PPHN - Persistent Pulmonary Hypertension of the Newborn

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Objectives

- Describe the normal physiologic transition of the cardiopulmonary system from fetal to neonatal circulation
- Identify risk factors for development PPHN
- Identify the clinical presentation of PPHN
- Describe nursing interventions to minimize progression of PPHN
- Identify current treatment strategies
- Explain significance of PPHN in the neonatal population
Fetal Circulation


2. The ductus venosus shunts oxygenated blood from the placenta away from the semilunar valves to the heart.

3. The ductus arteriosus connects the aorta with the pulmonic artery, allowing shunting blood away from the lungs and into the aorta.

4. Mixed blood travels to the head and body, and back to the placenta via the aorta.

5. The foramen ovale allows oxygenated blood in the right atrium to reach the left atrium.
Fetal Circulation: Quick Overview

- Organ of respiration is placenta
- Fetal lungs fluid-filled
- Pulmonary arteries constricted
- High right heart and lung pressures
- Low left heart pressures
- Open fetal shunts
Placenta

- Site for gas exchange in fetus
- Very vascular, large surface area
- High flow/low resistance circuit
- Responsible for delivering nutrients to and carrying waste products away from fetus
Open Fetal Shunts

- Ductus Venosus
- Foramen Ovale
- Ductus Arteriosus
- Purpose: shunt blood away from lungs, send well-oxygenated blood from placenta to fetus
Fetal Lungs

- Fluid-filled
- Low-flow, high-resistance circuit
- Only 10% cardiac output flows to lungs
- Only need blood flow for growth
Mixed blood travels to the heart and body, and back to the placenta via the aorta.

The ductus arteriosus connects the aorta with the pulmonary artery, further shunting blood away from the lungs and into the aorta.

The foramen ovale allows oxygenated blood from the right atrium to reach the left atrium.

Oxygenated blood from placenta enters right atrium via inferior vena cava.

The ductus venosus shunts oxygenated blood from the placenta away from the semifunctional liver and toward the heart.

Blood arrives via umbilical vein.
Lung Maturation Highlights

- **Fetal Breathing Movements**
  - Aid with lung fluid regulation, growth of lung tissue, strength of diaphragm

- **Antioxidant Defenses**
  - Scavenge/detoxify oxygen radicals from aerobic metabolism (toxic to cells)

- **Surfactant**
  - Reduces surface tension, aids lung expansion with lower pressures
  - Stabilizes alveoli, maintains FRC, prevents atelectasis
Lung Maturation

- Factors enhancing lung maturity
  - Stress
    - increased fetal catecholamines, cortosteroid levels
  - Chronic maternal hypertension, CV disease
  - Pre-eclampsia
  - IUGR
  - PROM
Lung Maturation

- Factors delaying lung maturation
  - IDM: high glucose/insulin level delays/interferes with surfactant production
  - rH isoimmunization with hydrops
  - Androgens delay Type II cell maturation (surfactant production)
    - Female fetal lung 1 week more mature
Surfactant

- Phospholipid
- Synthesized and secreted by Type II alveolar cells
- Unique: when layer is laterally compressed it changes physical nature from liquid to semisolid
- Forms protective oily layer on lung surface: antimicrobial properties
- Reduces surface tension, facilitates lung expansion with lower pressure
- Stabilizes alveolar surface during expiration so FRC is maintained
Lung Fluid

- Approximately 100 ml/kg/day secreted
- Becomes part of amniotic fluid
- Volume equivalent to FRC
- Function
  - Cell maturation/development
  - Formation, shape, size of airspaces
Lung Fluid

- Production slows late pregnancy
- Absorption during early labor
  - Active Na transport across epithelium
  - Liquid from lung lumen to interstitium, vasculature/lymphatics
- 35% original volume remains at birth
- Small amount squeezed out during vag delivery
- Delayed clearance with C-section
Fetal Pulmonary Vessels

- Greater amount of smooth muscle compared to adults
  - Increases tone of vessels, increases resistance to flow
- Constrictor response (reactivity) of smooth muscle is great (hypoxia)
- Number of vessels increases during fetal life
  - Decreases resistance to flow
Pulmonary Vascular Tone

- Central role: pulmonary endothelial cells
- Produce and release mediators that act on smooth muscle cells
- Delicate balance between vasoconstrictors and vasodilators maintain vascular tone
Pulmonary Vascular Tone

- Chemical and mechanical factors that decrease PVR include:
  - Oxygen
  - Nitric oxide, prostacyclines, some prostaglandins
  - Lung inflation
  - Structural changes in vessel walls -> thinning muscle
Pulmonary Vascular Tone

- Chemical and mechanical factors that increase PVR include:
  - Hypoxia, acidosis
  - Over or underinflation of the lungs
  - Increased chemical mediators:
    - Leukotrienes
    - Thromboxane
    - Endothelin
      - Protein: vasoactive peptide
      - Promotes vasoconstriction
      - Proliferation of SM cells in PA's
Pulmonary Vascular Tone

- Vascular tone increases with gestational age
- In **late** gestation, pulmonary pressures are equivalent to systemic pressures
- Major influences in utero favoring vasoconstriction
  - Low oxygen tension
  - High levels of endothelin-1 and leukotrienes
  - Low production of prostacyclines and nitric oxide
Pulmonary Vasculature

- Pulmonary hypertension with reduced PBF is normal state in fetus
- Fetus is physiologically hypoxemic (pO2~25): adequate for lung/cell growth
- Fetus is not hypoxic
- Adequate O₂ delivery to tissues in utero
  - High cardiac output
  - High hemoglobin level in term infant
  - Presence of fetal hemoglobin (high affinity for O₂)
Fetal Circulation in Detail

- **Umbilical Vein**
  
  One vessel
  
  From placenta to fetus
  
  Highest $O_2$ content
  
  (70%, 32-35 mm Hg)
  
  Branches into 2 parts inside the fetus
Fetal Circulation in Detail

- **Ductus Venosus**
  
  Majority of blood passes through DV
  
  From Umbilical Vein to IVC
  
  Blood then flows into Right Atrium
Fetal Circulation in Detail

- **Foramen Ovale**
  Majority of blood (> 50%) enters RA & flows through FO to LA

  Bypasses the lungs (2° to high PVR) so oxygenated blood gets to upper body through LV and aorta

  Pressure relationships keep FO open
Fetal Circulation in Detail

**Ductus Arteriosus**
Blood that does go from RA to RV to PA goes through DA to aorta

Again, bypasses the lungs (2º to high PVR) so oxygenated blood gets out to body through aorta

Pressure relationships, prostaglandins keep DA open
Fetal Circulation in Detail

- **Umbilical Arteries**
  
  Two vessels
  
  Deoxygenated blood from fetal circulation returns to placenta through umbilical arteries via the descending aorta
What Changes Have to Take Place at Birth for Successful Transition?

Have to switch gas exchange from the placenta to the lungs.
Transition: Critical Events

- Initiate respiratory movements
- Air into lungs, expansion of alveoli
- Establish FRC
- Increase pulmonary blood flow, redistribute cardiac output
Transition: Critical Events

- Oxygenation
  - Increases oxygen tension: pulm vessels dilate
  - Reduces PVR, increases PBF/venous return
  - Decreases ductal shunting

- Ventilation
  - Clears lung fluid/creates gas-fluid interface
  - Stimulates surfactant secretion
  - Stimulates pulm stretch receptors/increase PBF

- Cord clamping
  - Removes low resistance placenta
  - Increases SVR
First Breath

- Has to occur for other steps to follow
- Two important stimuli for infant to breathe
  - Cold
  - Chemoreceptor response to brief asphyxia
- Respiratory muscles
  - Contract, decrease intrathoracic pres
  - Air pulled into lungs
Establish FRC

- Volume of air retained in lung at end expiration (40% of fully expanded volume)
- Initial opening breath requires high pressure for expansion (40 - 60 cm H₂O)
- Next breath requires much less pressure, better inflation (need surfactant)
- Forces opposing air entry
  - Lung fluid
  - Surface tension in alveoli
Circulation Changes

- First breath causes rise in paO₂
- Pulmonary vessels dilate
- ↓ PVR, increased flow
  - Pulm vasculature becoming high-flow, low-pressure circuit
- ↓ R heart pressures
Circulation Changes

- Removal of low resistance placenta
- Increases systemic pressure/LV pressure
- Increases volume (venous return from lungs) left side of heart
- L heart pressures > R heart pressures
- Functional closure of the Foramen Ovale within minutes to hours after birth (anatomical closure 30 months or longer)
Circulation Changes

- Pressure in aorta becomes > pressure in PA’s: reverse flow through **Ductus Arteriosus**
- ↑ oxygen level, smooth muscle constricts to close the ductus
- PGE removed by lungs aids in closure
- Functional closure in healthy term baby by 96 hrs of age
- Anatomical closure later by tissue growth (up to 3 months)
Circulation Changes

- **Ductus venosus** functionally closes within hours after cord clamping when there is no longer blood flow from umbilical vein
- Anatomical closure by 10 to 14 days after birth
PPHN: Types and Associated Factors
PPHN – The Pathophysiology

- PVR does not fall
- PFO & PDA remain open shunting blood away from lungs
- Impaired gas exchange
- Progressive hypoxia & hypoxemia
- Increased cardiac afterload (right side)
- RVH, TI & heart failure
elevated PVR
deoxegenated + oxygenated blood
systemic circulation
hypoxemia
The Three Types of PPHN (What Causes Elevated PVR)

Underdevelopment

Maladaptation

Maldevelopment
A Little Physics
(Poiseulle’s law)

Volume Flowrate =

Pressure difference \times radius^4
Viscosity \times length
Small changes go a long way

(Taken from http://hyperphysic.phy-astr.gsu.edu)
Causes of Vasoconstriction

- Acidosis
- Hypoxia (acute or chronic)
- Asphyxia
- Vasoactive mediators
- Muscular hyperplasia
Arterial vasodilation

- Alkalosis
- Oxygen
- Vasoactive mediators
- Medications
Underdevelopment (Lung Hypoplasia)

- Decreased cross sectional area of pulmonary vasculature
- Examples: CDH, CCAM, renal agenesis, obstructive uropathy, IUGR
- Fixed elevated PVR
- High mortality
Maldevelopment
(Abnormal vasculature)

- Lung parenchyma develops normally
- Thick muscular layer around arterioles
- Vascular mediators are involved
- Genetic predisposition
- Excessive fetal perfusion of lungs
- Examples: post dates, premature closure of the ductus ateriosus
Maladaptation
(Pulmonary vasoconstriction)

- Normal pulmonary vascular bed
- Also known as secondary PPHN
- Active vasoconstriction at or after birth
- Examples: perinatal depression, hemorrhage, aspiration, asphyxia, lung disease, infections, hypoglycemia, hypothermia
Risk factors

- 1. Fetal closure of ductus arteriosus
- 2. Abnormal response to oxygen levels
- 3. Hypertrophy of pulmonary smooth muscles
- 4. Lung hypoplasia
- 5. Segmental alveolar underventilation
Risk factors cont’d…

- 6. Dysfunction or proliferation of vasoactive mediators
- 7. Presence of microthrombi in pulmonary vascular bed (polycythemia)
- 8. Maternal/perinatal factors
- 9. Airway obstruction, MSAF
Diagnosis
(How do you know it’s there?)

- “This baby just doesn’t look good”
- Severe cyanosis – a medical emergency!
- Low PaO₂ with normal PaCO₂
- Pre-ductal saturation higher than post-ductal
- Cardiac murmur (sometimes), CHF/TR
The Work-up

- Pre & post ductal saturations
- Hyperoxygenation test
- Chest x-ray
- Echocardiography (most definitive)
Echocardiogram

- Excludes congenital heart disease
- Measures pulmonary artery pressures (TR, TI, shunt velocities)
- Defines the presence, degree, and direction of intra-cardiac shunting
- Describe ventricular outputs and function
The Symptoms

cyanosis

respiratory distress

acidosis

PULMONARY VASOCONSTRICTION
Nursing Assessments and Management

- Antepartum
- Intrapartum
- Postpartum

- Crucial nursing assessment/intervention periods
Antepartum

- Good prenatal care!
- Prenatal education
Intrapartum

- Close intrapartum observation is key!
  - Careful fetal monitoring
  - Careful documentation!
Postpartum Preparedness

- Be prepared for high risk deliveries
- Suction equipment, Delee suction, ETT & laryngoscope, meconium aspirator, oxygen, PPV equipment
- Closely observe infant especially if respiratory distress present
Nursing Assessments

- Monitor HR, color closely
- If low Apgars or intubated
  - Frequent vital signs & respiratory assessments
  - Cord and post-natal blood gas analysis
  - Arterial stick for blood gas if not intubated
  - UAC if intubated or with high O2 requirement
Nursing Interventions

- Optimize oxygenation
  - Keep saturations in high 90’s
  - Oxygen challenge test
  - Wean very slowly if stable
- Correct metabolic acidosis
  - Fluid boluses
- Closely monitor perfusion and blood pressure
  - Color, CFT, pulses, temperature of skin
  - May need to treat hypotension/hypoperfusion with fluid boluses and/or inotropes
- Keep calm
  - May need sedation or paralysis if mechanically ventilated
  - Minimize O2 consumption
- Keep NPO
- Provide IVF and antibiotics
Assist with Medical Therapies

Goal: \(\downarrow \) PVR & \(\uparrow \) PaO2

- Mechanical ventilation
- Optimize Oxygenation
- Maintain Normal pH (7.35-7.45)
Other Medical Therapies & Diagnostic Tests

- High frequency ventilation
- Inhaled nitric oxide
- Surfactant administration
- ECMO – previously needed for 40% severe PPHN
Experimental Therapies

- Sildenafil
- Systemic steroids (for MAS)
- Magnesium sulfate
- Prostacycline
A Special Word: Nitric Oxide

- Produced endogenously
- Enzyme NO synthetase acts on arginine
- Increases levels of cGMP
- Potent smooth muscle relaxant
- Vasodilation
Inhaled Nitric Oxide

- Diffuses through the alveolar membrane
- Into the blood stream and deactivated
- No systemic effects
Inhaled NO
(Guidelines for Use)

- Clinical and echocardiographic signs of PPHN
- FIO$_2$ 1.0 already in use
- Access to ECMO
- Start at 20ppm, using a accurate delivery system
- Wean slowly when clinically stable
Side effects to Watch For

- Methemoglobinemia -
  - NO intereacts with oxyhemoglobin to form methemoglobin and nitrates
- Watch for rebound hypertension –negative feedback?
Provide Parental Support

- Explain! Explain! Explain!
- They can touch their infant, take pictures
- Prepare them for possible transport even before you know for sure it will happen
Prepare for Transport

- Ensure adequate IV access
- Suction ETT
- Sedation and maybe paralysis
- Continue 100% oxygen & iNO if applicable
Morbidity & Mortality

- Primary risks stem from:
  - 1. Delay in recognition of existence and severity of hypoxemia
  - 2. Delay in timely transfer to an ECMO center
  - 3. Lack of communication with an ECMO center especially if iNO is initiated
Outcomes of PPHN

- Before ECMO, mortality 12 to 50%
- Since ECMO, survival ~ 85%
- Significant morbidity still 10 to 45%
- Hyperventilation – some sensorineuronal hearing loss reported as high as 53%
- Higher risk for developmental delay & motor disability but most survivors are normal
Case Study

- 41 week 4.2 Kg female w/cyanosis & tachypnea immediately after vaginal delivery through meconium stained fluid
- APGARS 4 and 6
- Temp 36.9°C, HR 175, RR 110, BP 65/30
- Exam: Barrel chest w/retractions, poor aeration and bilateral rales

What is the primary problem for this child?

A. Meconium Aspiration
B. Pulmonary Hypertension
C. Respiratory Distress Syndrome
D. Air leak syndrome
13% of all live births
4-5% develop MAS

Classic findings:
- Barrel chest, rales and rhonchi
- CXR w/patchy areas of atelectasis alternating with over-inflation
- 10-20% have pneumothorax

Meconium Aspiration Syndrome
Mechanism of Injury
- Chemical pneumonitis
- Inactivation of surfactant
- Activation of complement (inflammatory pathways) and vasoconstriction
- Airway obstruction

Risk Factors
- Full term or post dates
- Fetal distress and in utero hypoxia
- Meconium stained amniotic fluid

Clinical
- Severe respiratory distress right after birth
Meconium Happens.

- **Pulmonary Function**
  - Decreased Lung Compliance
  - Decreased alveolar ventilation from air trapping
  - Decreased perfusion to poorly ventilated areas of lungs leading to hypoxia
  - Increased pulmonary vascular resistance due to local and general vasoconstriction
Current recommendations

- No benefit to suctioning the oral pharynx before delivery of the body
- No benefit to intubation of the vigorous infant
- Manage pulmonary hypertension
- Antibiotics
- Surfactant treatment to decrease risk of air leak or need for ECMO
- High frequency ventilation may decrease air trapping, improve lung compliance and diminish right to left shunts