Brain Injury during Fetal-Neonatal Transition

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Brain injury during fetal-neonatal transition

- Injury resulting during abnormal transition from fetal to stable neonatal physiology
- Pathophysiologies include
  - Compromised compensatory mechanisms
  - Immature anatomy / physiology
  - Abnormal systemic / cerebral circulation
- Focus will be on cerebral hypoxia-ischemia / reperfusion injury
Hypoxia-ischemia/reperfusion brain injury in the full-term infant

Systemic hypoxia-ischemia/reperfusion
- Transient severe asphyxia
- Prolonged partial asphyxia

Regional cerebral hypoxia-ischemia/reperfusion

Focal cerebral hypoxia-ischemia/reperfusion
- Arterio-occlusive insults (‘stroke’)
- Veno-occlusive insults
Definition of Perinatal Asphyxia

- Perinatal asphyxia is an acquired metabolic condition that results when gas exchange is impaired between the maternal and fetal circulations, or in the early newborn period.

- The initial effects are a decrease in circulating arterial oxygen (hypoxemia) and an accumulation of circulating carbon dioxide (hypercarbia) causing fetal respiratory acidosis.

- If fetal hypoxemia is sustained, tissue oxygen levels begin to fall (hypoxia), and the anaerobic metabolism that ensues leads to lactate accumulation, metabolic acidosis, and eventual energy failure.
Systemic fetal hypoxia-ischemia/reperfusion

1. Prolonged partial asphyxia
   - Placental failure with prolonged labor
   - Tetanic uterine contractions
   - Nuchal cord
Systemic fetal hypoxia-ischemia/reperfusion

1. Partial Prolonged Fetal Hypoxia

Centralization of perfusion

Cortex

Basal Ganglia

Brainstem

Heart

Liver

Kidneys
Major Cerebral Arterial Supply Territories

ANTERIOR CEREBRAL ARTERY

MIDDLE CEREBRAL ARTERY

POSTERIOR CEREBRAL ARTERY
Prolonged Partial Insult Parasagittal Injury
Prolonged Partial Asphyxia

“Circulatory centralization” eventually collapses when
- tissue lactate accumulation causes vasodilation, overriding adrenergic vasoconstriction
- myocardial lactate accumulation and glycogen depletion causes hypotension

Cerebral pressure autoregulation fails with progressive hypoxemia and hypercarbia

Hypotension and pressure-passive cerebral circulation cause serious cerebral circulatory insufficiency

Systemic end organ injury prominent; often severe acidosis
Fetal asphyxia causes sustained disruption of cerebral pressure autoregulation.
Fetal asphyxia causes sustained disruption of cerebral pressure autoregulation.
Systemic fetal hypoxia-ischemia/reperfusion

2. Transient severe asphyxia
   - Uterine rupture
   - Placental abruption
   - Cord prolapse
Systemic fetal hypoxia-ischemia/reperfusion

2. Transient Severe Fetal Hypoxia

Centralization of perfusion fails
Transient severe fetal hypoxia
Transient severe asphyxia
Basal ganglia-thalamic injury
Transient Severe Perinatal Asphyxia

- Topography of brain injury
  - Basal ganglia: putaminal
  - Thalamus: dorsolateral
  - Brainstem: dorsal
  - Cerebral: sensorimotor gray/white

- Systemic end organ injury may be mild-absent

- Cord blood gases may *not* show severe acidosis
Regional cerebral intrapartum hypoperfusion

- Prolonged obstructed labor with cranial compression
- Shoulder dystocia
- Pattern of injury resembles prolonged partial HI/R but has additional features of venous ischemia and hemorrhage
Focal cerebral hypoxia-ischemia/reperfusion

Neonatal arterial stroke

- Etiology often unclear
- ? Role of transitional circulation
Fetal-transitional circulation

- Ductus arteriosus
- Superior vena cava
- Pulmonary vein
- Crista dividens
- Oval foramen
- Inferior vena cava
- Ductus venosus
- Sphincter in ductus venosus
- Portal vein
- Inferior vena cava
- Umbilical vein
- Umbilical arteries
- Pulmonary vein
- Pulmonary artery
- Descending aorta
Importance of timing of injury

- Increasingly important for management (therapeutic windows)

- Medicolegal issues
Phases of cerebral energy failure

Hypoxia

Reperfusion

Primary energy failure

8 - 24 hours

Secondary energy failure

ATP ↓
Lactate ↑
$pH_i$ ↓

ATP N
Lactate N ↑
$pH_i$ N

ATP ↓
Lactate ↑
$pH_i$ N
Ongoing challenges for the management of perinatal brain injury

Establishing the

• Severity of the initial insult
• The nature of the insult
• The timing of the insult
• The acute response to treatment
Summary and conclusions