

# PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

Travis W Anschutz, MD  
Neonatologist

# Disclosure Statement

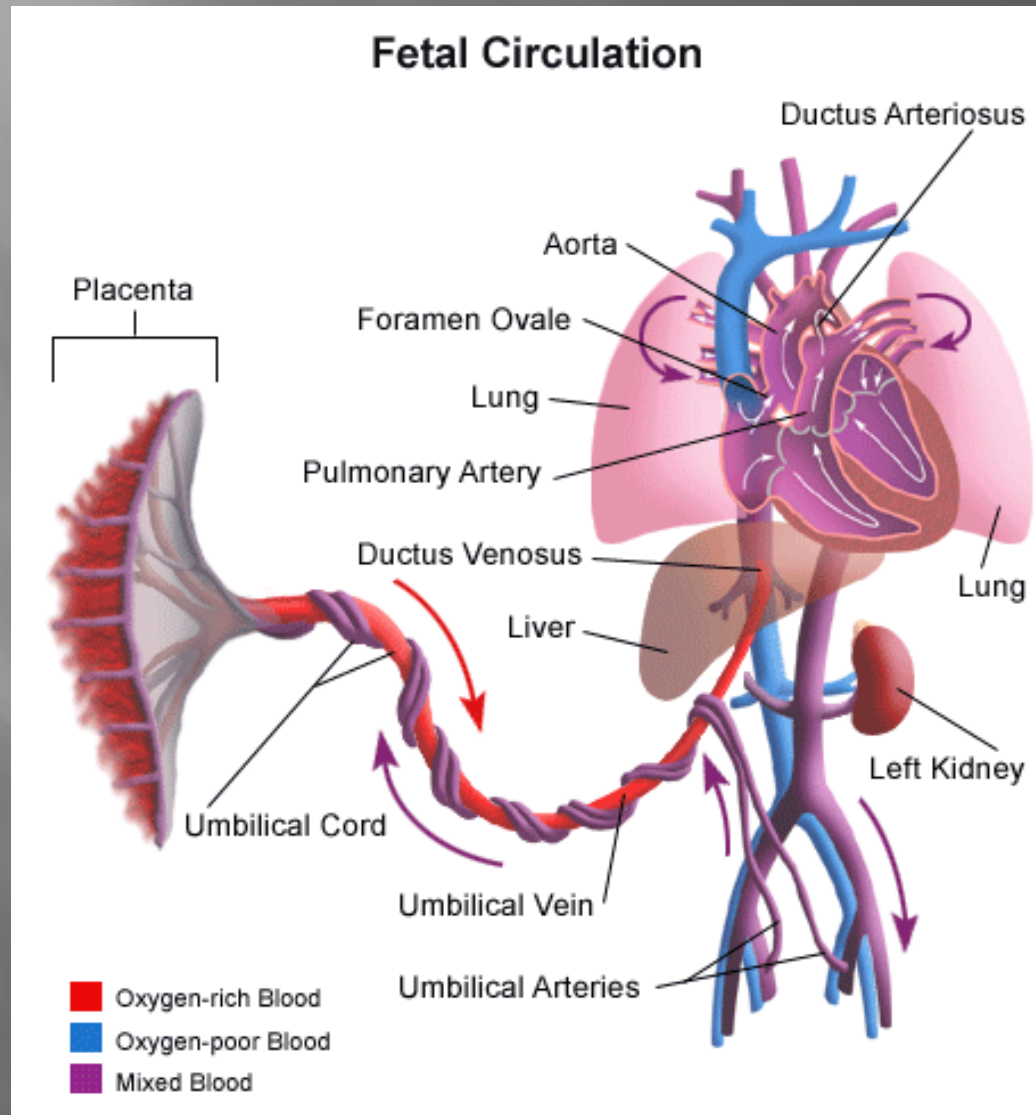
- ▣ I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

# Objectives

- ▣ Briefly Understand Fetal Circulation
- ▣ Define Pulmonary Hypertension
- ▣ Understand Nitric Oxide Metabolism
- ▣ Understand Epidemiology, Morbidity, Mortality
- ▣ Understand Etiologies of PPHN
- ▣ Be Able to Recognize PPHN Clinically
- ▣ Understand Initial Treatment Strategies
- ▣ Review Calculation of OI
- ▣ Know Therapies For PPHN
- ▣ Understand Who Goes on ECMO

# Fetal Circulation

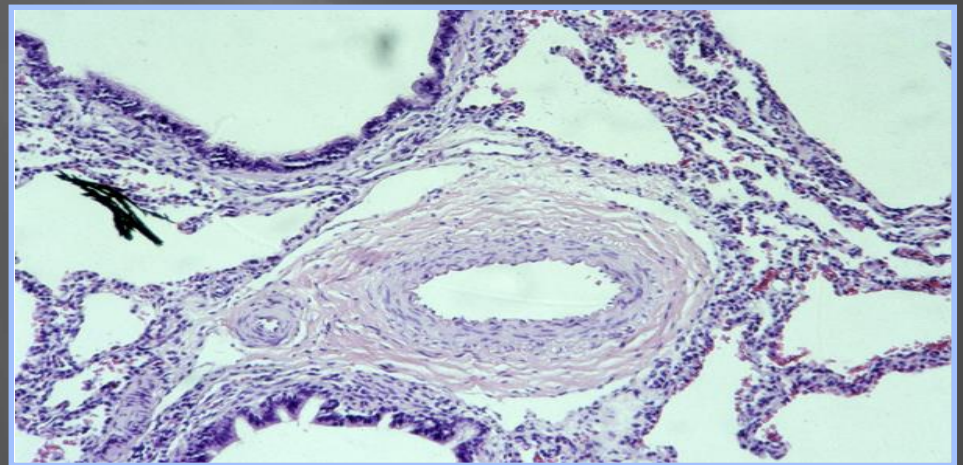
13-20%  
pulmonary  
blood flow



\*1,2,3, 4

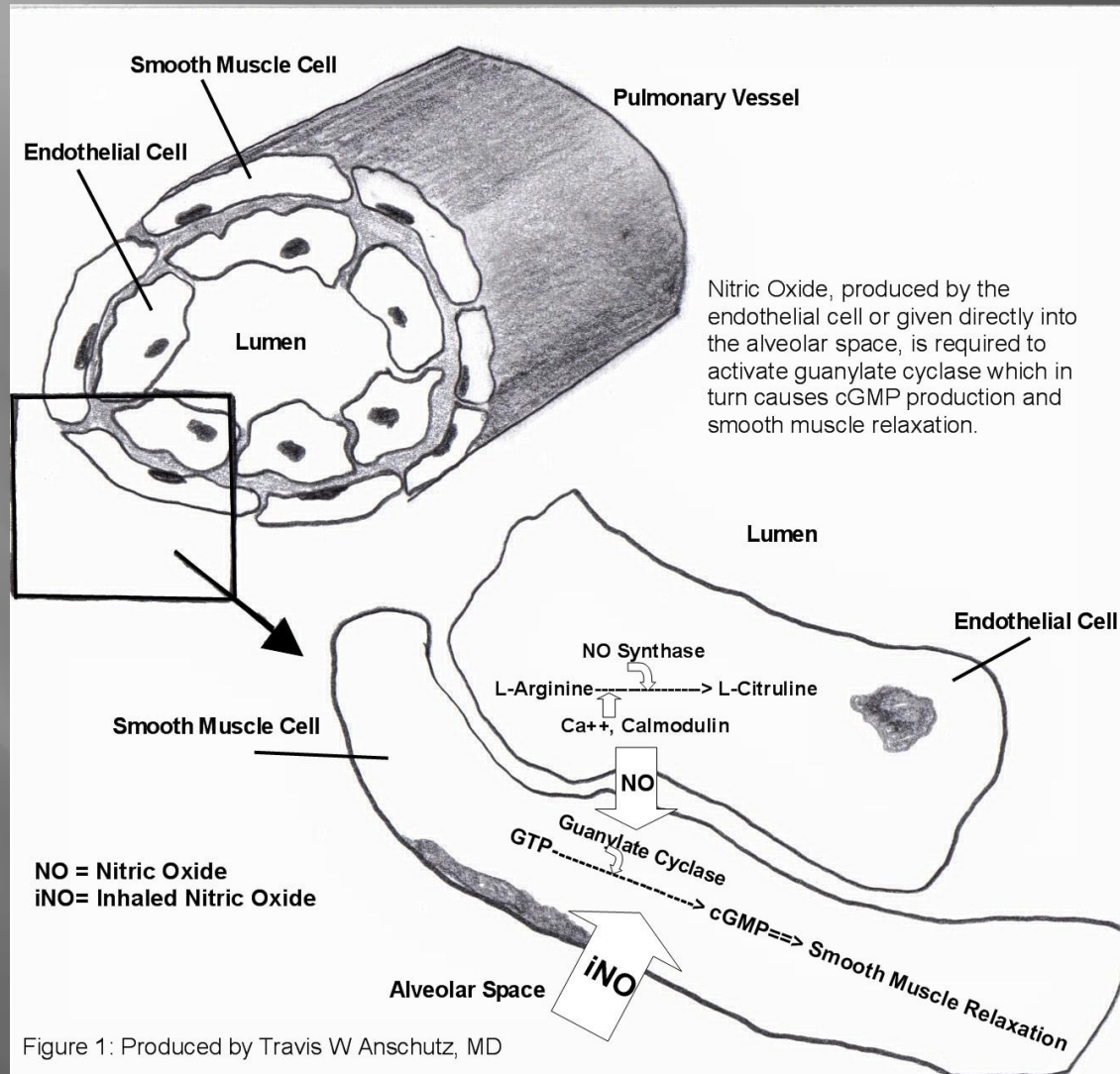
# Persistent Pulmonary Hypertension of the Newborn

- ▣ Failure of the normal transition to the extra uterine circulation secondary to sustained high pressures in the pulmonary circulatory system.
- ▣ 1969- Gersony- Persistence of Fetal Circulation
- ▣ Pulmonary Artery Pressure  $>2/3$ -  $3/4$  Systemic Pressure ( $>30\text{mmHg}$ )
- ▣ Leads to:
  - Hypoxemia
  - Acidosis
  - End Organ Damage
  - Dev Delay
  - Hearing Loss
  - Death





# Nitric Oxide Metabolism



# Epidemiology

- ▣ USA- 4,000,000 Births per year
- ▣ 2-6 per 1,000 Live Births
- ▣ 8,000- 24,000 PPHN cases per year

# Morbidity/ Mortality

- ▣ 1992
  - Mortality-40-60%
  - Morbidity- up to 60% of survivors
    - ▣ Hypocarbia, Magnesium, Volutrauma, Alkalinization
- ▣ ECMO
  - Reduced Mortality from 60-30%
- ▣ 2014
  - Mortality- <10%
  - Morbidity- 15-20%

\*1,2,3,4



# Etiology/ PathoPhys

## **Maladaptation/Parenchymal Lung Diseases**

- Meconium Aspiration Syndrome
- Pneumonia/ Sepsis
- Extreme Preterm/ RDS/ BPD

## **Maldevelopment/ Idiopathic (Black Lung PPHN)**

- Abnormally remodeled vascular bed
  - Premature Closure of PDA
- Maternal use of NSAIDs, SSRIs last half of pregnancy
- Capillary Alveolar Dysplasia

## **Underdevelopment/ Pulmonary Hypoplasia**

- Congenital Diaphragmatic Hernia
- Renal Disease/ PPRM/ Oligohydramnios sequence

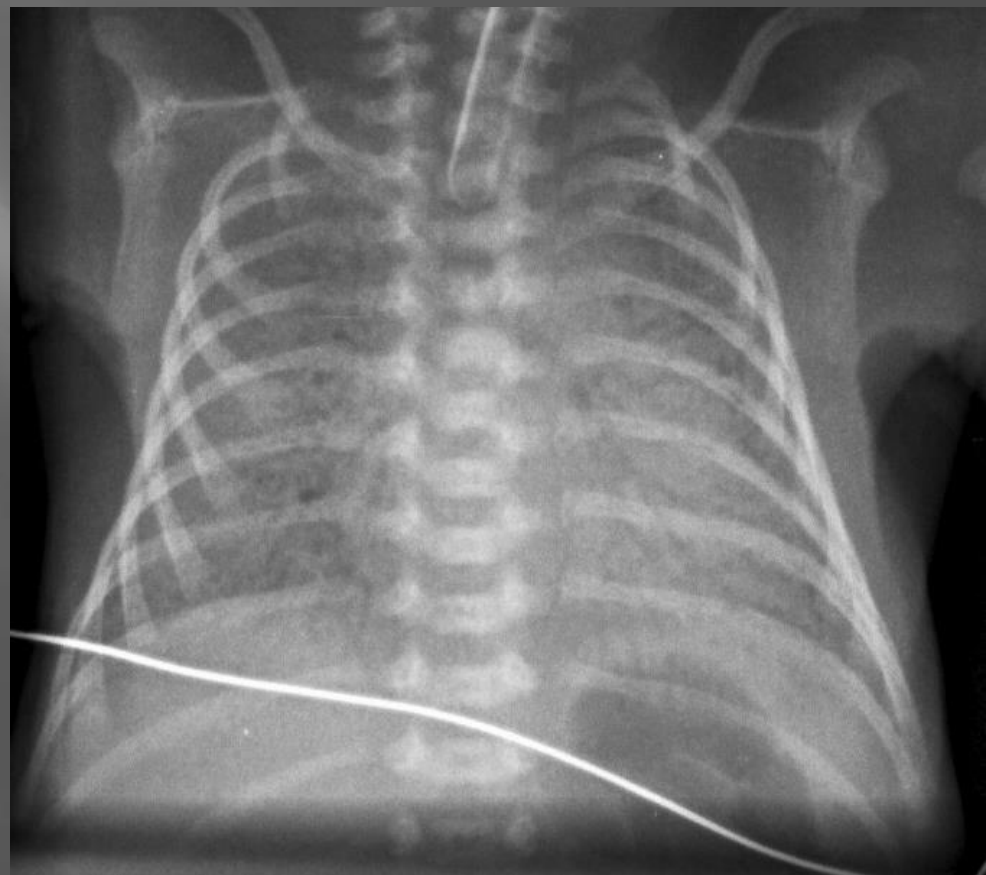
# Etiology

- ▣ Transient Pulmonary Hypertension
  - Hypoxia
  - Acidosis
  - Hypoglycemia
  - Polycythemia

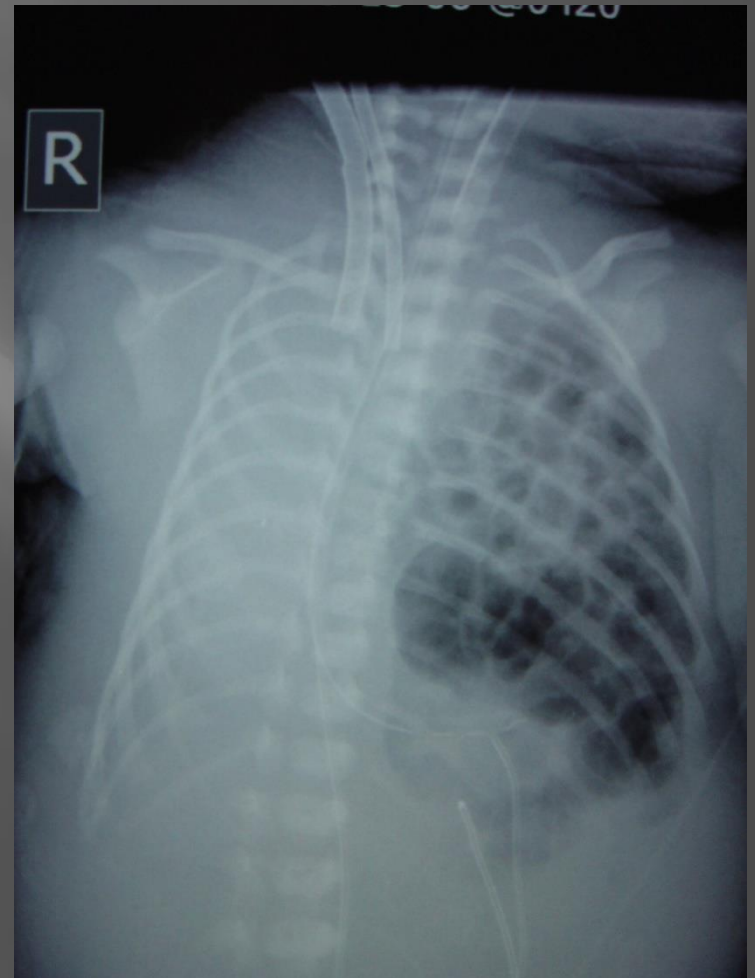
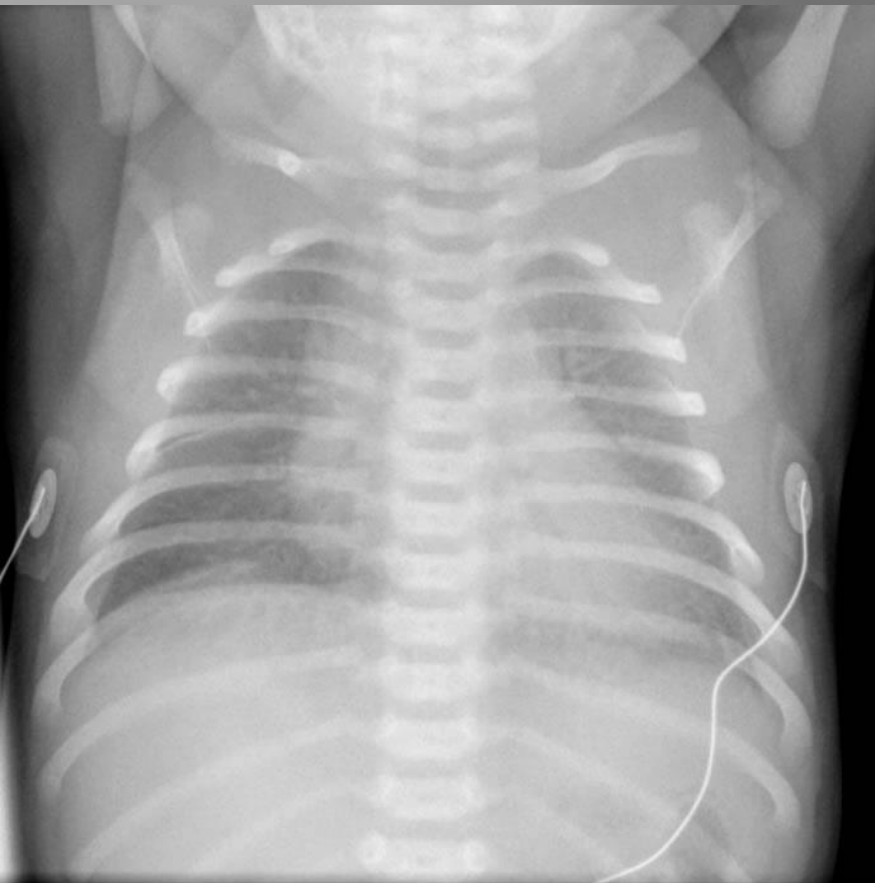
# Etiology

- ▣ Persistent Pulmonary Hypertension
  - *Meconium Aspiration (Most Common Cause)*
  - *Idiopathic/ Black Lung PPHN (2<sup>nd</sup> Most Common Cause)*
  - Amniotic Fluid Aspiration
  - Sepsis
  - Pneumonia
  - Pulmonary Hypoplasia
  - RDS
  - Surfactant Protein Mutations
  - CDH
  - Potter Sequence/ Oligohydramnios
  - Chronic Intrauterine Asphyxia
  - Premature Closure of Ductus
  - Maldevelopment of Pulmonary Vessels
  - SSRI use in Expectant Mothers

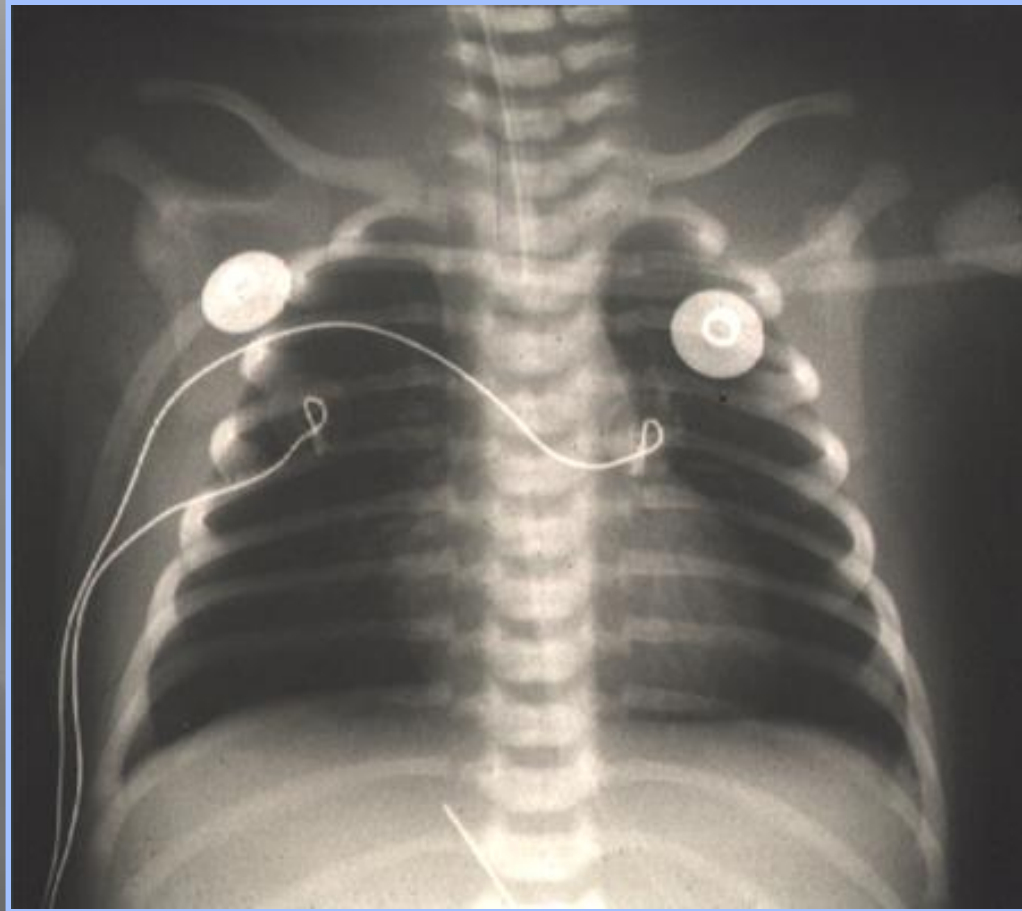
# Radiographs



# Radiographs



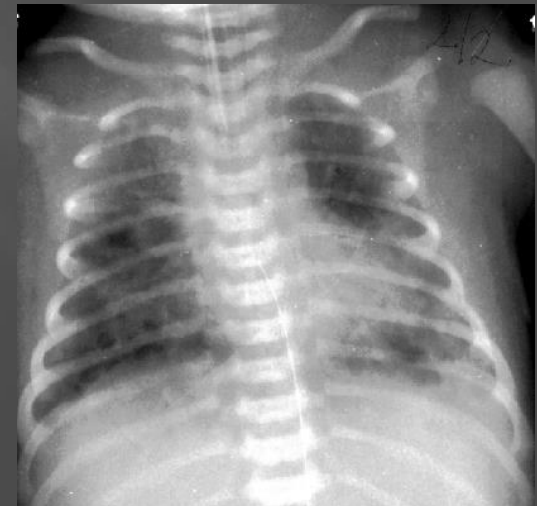
# Black Lung PPHN





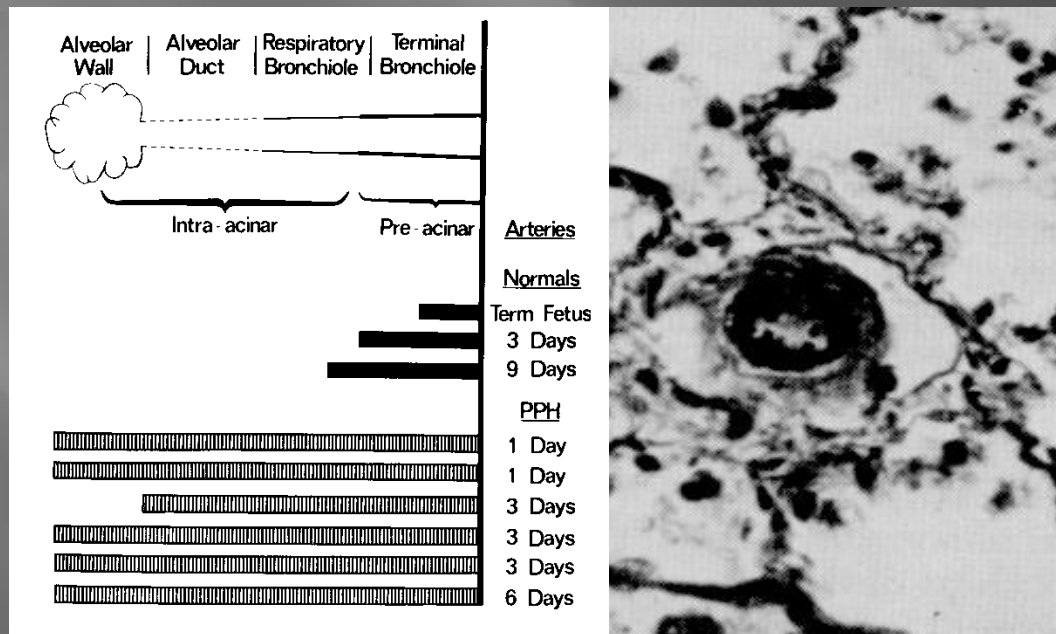
# Etiology PPHN

- ▣ Most Common Cause- Meconium Aspiration
  - 25-30,000 infants annually
  - 1,000 Deaths annually
  - (=3% mortality rate from MAS)
    - ▣ 13% of all live births have Meconium Stained Fluid
    - ▣ 5% of these develop MAS
    - ▣ \*Most aspirations occur in utero



# Etiology PPHN

- ▣ Second Most Common Cause= Idiopathic
  - >34 wks GA- Late Preterm/ Term
  - NSAIDs, SSRIs



# Clinical Recognition

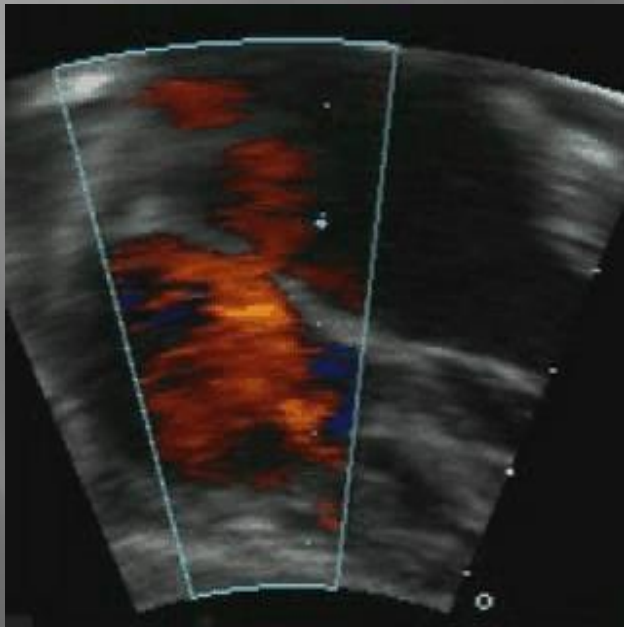
- ▣ History/ Underlying Etiology
- ▣ Hypoxia, Hypoxemia
  - Out of proportion to distress/ X Ray
- ▣ Metabolic Acidosis
- ▣ Pre-Post Ductal Splitting ( $>10$ )
  - R arm, Leg
- ▣ Respiratory Distress +/-
- ▣ Hypotension +/-
- ▣ Tachypnea

**LABILITY**

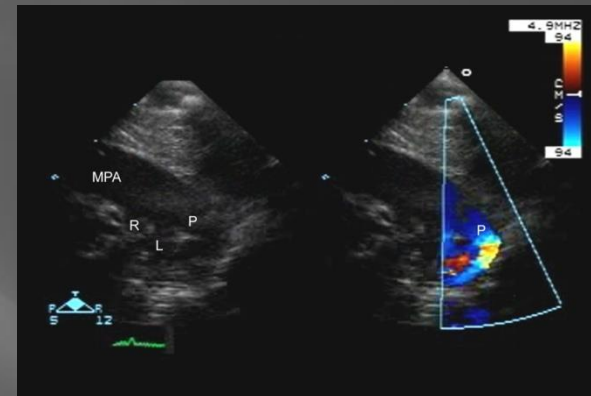


# Diagnosis

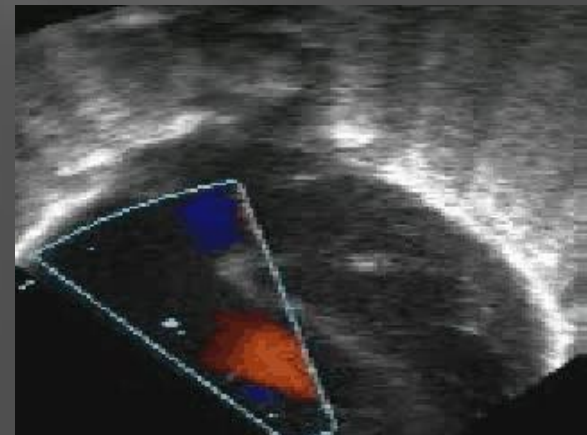
- ▣ Clinical
- ▣ Echocardiography
- ▣ Response to Tx- iNO



R→L Shunt PFO



R→L Shunt PDA



Tricuspid Regurgitation

# Echocardiogram

- ▣ Estimation of Right Ventricular Pressure
  - To estimate Pulmonary Arterial Pressure
  - $> 2/3 - 3/4$  Systemic Pressure
  - Calculation based upon Tricuspid Regurg Jet
  - $\pm 10\text{mmHG}$  in 48% cases
  - Underestimates more often than Overestimates

# Pulmonary Vascular Resistance

<i>Increase PVR</i>	<i>Decrease PVR</i>
Hypoxia	High FiO <sub>2</sub>
Hypercarbia	Adequate Ventilation
Acidosis	7.35-7.40
Hypotension	Bolus/ Pressor
Stimulation	Sedation
Thromboxanes	Limit Lipids
Over/Underinflation	9 Ribs



# Initial Treatment

- ▣ Prompt Recognition
- ▣ Provide Antibiotic Coverage
- ▣ Decrease Stimulation
  - Cover Eyes, Ears
  - Limit Painful Procedures/ Sticks
  - Try to Limit Hands on Care
- ▣ Provide Oxygen
  - Keep SaO<sub>2</sub> >95



# Next Step in Therapy

- ▣ Mechanical Ventilation
  - Conventional vs HFOV
- ▣ Tx Underlying Cause
- ▣ Surfactant
- ▣ Prevent Hypocalcemia
- ▣ Sedation
  - Fentanyl, Versed
- ▣ Correct Acidosis
- ▣ Correct Hypotension/ Boost Systemic Pressure
  - Fluid Bolus
  - Dopamine/ Dobutamine/ Hydrocortisone/ Norepinephrine
- ▣ Maximize Oxygen Carrying Capacity- PRBCs
- ▣ ?Paralysis?



# How Are We Doing?

- OI- Oxygenation Index

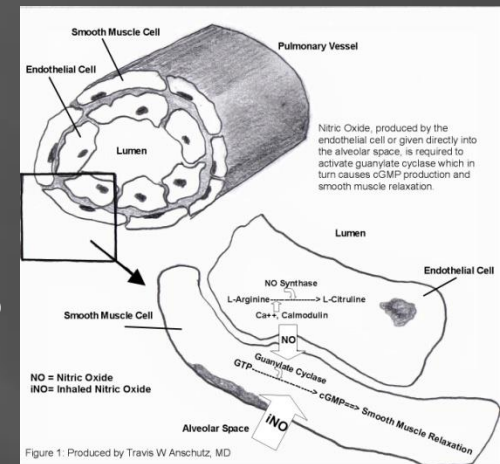
- $$OI = \frac{MAP * \%FIO_2}{PaO_2}$$

- > 15-20 initiation of iNO @ 20 PPM
    - Usually can be weaned off in <5 days



# Other Pharmacologic Agents

- ▣ Milrinone
  - Inhibitor of cAMP Phosphodiesterase
  - Improves Cardiac Output
  - Vasodilation
- ▣ Sildenafil ???
  - Inhibitor of Phosphodiesterase Type 5
  - Prevents breakdown of cGMP
- ▣ Inhaled Prostacyclin
  - Pulmonary vasodilation
  - Inhibits platelet aggregation



# Indications for ECMO

- ▣ Candidate?
  - GA >34 wks
  - >2000 gms
  - Reversible Lung Disease
  - <Grade III IVH
  - No Lethal Cong Anomalies
  - No Non Surgical CHD Patients
  - Mechanical Ventilation <14 days
- ▣ Criteria
  - If Meet above Criteria+
  - Irreversible Hypotension
  - PaO<sub>2</sub><30-40 on consecutive gases
  - pH< 7.25 for 2 hours
  - OI> 40 on 2 ABGs





# References

1. ***Persistent Pulmonary Hypertension of the Newborn***: Sharma et al. Maternal Health, Neonatology, and Perinatology. DOI 10.1186/s40748-015-0015-4
2. ***Advances in the Diagnosis and Management of Persistent Pulmonary Hypertension of the Newborn (PPHN)***: G. Konduri, MD, Olivia Kim, MD. Pediatr Clin North Am. 2009 June; 56(3):579
3. ***Update on PPHN: Mechanisms and Treatment***: J. Nair, MD, S. Lakshminrusimha, MD. Semin Perinatol. 2014 March; 38(2): 78-91.
4. ***Persistent Pulmonary Hypertension of the Newborn: Recent Advances in the Management***: A. Agrawal, MD, R. Agrawal, MD. Clin Pediatr; 2013;2(1):1-11
5. ***Accuracy of Doppler Echocardiography in the Hemodynamic Assessment of Pulmonary Hypertension***: M. Fisher MD, et al. Am J Respir Crit Care Med; Vol 179: 615-621
6. ***Randomized, Multicenter Trial of Inhaled Nitric Oxide and High-Frequency Oscillatory Ventilation in Severe, Persistent Pulmonary Hypertension of the Newborn***: Kinsella, et al. Journal of Pediatrics. 1997:Vol131;55-62
7. ***Pfizer Announces Results From Phase 3 Trial of Revatio (Sildenafil Citrate) in Newborns with Persistent Pulmonary Hypertension***: Bloomberg Business. June 2019