Prematurity

Prematurity involves multisystem physiologic / anatomic changes which should be considered during the neonatal period and beyond: these include changes in airway anatomy, rapid desaturation, risk of postoperative apnea, reactive pulmonary vasculature, PDA, cardiac output dependent on heart rate / preload, immature SNS leading to bradycardia, risk of fluid / electrolyte / glucose derangements, anemia, altered pharmacodynamics / -kinetics and decreased ability to deal with temperature fluctuations; prematurity is also associated with several conditions including RDS, BPD, ICH (esp. IVH), NEC and ROP (see below for acronyms)

ANESTHETIC CONSIDERATIONS:

- Anatomical and physiological considerations of prematurity:
  - **Changes in airway anatomy** – large head / tongue / epiglottis, small jaw / anterior larynx, short trachea → risk of subglottic stenosis, tracheomalacia in ex-prems. Narrow nares. Narrowest a/w at cricoid.
  - ↓ FRC, ↑ MVO_2, ↑ WOB → **rapid desaturation**
  - Immature central control of respiration → **postoperative apnea risk**
  - **Reactive pulmonary vasculature** (persistent pHTN), open or reversibly contracted **ductus arteriosus** (risk of shunting, pulmonary edema, CHF)
  - Immature LV → **HR / preload dependent** to ↑ CO; relatively hypertrophied RV
  - Immature SNS→ ↑ **bradycardia risk**
  - ↓ Glycogen stores → tendency toward **hypoglycemia** (treat if BS < 2.2)
  - ↓ Renal ability to concentrate urine / ↑ insensible water loss → prone to **hypovolemia and electrolyte disorders**
  - ↓ Hepatic function → kernicterus, ↓ drug metabolism
  - **Anemia**
  - Susceptible to **hypothermia** d/t relatively greater BSA / ↓ subcutaneous fat / thin skin / ↓ non-shivering thermogenesis (brown fat) vs. term / hypotonia
  - Difficult IV access
- Common conditions of prematurity:
  - **Hyaline membrane disease** – surfactant deficiency from immature type II pneumocytes
    - **Respiratory distress syndrome** (RDS) – increased risk of PTX
  - **Bronchopulmonary dysplasia** (BPD) – chronic pulmonary disease from prolonged ventilation
  - **Patent ductus arteriosus** (PDA), congenital cardiac defects
  - **Intracranial hemorrhage** (ICH) – intraventricular most common (IVH)
  - **Necrotizing enterocolitis** (NEC)
  - **Retinopathy of prematurity** (ROP)
  - Other congenital syndromes
- Altered pharmacokinetics / pharmacodynamics:
  - ↑ VD, ↓ clearance, ↓ protein binding, ↓ drug metabolism (cytochrome p450)
  - Increased sensitivity to opioids / inhalational agents (↓ MAC compared to term)

ANESTHETIC GOALS:

- Ensure optimization of multisystem derangements including respiratory, cardiovascular, hepatic, renal and hematological
- Anticipate fluid / electrolyte / glucose derangements and optimize preoperatively
- Ensure continuous temperature monitoring and maintain normothermia

HISTORY

- Gestational age at birth and the current post-conceptual age
- Obstetric and perinatal history including birth details, resuscitation, APGARs, need for intubation / ventilation / ICU care
  - C-section (increase risk of RDS since more water in lungs)
  - Birth asphyxia (risk of cerebral vascular dysregulation and IVH)
  - Maternal drug abuse
    - Heroine, cocaine for risk of withdrawal and PPH
    - Benzos and barbiturates show withdrawal about day 5-10
    - ASA and acetaminophen risk for pHTN and PPH
- Consider presence of associated disorders of prematurity as well as congenital abnormalities including heart disease and any treatments being utilized
  - BPD, RDS, PDA, IVH, NEC, ROP

PHYSICAL

- **GENERAL** - will focus on vital signs IV access / IV infusion + rate / U/O
- **RESP** - Intubated?, ventilation parameters, airway pressures and FiO_2 requirements, RR, spontaneous respiratory effort, work of breathing, crackles of pneumonia or failure, wheezes of airway resistance, signs of PTX
- **CVS** - murmur, signs of adequate skin perfusion, volume assessment (HR / BP / fontanel / skin color and turgor / urine output), look for PDA ($3\text{-}5^{th}$ day of life develops L to R shunt → bounding pulses wide pulse pressure, gallop rhythm, tachycardia), CHF (retractions, decreased a/e, crackles, decreased perfusion, cap refill, edema, hepatomegaly, new onset apneas)
- **CNS** - twitches, seizures (may indicate ↓ Ca^{++}), signs of CP

INVESTIGATIONS

- **Labs**
  - CBC (signs of sepsis); lytes / BUN / Cr (immature kidneys, TPN, diuretics); glucose; bilirubin; ABG (r/o acidosis)
    - ↓ Hb / HCT (< 30%) → increases risk of apneas
    - ↓ PLT if asphyxiated at birth
    - ↓ clotting factors (↑ PTT / INR) if asphyxiated at birth
    - ↓ Ca++ (can cause seizures)
    - ↑ Na+ (dehydration or excess Na+ administration)
    - ↓ K+ (diuretics)

- Normal ABGs in a preterm baby:

	3-5 hours	12-24 hours	5-10 days
pO_2	60	67	80
pCO_2	47	**27**	36
pH	7.32	**7.46**	7.38

- **Imaging**
  - CXR - BPD, CHF
  - AXR - NEC
  - ECHO PRN (biventricular function / congenital anomalies); cranial U/S if concern of ICH

OPTIMIZATION

- NICU / SCN / neonatology consults & medical optimization
- PDA: dehydrate (via fluid restriction) and Indomethacin (for medical closure) +/- surgical closure
- Early surfactant treatment as required (ie. BLES)
- Keep SpO_2 86-92% (PO_2 60-80 mmHg) to avoid ROP
- Keep Hb > 100 if cardiorespiratory disease, > 70 if otherwise well
- Vitamin K 1 mg if NPO since birth, or on IV antibiotics
- NPO (2 hrs clear fluids, 4 hrs breast milk)
- Correct acidosis (base excess x 0.5 x weight)
- Correct hypocalcemia ($CaCl_2$ 100 mg/kg)

ANESTHETIC OPTIONS

- Local, regional (e.g. inguinal hernia repair under spinal / epidural / caudal frequent in some centers), GA

ANESTHETIC SETUP

- **Drugs**
  - Standard emergency drugs
- **Equipment**
  - Standard CAS monitors + temperature
  - Temperature considerations – increase the OR temperature, use radiant heater pre-induction and forced air intraoperatively, and monitor temperature continuously (don't overheat)
  - Precordial stethoscope
  - Preductal SpO_2 (right limb or head)
  - Consider location of arterial line if there is PDA or other known shunt (i.e. right radial will reflect brain oxygen delivery as it is pre-ductal in location)
  - End-tidal CO_2 not a good reflection of $PaCO_2$ due to large dead space of the circuit
  - Appropriate sizes of circuits, masks, ETTs and consider cuffed ETT if expecting high ventilatory pressures, spirometry

MANAGEMENT OF ANESTHESIA

- **Induction**
  - Avoid strong sympathetic response (risk of IVH)
    - Fentanyl 1-3 mcg/kg + STP 2-5 mg/kg / propofol 2-5 mg/kg until lid reflex gone
    - Muscle relaxant usually not required for intubation
      - SCh 2 mg/kg, rocuronium 0.3-0.4 mg/kg, pancuronium 0.1 mg/kg
      - Avoidance of muscle relaxants (and opioids) in ex-premature infants recommended to avoid postoperative apnea
    - Consider Atropine 10-20 mcg/kg on induction to prevent bradycardia
  - ETT: allow leak at 20 cmH_2O
    - Watch for kinking of ETT and high risk of endobronchial displacement (short distance to carina)
- **Maintenance**
  - Anesthetic maintenance recognizing decreased MAC requirement (80% of adult) and increased cardiovascular depression with volatiles
    - If returning to SCN / NICU intubated then may use higher dose opiates and lower dose volatiles
    - If planning to extubate then watch narcotic dose (sevoflurane and remifentanil maintenance have been recommended) and use RA when applicable + appropriate apnea monitoring
  - Watch ventilatory pressures and expiratory times if BPD and consider pneumothorax if abrupt oxygenation problem or high peak airway pressures
  - Dextrose maintenance / NS replacement
  - Prevent air embolism
  - Consider FiO_2 → brief ↑ PaO_2 intraoperatively unlikely to be major factor in ROP (multiple factors postulated) but reasonable to minimize when possible
- **Emergence**
  - Reverse any muscle relaxation at end of the procedure if considering extubation
  - Dependent on disposition (SCN / NICU) and any underlying problems (smooth emergence is always a goal to strive for)

DISPOSITION & MONITORING

- **Post operative apnea in infants (see also below in Pathophysiology):**
  - Occurs in infants with history of prematurity and current PCA < 52 weeks and also in infants with history of apneas or chronic lung disease
    - Debate as to when apnea risk is normal between 50-60 weeks
    - Term + 4 weeks for term infants (i.e. at least 42-44 weeks PCA) → apnea monitoring
  - 20% of these patients have postoperative apnea
  - Due to prolonged action of anesthetics, shift of CO_2 response curve, immaturity of respiratory control or fatigue of respiratory muscles
  - Suggest admission and post-operative monitoring for at least 12 apnea free hours
  - Regional anesthesia alone may help reduce incidence but not if combined with sedative

- Avoid opioids and muscle relaxants as much as possible
- Prophylaxis with caffeine thought to be effective → 10 mg/kg IV (Cochrane review – 2003)
- **Risk Factors:**
  - Prematurity and ↑ risk with ↓ PCA
  - HCT < 30% (Hb < 100)
  - Apnea at home
  - Chronic respiratory disease (e.g. BPD)
  - Neurological disease (IVH, seizures, AVMs, congenital hypoventilation syndrome)

- **Walther-Larsen & Rasmussen (2006)**
  - Infants with a post-conceptual age of less than 46 weeks should be admitted for continuous monitoring for at least 12 h post-operatively
  - In infants with a post-conceptual age (PCA) between 46 and 60 weeks, a careful assessment of the child is mandatory and 12 h of respiratory monitoring is recommended if the patient's history reveals episodes of apnea at home, chronic lung disease (CLD), neurological disease or anemia
  - The otherwise healthy infant could be scheduled for theatre as the first patient on the list and subsequently monitored in the post-anesthetic care unit for 6 h
  - The risk of apnea in former preterm infants can be further reduced by the administration of intravenous caffeine (10 mg/kg)
  - All of these patients should be referred to a tertiary centre for anesthesia and surgery

PATHOPHYSIOLOGY

- Incidence: ~6% of deliveries
- Definition: < 37 weeks or < 2500 grams
  - Borderline = 36-37 wks
  - Moderate = 31-36 wks
  - Severe = 24-30 wks
- Intrauterine asphyxia is common
- Anesthetic morbidity increases with degree of prematurity → higher perioperative complication rates even after minor surgery
  - Therefore, only take to OR for strong indications

- **Impaired thermoregulation:**
  - ↑ BSA:volume → ↑ heat loss
  - Lack of fat insulation
  - ↓ Brown fat stores vs. term infants (NE stimulates non-shivering thermogenesis)
  - Thin skin → ↑ heat and insensible water loss
- **Hypothermia:**
  - May cause hypoglycemia, apnea, bradycardia, and metabolic acidosis
- **Respiratory distress syndrome (hyaline membrane disease):**
  - Rare > 34 weeks / ↑ 3x in C-section vs. vaginal delivery
  - Accounts for 50-75% premature deaths
  - Deficiency of surfactant (immature type II pneumocytes) → alveolar collapse, R→ L shunting, hypoxemia, and metabolic acidosis
  - Artificial surfactant has reduced mortality
- **Bronchopulmonary dysplasia:**
  - Definition: Continued oxygen requirement at 28 days of life with history of RDS
  - Chronic disorder → the more severe the RDS the greater the degree of BPD
  - Risk factors include: ↑ FiO_2, PPV, infection, PDA, and fluid overload in first 5-6 days of life, hypercarbia
  - Characterized by ↑ airway resistance, ↓ compliance, V/Q mismatching, ↓ PaO_2, tachypnea, ↑ MVO_2, ↑ pulmonary infections
  - May cause pHTN and cor pulmonale from severe BPD and PDA
- **Apnea:**
  - Definition: > 15-20s or cyanosis and bradycardia (HR < 100 bpm lasting at least 5s) associated with shorter episodes
  - All premature infants have degree of periodic breathing (3 apneic pauses of 3s interrupted by breathing for < 15-20s)
  - Increased risk with decreased GA
  - Increased postoperative apnea risk < 44 weeks (with reduction of risk between 44-60 weeks)
  - Postoperative apnea risk factors: prematurity, anemia (HCT < 30%), hypothermia, sepsis, neurological abnormalities
  - Treatment: caffeine IV 10 mg/kg to prevent postoperative apnea
  - Summary recommendations of recent review (Walther-Larsen & Rasmussen 2006):
- **Patent ductus arteriosus:**
  - L→R shunt, LVH, ↑ pulmonary blood flow, may cause CHF and respiratory failure
  - Medical closure (Indomethacin) vs. surgical (ligation)
- **Intracranial hemorrhage:**
  - 4 types: subdural, SAH, periventricular-intraventricular (most common) and intracerebral
  - Unusual beyond 10 days of life, most within 1st 3 days
  - Mechanisms:
    - Impaired autoregulation
    - Hypoxemia and hypercapnia
    - Hyperosmolality
- **Necrotizing enterocolitis:**
  - Small prems at greatest risk (< 32 weeks and < 1500g)
  - Hypoperfusion of gut? → ischemia
  - Abdominal distension, bloody stools, perforated bowel
  - Hypovolemia / volume resuscitation may cause intracranial hemorrhage or re-opening of ductus if too vigorous
  - Associated with DIC
  - Avoid nitrous

- **Retinopathy of prematurity:**
  - Inversely related to BW (< 1000g greatest risk)
  - Multiple factors aside from FiO_2
  - Little evidence that brief exposures to 100% O_2 is risk factor
  - Generally aim for PaO_2 60-80 mmHg
- **Infections:**
  - Decreased immunity / increased incidence pneumonia, sepsis, meningitis
  - May not exhibit leukocytosis or fever
  - Apnea, bradycardia, or acidosis may be only signs

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