Persistent pulmonary Hypertension of the newborn

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Objectives

1. Describe the differences between fetal and newborn cardiovascular physiology
2. Discuss common causes of PPHN
3. Evaluate common approaches to the treatment of PPHN
First described in 1969 by Gersony et al

First described as “persistent fetal circulation”

- Systemic blood flow through fetal shunts (PDA and PFO)
- Systemic hypoxia
- Similar to fetal circulation
Case Presentation

- 37 week twin gestation, di-di twins
- Uncomplicated pregnancy
- C-section for transverse
- A-female, healthy, mild resp. distress, tx to NICU
- B-significant respiratory distress soon after delivery, transfer to NICU
Case Presentation

A-female
- X-ray consistent with TTN
- Transferred to NICU
- Within 2 hours, respiratory distress resolved
- Roomed in

B-male
- Continued respiratory distress
- X-ray with pneumothorax
- Chest tube, CPAP
- PaO₂ 50 mmHg on 100% oxygen
What is wrong?

- Is this PPHN or something else?
- Is it the heart?
- How do you figure it out?
- What are the treatments?
PPHN-Background

- PPHN is defined by a failure of pulmonary vascular resistance to decrease after delivery
- Results in failure of systemic oxygenation (hypoxia)
  - Multi-organ system failure
- Absence of congenital heart disease
PPHN-Background

- Low oxygen levels normal as fetus
- Low oxygen levels not well tolerated after delivery
- Spectrum from mild respiratory symptoms to complete collapse needing advanced neonatal intensive care
PPHN-Background

- Incidence 2/1000 live births
- Prompt diagnosis important
- Mortality <10%
  - 11-34% in 1980’s
- Early treatment improves outcome
  - Referral to tertiary care center
FETAL CARDIOVASCULAR AND TRANSITIONAL PHYSIOLOGY
Fetus characteristics that allow for low oxygen levels

- No heat generation
- No significant respiratory effort
- No digestion
- Reduced movement
Fetus Cardiovascular Characteristics

- Oxygen consumption reduced in the fetus
- Lower PaO2/saturations in the fetus
- When delivered
  - Increased oxygen demands
Fetal Oxygen Saturations

- SVC
- Ascending Aorta
- Aorta
- Pulmonary Artery
- DA
- LA
- RA
- IVC
- LV
- LA

http://www.embryology.ch/anglais/pedcardio/p9umstellung/oxygendvorr.html
Changes at Birth - Lungs

- The lungs become the organ of gas exchange
- Continuous breathing
- Expansion of lungs with air
- Surfactant synthesis
- Fetus becomes more oxygenated
Changes at Birth - Cardiovascular

- Removal of the placental circulation
- Decreased pulmonary vascular resistance (PVR)
- Increase in pulmonary blood flow
- Closure of the ductus arteriosus, foramen ovale, and ductus venosus
Changes at Birth - Other

- Glucose homeostasis
- Thermogenesis
- Hormonal and metabolic
Review

before birth

after birth

http://www.embryology.ch/anglais/pcardio/umstellung02.html
Fetal Oxygen Saturations

- SVC
- Aorta
- Pulmonary Artery
- DA
- LA
- RA
- IVC
- LV

Ascending Aorta

http://www.embryology.ch/anglais/peurc/acardio/p9umstlungen/oxygenmach.html
COMMON CAUSES OF PULMONARY HYPERTENSION
Common to All Causes of PPHN

- Pulmonary vasospasm
- Altered pulmonary vascular reactivity
- May have increased muscle mass in the pulmonary vascular bed
Factors exerting control over pulmonary vascular tone

- Hypoxemia
- Acidosis
- Endogenous substances
  - Vasoconstrictors: leukotrienes, thromboxane, endothelin, etc
  - Vasodilators: oxygen, Nitric Oxide (NO), prostacyclin
- Systemic hypotension
  - Blood flows along pressure gradient – i.e.: path of least resistance
Causes of PPHN

- Parenchymal lungs disease
- No known lung disease (primary PPHN)
- Genetic or developmental lung abnormalities
Parenchymal Lung Disease

- Meconium aspiration syndrome
  - Most common cause
- Hyaline membrane disease (RDS)
  - Third most common
  - Especially in 34-37 weeks
    - Increased pulmonary vasoreactivity
Parenchymal Lung Disease

- Pneumonia/sepsis
  - Release of endotoxins
  - Hypotension
  - Acidosis
- Pneumothorax
  - Hypoxia and/or acidosis
Primary PPHN

- No recognizable lung disease or predisposition
- Second most common cause
  - Prenatal constriction of ductus arteriosus implicated
  - NSAID
- SSRI’s
Genetic or developmental lung abnormalities

- Pulmonary hypoplasia
  - Congenital diaphragmatic hernia
  - Oligohydramnios
    - PPROM
  - Fewer vessels, more reactivity
- Lethal forms
  - Alveolar capillary dysplasia
  - Surfactant deficiencies
Summary: Causes of PPHN

Diagnosis of PPHN

- Respiratory distress
- Labile oxygenation
- Hypoxia out of proportion to degree of lung disease
- Exam

  - Respiratory distress, grunting, retractions, cyanosis
  - Murmur from tricuspid regurgitation
Diagnosis of PPHN

- Overlap with cyanotic heart disease
- Chest x-ray
- Arterial blood gas*
- Pre and post ductal pulse ox
  - ½ of babies with have a shunt across PDA
- Echocardiography
Hyperoxia Test

- Arterial blood gas obtained prior to and 5-10 minutes after administration of 100% Oxygen
  - PaO2 < 50 mmHg - cyanotic congenital heart disease or PPHN
  - PaO2 < 150 mmHg - PPHN
  - PaO2 > 150 mmHg - parenchymal lung disease
  - PaO2 > 300 mmHg - normal
Echocardiography

- Pediatric trained echo techs needed
- Look for congenital heart disease
- Right to left/bidirectional shunts
- Flat intraventricular septum
- Dilated right ventricle
- Tricuspid regurgitation to estimate pulmonary artery pressures
APPROACHES TO TREATING PULMONARY HYPERTENSION
Anticipation and Transition

- Anticipating at risk infants
  - MAS, sepsis, CDH, etc.
  - Prompt treatment and evaluation
- Ensuring appropriate transition
  - Thermoregulation, glucose homeostasis, blood pressure, antibiotics
Principles of Treatment

- Restore cardiopulmonary transition while avoiding lung injury
- Avoid oxygen toxicity
- Avoid compromise of systemic perfusion
Treatment

- Correct underlying metabolic derangements
  - Body Temperature
  - Acidosis
  - Surfactant
  - Glucose homeostasis
  - Electrolyte abnormalities
  - Treat anemia
Respiratory Treatment

- Mild respiratory distress
  - Treat with nasal cannula or CPAP
  - Follow ABG closely
  - Low threshold for UAC/UVC
  - Low threshold for ventilation
- Moderate to severe disease must be treated aggressively
Treatment

- Goal in moderate to severe disease is to
  - Reverse right-to-left shunts
  - Reduction of PVR
  - Maintain systemic blood pressure
Respiratory Treatment

- Ventilation / oxygenation
  - High PaO2 (>100 mm Hg) and low PCO2 used traditionally
    - Does not improve outcomes, potentially harmful to lungs and cerebral perfusion
    - No significant reduction in PVR with PaO2 > 100 mm Hg
    - Sometime need >100 mm Hg due to lability (flip flop)
  - High frequency ventilation
Cardiovascular Treatment

- Increase systemic blood pressure
  - Reduce right-to-left shunts
  - Dopamine, dobutamine, epinephrine
    - Optimize (not maximize) cardiac function
  - Want normal to high blood pressure
Pulmonary vasodilators

- Inhaled nitric oxide
  - Most significant advancement in treatment
  - Selective pulmonary vasodilator
  - Supported by several large trials
  - Decreased mortality and need for ECMO
- Milrinone, sildenafil (off label use)
Sedation/Paralytics

- Minimize stimulation
  - Quiet, minimize movement of patient
  - Sedation / neuromuscular blocking agents?
    - Reduce oxygen consumption
    - Comfort
    - Not tested in randomized trials
ECMO

- Extracorporeal membrane oxygenation
- First used in the 1970’s
  - Used as rescue therapy for neonates with greater than 80% predicted mortality
- Respirator and cardiac support
ECMO

- Allows lungs to recover while on ECMO
- Only for >34 weeks
  - Complications greater in less mature
- Reduced numbers of ECMO cases
- ACH the busiest neonatal ECMO center in world in recent years
ECMO

- Early referral for PPHN and ECMO essential
  - iNO started on ECMO candidate, should transfer to ECMO center
  - ECMO not a replacement for early, optimized therapy for PPHN
Case Presentation - Resolution

- Twin B placed on vent
- Echo showed flat septum, TR jet systemic
- Surfactant replacement
- Able to rapidly wean oxygen
- Improved oxygenation, extubated DOL 6
- Discharged to home at 16 days
Summary

- Understanding fetal circulation and transition is to understand PPHN
- Good transitional care important in the prevention of PPHN
- The most common causes of PPHN are MAS, RDS, and infection
- Treating PPHN includes providing adequate oxygenation and restoration of cardiopulmonary transition using optimal (not maximal) therapies appropriate to the cause of the PPHN
References

- Klaus and Fanaroff, Care of the High-Risk Neonate, 5th edition.