Problems with Prematurity

Part I: Physiology & Pathophysiology

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Objectives

• Describe common problems associated with premature birth as they relate to the brain, eyes, lungs, heart, gut, and thermoregulation

• Review anesthetic implications as they pertain to problems of prematurity
Conflicts of Interest

• None
Common Complications of Prematurity

- Intraventricular Hemorrhage
- Post-hemorrhagic Hydrocephalus
- Periventricular White Matter Injury
- Retinopathy of Prematurity
- Bronchopulmonary Dysplasia
- Apnea of Prematurity
- Patent Ductus Arteriosus
- Necrotizing Enterocolitis
- Hypothermia
## Prematurity

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Prematurity Group</th>
<th>Birth Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>36-37 Weeks</td>
<td>Borderline Premature</td>
<td>&lt; 2500 g</td>
</tr>
<tr>
<td>31-35 Weeks</td>
<td>Moderately Premature</td>
<td>&lt; 1500 g</td>
</tr>
<tr>
<td>24-30 Weeks</td>
<td>Severely Premature</td>
<td>&lt; 1000 g</td>
</tr>
</tbody>
</table>

Peiris & Fell. 2009
Figure 4. Preterm birth rates, by race and Hispanic origin of mother: United States, 2007–2014

Factors Associated with Preterm Birth

Social, Personal, and Economic Characteristics
- Low or high maternal age.
- Black race.
- Low maternal income or socioeconomic status.

Medical and Pregnancy Conditions
- Infection.
- Prior preterm birth.
- Carrying more than 1 baby (twins, triplets, or more).
- High blood pressure during pregnancy.

Behavioral
- Tobacco and alcohol use.
- Substance abuse.
- Late prenatal care.
- Stress.

Head Problems
Intraventricular Hemorrhage (IVH)

- Incidence and severity inversely related to gestational age
- Germinal matrix
- Causes of IVH are multifactorial

Peiris & Fell (2009); Ballabh (2010)
Robinson (2012). J Neurosurg Pediatrics
Post-hemorrhagic Hydrocephalus (PHH)

- Increase in the amount of CSF due to impaired reabsorption
- Exact mechanism of PHH is not understood
- Ventriculoperitoneal (VP) shunt is the current most common treatment mode for PHH

Robinson (2012)
Anesthetic Implications for VP Shunt

• Supine or slightly lateral position
• Elevate HOB if ICP ↑
• If ICP ↑, hyperventilate to PaCO₂ 25-30 mm Hg

http://radiopaedia.org/cases/neonatal-ventriculoperitoneal-shunt

Gregory & Andropoulos (2012)
Periventricular White Matter Injury

• VLBW (<1500 g) especially at risk
  – 10-15% diagnosed with cerebral palsy
  – 25-50% have cognitive, attentive, behavioral, or socialization problems

• “Encephalopathy of prematurity”

• Pathophysiology incompletely understood

• Cause is multi-factorial

Cerebral Palsy

- Non-progressive, changing
- Movement and posture disorder
- Spastic quadriparesis is most common
- Multifactorial, but hypoxia

Anesthetic Implications for Cerebral Palsy

- Secretions
- Positioning
- GERD
- Scoliosis
- Hypothermia
- Succinylcholine

Retinopathy of Prematurity (ROP)

- Progressive overgrowth of retinal vessels
- Can lead to intraocular hemorrhage
- Retinal hypoxia
  - Vascular Endothelial Growth Factor production
  - vascular proliferation
  - hemorrhage → retinal detachment

McCann & Soriano (2014), Gregory & Andropoulos (2012)
Retinopathy of Prematurity (ROP)

- Oxygen is a major contributing factor
- \( \text{PaO}_2 \) 150 mm Hg for as little as 1-2 hours has caused ROP!
- Preterm infants whose \( \text{SaO}_2 \) was kept between 80-96% had less ROP than those with higher \( \text{SaO}_2 \)

McCann & Soriano (2014), Gregory & Andropoulos (2012)
<table>
<thead>
<tr>
<th>Stage of ROP</th>
<th>Events</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mildly abnormal blood vessel growth</td>
<td>Resolves on its own</td>
</tr>
<tr>
<td>2</td>
<td>Moderately abnormal blood vessel growth</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Severely abnormal blood vessel growth</td>
<td>Treatment at this point has a good chance of preventing retinal detachment</td>
</tr>
<tr>
<td>4</td>
<td>Partially detached retina</td>
<td>If the eye is left alone at this stage, the baby can have severe visual impairment and even blindness</td>
</tr>
<tr>
<td>5</td>
<td>Completely detached retina</td>
<td></td>
</tr>
</tbody>
</table>
Anesthetic Implications for ROP

• Unknown if exposure to $\uparrow \text{FiO}_2$ can worsen pre-existing ROP
• Better to target a lower $\text{SaO}_2$ (i.e. 87-92%)
• Avoid $\text{N}_2\text{O}$ in case surgeon injects air into eye

Gregory & Andropoulos (2012)
Heart and Lung Problems
Stages of Lung Development, Potentially Damaging Factors, and Types of Lung Injury.

Bronchopulmonary Dysplasia (BPD)

- Impaired alveolar growth
- Airway inflammation
- Dysplastic pulmonary vasculature
- Enlarged alveoli
- Fewer alveoli
- Decreased septation

Decreased septation → Alveolar Hypoplasia → Fewer, larger alveoli → DECREASED GAS EXCHANGE

Pediatric Anesthesiology
Comparison of Normal Lungs and New BPD

A. 5-month-old infant born at term.  
B. Infant who has BPD, born at 28 weeks’ gestation, lung biopsy at 8 months.

Jobe, A. NeoReviews Vol.7 No.10 2006 e531 2006.
<table>
<thead>
<tr>
<th>Severity of BPD</th>
<th>Oxygen Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Now on Room Air</td>
</tr>
<tr>
<td>Moderate</td>
<td>Now needs &lt; 30% FiO₂</td>
</tr>
<tr>
<td>Severe</td>
<td>Now needs ≥ 30% FiO₂ and/or Positive Pressure Ventilation</td>
</tr>
</tbody>
</table>

For babies born at < 32 weeks’ GA who are assessed at hospital discharge or 36 weeks PCA, as having needed oxygen supplementation for at least 28 days

Gregory & Andropoulos (2012)
Pulmonary Arterial Hypertension (PAH)

- PAH = mPAP > 25 mm Hg at rest
- Triggers for PAH crisis
- Clinical picture of hemodynamic deterioration: RV failure

RV failure

↓coronary perfusion

↑RV wall stress

↑RVEDV

R to L septal shift

↓CO ↓MAP

↓LV performance / SV

Self-perpetuating Cycle of PAH Crisis

Pulmonary Arterial Hypertension (PAH)

• Signs and symptoms
  – dyspnea
  – pallor
  – cyanosis
  – syncope
  – bradycardia
  – RV heave
  – bronchospasm

Friesen & Williams (2008)
Goals & Treatment for PAH Crisis

↑ oxygenation
↓ pulmonary vasoconstriction
↑ systemic pressure, perfusion

(Petros & Pierce, 2006)
Goals & Treatment for PAH Crisis

↑ oxygenation
  • give oxygen

↓ pulmonary vasoconstriction
  • hyperventilate
  • pulmonary vasodilators
  • relieve noxious stimuli

↑ systemic pressure, perfusion
  • fluid, inotropes, vasopressors

Anesthetic Drugs and PAH

- Benzodiazepine
- Opiate
- Volatile agents
- Propofol
- Ketamine

Friesen & Williams (2008)
Hemodynamic response to ketamine in children with pulmonary hypertension


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What is already known
- In children with pulmonary hypertension, ketamine administration has been associated with significant increases in pulmonary artery pressure and vascular resistance in some studies and insignificant changes in others.
- Factors such as airway management and co-administration of pulmonary vasodilators have been incompletely controlled in several prior studies of ketamine and pulmonary hypertension.

What this article adds
- Under controlled airway and ventilation conditions without co-administration of pulmonary vasodilating anesthetics, ketamine was not associated with significant changes in pulmonary hemodynamics in children with pulmonary hypertension.
Apnea of Prematurity

• Considered pathologic when
  – Cessation of breathing for > 20 seconds
  – Cessation of breathing for < 15 seconds with bradycardia, cyanosis, pallor, or hypotonia

• Central and obstructive, or both

Apnea of Prematurity

• Central apnea
  – diminished response to hypercapnia
  – ventilatory depression due to hypoxia

• Obstructive apnea
  – nasal occlusion
  – occlusion of hypopharyngeal soft tissues

Peiris & Fell (2009)
Apnea of Prematurity

- Underlying problem is immature CNS!
- Exacerbated by:
  - anemia (Hgb < 10 mg/dL)
  - hypoxia
  - hypo- or hyperthermia
  - intracranial hemorrhage
  - opioids
  - ANESTHETIC DRUGS

Gregory & Andropoulos (2012)
What can we do?

• Tactile Stimulation (DO wake the baby!)
• Oxygen
• Continuous positive airway pressure (CPAP)
• Methylxanthine
  – caffeine (5-10 mg/kg)
• Intubation with mechanical ventilation

Gregory & Andropoulos (2012)
Patent Ductus Arteriosus (PDA)

- 50% of full-term infants close PDA within 24 hours
- Gestational age $\geq 30$ weeks close PDA within 96 hours
- PDA in younger neonates may remain open
- Symptoms appear in 3rd-5th DOL

Gregory & Andropoulos (2012)
Degree of shunting depends on

- Size of PDA
- Ratio of PVR:SVR

Andropoulos et al. (2015)
Anesthesia for an infant with known PDA

- Large volume IV access
- Warming device
- Avoid triggers for ductal re-opening

McMann & Soriano (2014)
Other Problems
Necrotizing Enterocolitis (NEC)

- NEC primarily affects preterm infants
- Age of onset is inversely related to PMA
- More than 85% of NEC cases occur in VLBW or very premature (< 32 weeks) infants
- 10-50% mortality

Sharma & Hudak (2013)
What causes NEC?

• Inflammatory response

• Interaction between milk substrate, microbes, immature immune system
  – oral feeding
  – excessive feeding
  – overgrowth of normal flora

• Hypoperfusion

Sharma & Hudak (2013)
Aggressive feeding

Milk stasis

Intestinal dilation

Inflammation & necrosis
Signs of NEC

• Early signs
  – feeding intolerance (vomiting)
  – increased work of breathing
  – lethargy
  – temperature instability

• Late signs
  – hypotension (shock)
  – abdominal distention, bloody stool
  – apnea
  – thrombocytopenia / coagulopathy

Cote et al. (2009, Gregory & Andropoulos (2012))
Hypothermia

• High surface area : body weight
• ↓ brown fat stores
• Non-keratinized skin
• Flaccid, open posture
• Dry gases in the operating room

Peiris & Fell (2009), Gregory & Andropoulos (2012)
A. Conduction

B. Convection

C. Evaporation

D. Radiation

Consequences of Hypothermia

• Increased metabolic rate
• Periodic breathing or apnea
• Metabolic acidosis
• Hyperglycemia
• Delayed drug metabolism

Measures to conserve heat

- Uncomfortably warm operating room (78-86°)
- Heat lamps over the bed
- Covering the patient with clear plastic
- Cap on the head
- Forced air warming device
- Warming pad on the table
- Warmed prep solution

Gregory & Andropoulos (2012)
References


References


References


