamic status, acid-base balance, and possible infection is important. Secondary hypoxia or hypotension due to complications of HIE must be prevented. Aggressive treatment of seizures is critical and may necessitate continuous EEG monitoring.

Prognosis depends on:

1. initial cord or initial blood pH < 6.7 have a 90% risk for death or severe neurodevelopmental impairment at 18 mo of age.

2. infants with Apgar scores of 0-3 at 5 min, high base deficit (> 20-25 mmol/L), decerebrate posture, and lack of spontaneous activity are also at increased risk for death or impairment.
3. Gestational age

4. The severity of encephalopathy:
   severe encephalopathy, characterized by flaccid coma, apnea, absence of oculocephalic reflexes, and refractory seizures, is associated with a poor prognosis.

5. A low Apgar score at 20 min, absence of spontaneous respirations at 20 min of age, and persistence of abnormal neurologic signs at 2 wk of age also predict death or severe cognitive and motor deficits.

6. Severe MRI and EEG abnormalities predict a poor outcome as microcephaly and poor head growth during the 1st year of life.