Birth Asphyxia

- May occur in utero, during labor/delivery or during the neonatal period
- Condition of impaired blood gas exchange that leads to progressive hypoxemia and hypercapnia with metabolic acidosis.
- ACOG and AAP discourage the term “asphyxia” as imprecise, prefer the term “depression”
- Death or severe neurological impairment following perinatal asphyxia in 0.5-1/1000 live births

Risk Factors – maternal

- Hypertensive disorders
- Cardiac disease
- Pulmonary disease
- Diabetes
- Sickle cell disease
- Renal disease
- Premature rupture of membranes
- Vaginal bleeding
- Severe anemia
- Rh/ABO sensitization
- Uterine or pelvic anatomic abnormalities
- Previous fetal or neonatal death

Risk Factors – fetal

- Multiple birth
- Post-dates
- IUGR
- Premature
- Polyhydramnios
- Meconium stained amniotic fluid

Risk Factors – Intrapartum

- Abnormal presentations
- Forceps (other than low)
- C-section delivery
- Prolapsed cord
- Abnormal heart rate or rhythm
- Prolonged general anesthesia
- Anesthetic complications (hypotension, hypoxia)
- Nuchal cord
- Prolonged or precipitous labor
- Uterine hypertonus
- Infection
Pathophysiology

- Definitions
  - Hypoxemia: low blood oxygen levels
  - Hypoxia: lack of oxygen in the tissues of the body
  - Ischemia: reduction or loss of blood flow to an organ
- The fetus and neonate are more resistant to asphyxia than adults—good at redistributing preferentially, oxygenated blood to the heart, brain and adrenals

Pathophysiologic sequence

- Can occur at any time, well defined series of events
- Onset of asphyxia results in period of rapid breathing followed by primary apnea
- Primary apnea is followed by irregular gasping and secondary apnea by 10 minutes
- Heart rate initially increases during the rapid breathing then falls along with the pH, BP and cerebral, pulmonary and renal perfusion.

Pathophysiologic sequence

- The infant’s response to resuscitation will depend on duration of the asphyxia
  - Will respond to stimulation if born during primary apnea
  - Will need PPV if delivered during gasping or secondary apnea

Pathophysiologic sequence

- As hypercapnia, hypoxemia and acidosis worsen, cerebral blood flow (CBF) becomes pressure passive which leaves the infant at risk of cerebral ischemia with systemic hypotension and cerebral hemorrhage with systemic hypertension.
- Prolonged asphyxia results in decreased cardiac output, hypotension and decreased CBF, risking cerebral ischemia and cell injury.
- As less oxygen is available anaerobic metabolism ensues.

Aerobic vs Anaerobic Metabolism

Systems Affected by Asphyxia

- Neurologic
  - Hypoxic — ischemic encephalopathy (HIE)
  - Seizures
  - Cerebral edema or hemorrhage
- Cardiovascular
  - Poor contractility—failure
- Pulmonary
  - Delayed onset of respirations→shunting→PPHN risk
  - Risk of MAS
Systems Affected by Asphyxia

- Renal
  - Acute Tubular Necrosis (ATN) → risk of failure
  - Syndrome of Inappropriate Antidiuretic Hormone (SIADH)
- GI
  - Risk of necrotizing enterocolitis (NEC)
- Hematologic
  - Disseminated intravascular coagulation (DIC)
- Metabolic
  - Hypoglycemia, hypocalcemia, altered electrolytes
- Hepatic
  - Abnormal liver function tests (LFTs), clotting factors

Hypoxic-Ischemic Encephalopathy (HIE)

- Neuronal death occurs in two phases after a reversible hypoxic-ischemic global insult
  - First phase: immediate neuronal death related to cellular hypoxia and exhaustion of the cells energy stores
  - Second phase: 6+ hrs after insult delayed neuronal death occurs due to several mechanisms including: hyperemia, cytotoxic edema, mitochondrial failure, accumulation of toxins, nitric oxide synthesis and free radical damage (assoc w/ incr seizure activity and accounts for significant portion of final cell loss)

Assessment for HIE

- No particular lab test to rule HIE in or out
- Clinical presentation is the best indicator
- Degree of other system involvement, electrolyte abnormalities are dependent on the severity of the insult
- EEG and MRI correlation have predictive value
- Sarnat and Sarnat’s 3 Clinical Stages of Perinatal Hypoxic Ischemic Brain Injury (1976)
Mild HIE

- Mildly increased muscle tone, brisk deep tendon reflexes during the first few days
- Transient behavioral abnormalities: poor feeding, irritability, irritated crying, sleepiness
- Normal CNS findings by 3-4 days of life

Moderate HIE

- Lethargic infant with significant hypotonia and decreased deep tendon reflexes
- Grasping, Moro and sucking reflexes sluggish or absent
- Occasional periods of apnea
- Seizures usually occur in the first 24hrs of life
- Full recovery in 1-2 weeks is possible and associated with a better long term outcome

Severe HIE

- Stupor or coma is typical
- Irregular breathing, generally requires vent support
- Hypotonia and depressed deep tendon reflexes
- Neonatal reflexes (sucking, Moro, etc) are absent
- Pupils can be dilated, fixed or poorly reactive to light
- Seizures occur early and often and may worsen over the initial hours of recovery secondary to reperfusion injury
- Fontanel may bulge with increasing cerebral edema
- HR and BP irregularities are common secondary to cardiorespiratory failure
- Multiple organ involvement common

HIE outcomes

- Dependent on severity
- Mild (Stage I) HIE—generally normal neurological outcome
- Moderate (Stage II) HIE—some with normal outcomes, resolution of neurological symptoms and normal nipple feeding by 1-2 wks is a good prognostic sign
  - 30-50% with serious long term complications (CP, mental retardation)
  - 10-20% with minor neurological morbidities
- Severe (Stage III) HIE
  - Mortality rate of 50-75%, most during the first month
  - 80% of the survivors develop serious complications: mental retardation, epilepsy, CP
  - 10-20% with moderately serious disabilities
  - Up to 10% are normal
  - One study showed school age children with a history of moderate to severe HIE but neurologically normal, 15-20% had significant learning disabilities

Management

- First goal is always prevention—identify infants at risk and be prepared
- Immediate resuscitation, NRP
- In the neonatal period:
  - Maintenance of adequate ventilation—hypercarbia can increase cerebral intracellular acidosis and impair cerebral vascular autoregulation
  - Maintenance of adequate oxygenation—PaO2 >40 in preterm, >50 in term, avoid hyperoxia
Management, cont.

- In the neonatal period, cont.
  - Cooling is the standard of care
  - Maintenance of adequate perfusion—maintain BP in the normal range for GA, volume and inotropes are often necessary, stable BP necessary with loss of cerebrovascular autoregulation
  - Correct metabolic acidosis
  - Maintain normal electrolytes and glucose—often hyper then hypoglycemic, hyponatremia common

- Prevention of cerebral edema—avoid fluid overload. Often have to restrict fluids to 60ml/kg/d, can decrease to 50ml/kg/d.
- Control of seizures—Phenobarbital is the first choice: loading dose of 20mg/kg IV. If unresponsive, 5mg/kg doses up to 40mg/kg.
- If unable to control seizures with Phenobarbital start Ativan (lorazepam) 0.1mg/kg/dose—repeat as necessary to control.

Seizures

- Common with HIE
- Must be distinguished from
  - Jitteriness: usually normal eye movement, extremities are containable, fine movements
  - Benign myoclonic activity: nonrepetitive, isolated jerky movements, generally occur during sleep
- Consider other causes: metabolic disturbances (hypoglycemia/calcemia), inborn errors of metabolism, cerebral infarction, intracranial hemorrhage, infection (meningitis, TORCH, sepsis), neonatal drug withdrawal, developmental abnormalities

Seizures, cont.

- The earlier the onset the more ominous the prospects for recovery
- Important to recognize:
  - Seizure activity can further damage the brain
  - Suggestive of serious illness/injury which needs careful management
  - Subtle seizure activity requires astute observation
  - Obtain EEG as soon as practical

Seizures—Pathophysiology

- Neurons are depolarized by an inward migration of sodium
- They are repolarized by an efflux of potassium.
- Seizures occur due to excessive depolarization which results in excessive synchronous electrical discharge.

Seizures—Pathophysiology, cont.

- Volpe (2001) proposed four possible reasons for the excessive depolarization
  - Failure of the sodium-potassium pump secondary to a disturbance of energy production.
  - Relative excess of excitatory vs inhibitory neurotransmitter.
  - Relative lack of inhibitory vs excitatory neurotransmitter.
  - Alteration in the neuronal membrane resulting in an inhibition of sodium movement
Seizure activity in 4 day old with HIE

Seizures: Subtle & Clonic
- Subtle
  - Apnea
  - Staring, eyelid fluttering
  - Sudden VS changes: BP fluctuations, tachycardia
  - Cycling
  - Most common type in preterm infants
- Clonic
  - Multifocal: rhythmic, repetitive movement of one or two extremities that migrate to others in a non-orderly fashion
  - Focal: rhythmic, repetitive movement of one extremity

Seizures: Tonic & Myoclonic
- Tonic
  - Decerebrate or decorticate posturing
    - Decerebrate: extremities are stiff and extended
    - Decorticate: rigidly still with arms flexed, wrists clenched and legs extended
  - Eye signs, occasional clonic movements
- Myoclonic
  - Single or multiple jerky movements with flexion of upper or lower limbs
  - Rare in neonates, but seen occasionally in metabolic problems

Management
- Assure adequate airway/ventilation
- Close CRM/oximetry monitoring
- Access for anticonvulsants
- Stat glucose, calcium, sodium and magnesium levels

Selective Head Cooling
- Research has shown that hypothermia can be neuroprotective
  - May modify cells programmed for apoptosis, leading to their survival
  - Reduced metabolic rate
  - Decreased excitotoxicity
  - Decreased edema
  - Reduced alterations in ion flux
- Head cooling vs whole body cooling
CoolCap Study Group

- 234 term infants with moderate to severe neonatal encephalopathy and abnormal EEG randomized to control or study group
- Head cooling was initiated within 6hrs and continued x 72hr when infant was gradually rewarmed
- Infants were cared for on a radiant warmer with temp adjusted to maintain rectal temp of 34-35 degrees
- CoolCap water temp started at 8-12 degrees
- Outcomes—no change in those with the most severe EEG changes, but beneficial to those less effected

Cochrane Review 2007

- Systematic review of eight randomized trials (n=638) found that therapeutic hypothermia is beneficial to term newborns with HIE
- Found that cooling reduces mortality without increasing major disability in survivors

Seattle Children’s Protocol

- Now encouraging cooling of eligible infants prior to and during transport
  - Core/rectal temp goal 33.5C (check q15min)
  - Passive cooling only
  - Start prophylactic antibiotics
  - Adequate sedation (avoid shivering) with morphine
  - Phenobarbital for clinical seizures only
  - Monitor electrolytes closely
  - Avoid over ventilation and oxygenation

Seattle Children’s cooling criteria

- Inclusion
  - ≥ 36wk GA
  - Perinatal depression based on one or more of the following:
    - APGAR ≤ 5 at 10min
    - need for resuscitation at 10 min
    - cord pH < 7 or arterial pH < 7 within 1hr of birth
    - Base deficit ≥12 in cord or blood gas within 1hr of birth
  - Moderate to severe encephalopathy based on one of more of the following:
    - Lethargy, stupor or coma, hypotonia
    - Abnormal reflexes including oculomotor or pupillary abnormalities
    - Absent or weak suck
    - Clinical seizures or hyper-alert state
Seattle Children’s cooling criteria, cont.

- Exclusion
  - IUGR (BW < 1.8kg)
  - Microcephaly (OFC <2SD for GA)
  - Infant older than 6-12 hrs of age
  - Infant likely to die or for whom withdrawal of care is being considered

Selected References