

Respiratory Failure, ARDS and Pulmonary Hypertension

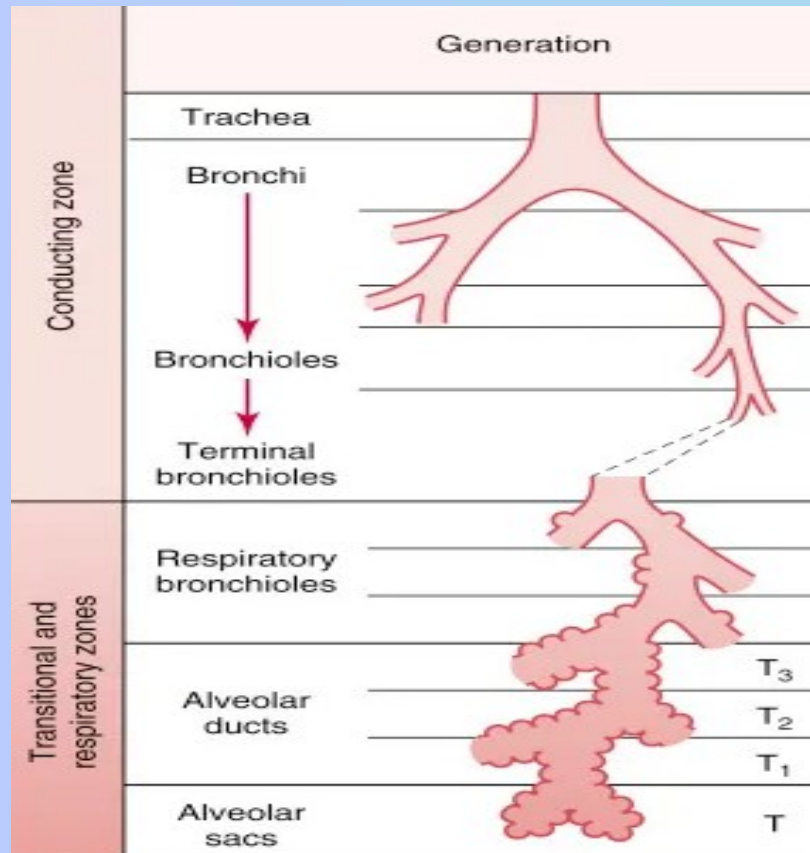
By Thomas Dlugosz

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The Respiratory Tree and Gas Exchange

Pulmonary Gas Exchange: The diffusion of oxygen gas from the lungs into the blood and of carbon dioxide from the blood into the lungs across the alveolar capillary membrane



Conducting Zones simply contain air. This is called **anatomical dead space**.

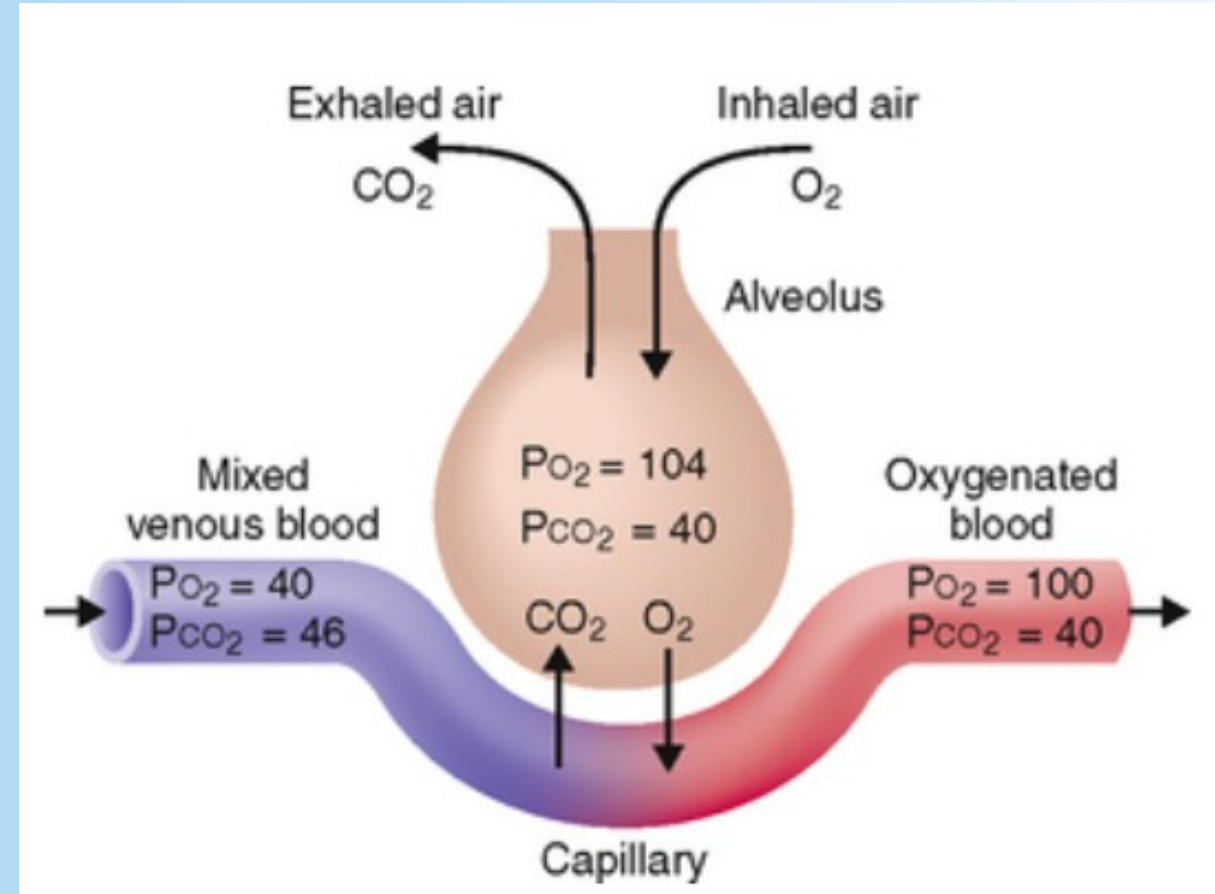
Respiratory zones is where pulmonary gas exchange occurs!

Gas Exchange Normal Values

Alveolar PO₂ (PAO₂) = 100mm Hg
Alveolar PCO₂ (PACO₂) = 40mm Hg

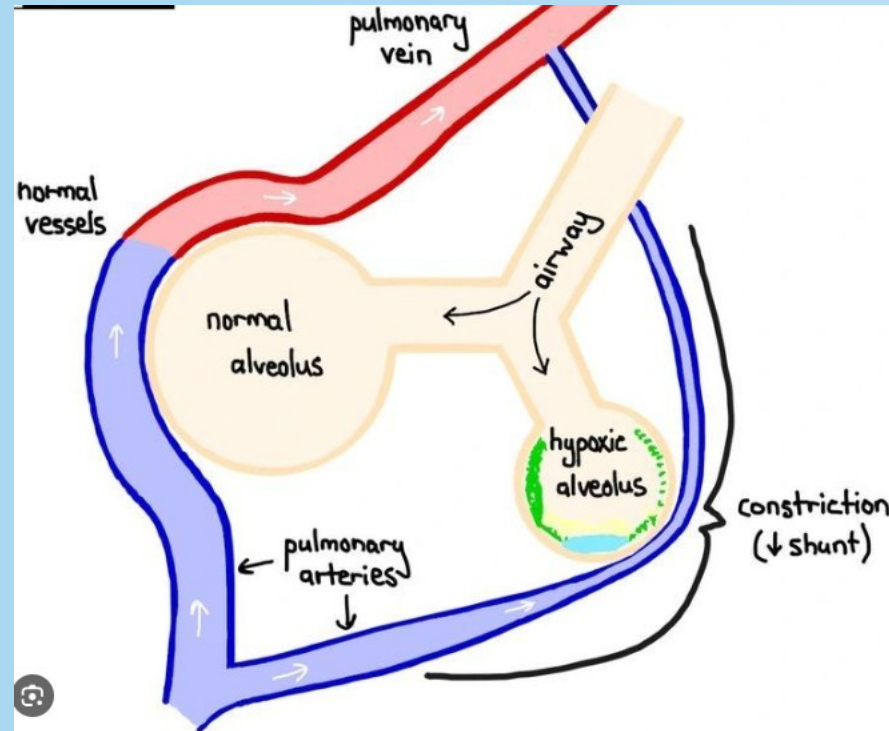
Venous PO₂ (PvO₂) = 40mm Hg
Venous PCO₂ (PvCO₂) = 46 mm Hg

Arterial PO₂ (PaO₂) = 100mm Hg
Arterial PCO₂ (PaCO₂) = 40mm Hg



Hypoxic Pulmonary Vasoconstriction

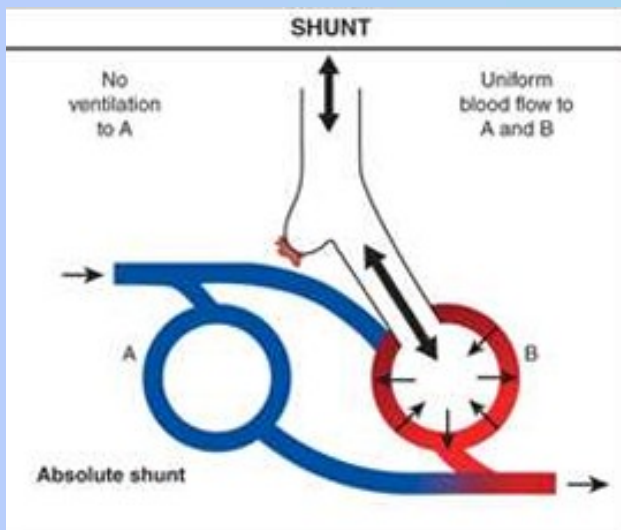
- The pulmonary arteries constrict when local alveolar PO_2 is low and dilate when the local alveolar PO_2 is high!



- **Effect:** Redistribution of blood flow to regions with higher alveolar PO_2

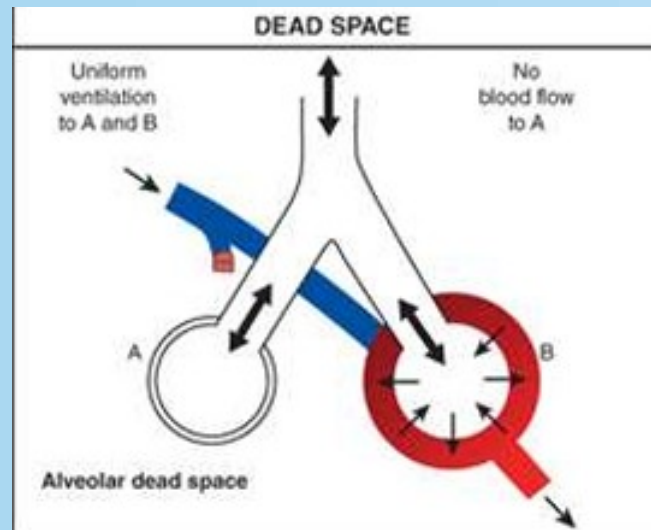
Ventilation (V) and Perfusion (Q)

- For efficient gas exchange, we want to match perfusion to the ventilation of the alveolus → **Ideal V/Q ratio is 1**
- Spirometry studies have found that typical resting alveolar ventilation is about 4 L/ min and pulmonary blood flow is 5L/min → **Normal V/Q ratio is about 0.8**



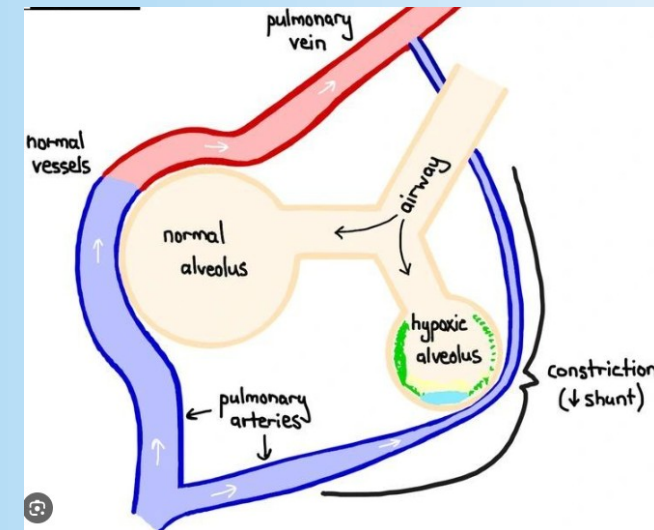
Shunt- Pulmonary arterial blood bypasses gas exchange and mixes with ventilated blood.

$$V/Q = 0$$



Alveolar Dead Space- A ventilated alveolus with no perfusion.

$$V/Q \rightarrow \infty$$



Compensated- HPV adjusts for poor ventilation

$$V/Q = 1$$

CO₂ elimination depends on ventilation only.

Oxygenation depends on Ventilation, perfusion, and diffusion

Alveolar Capillary Membrane

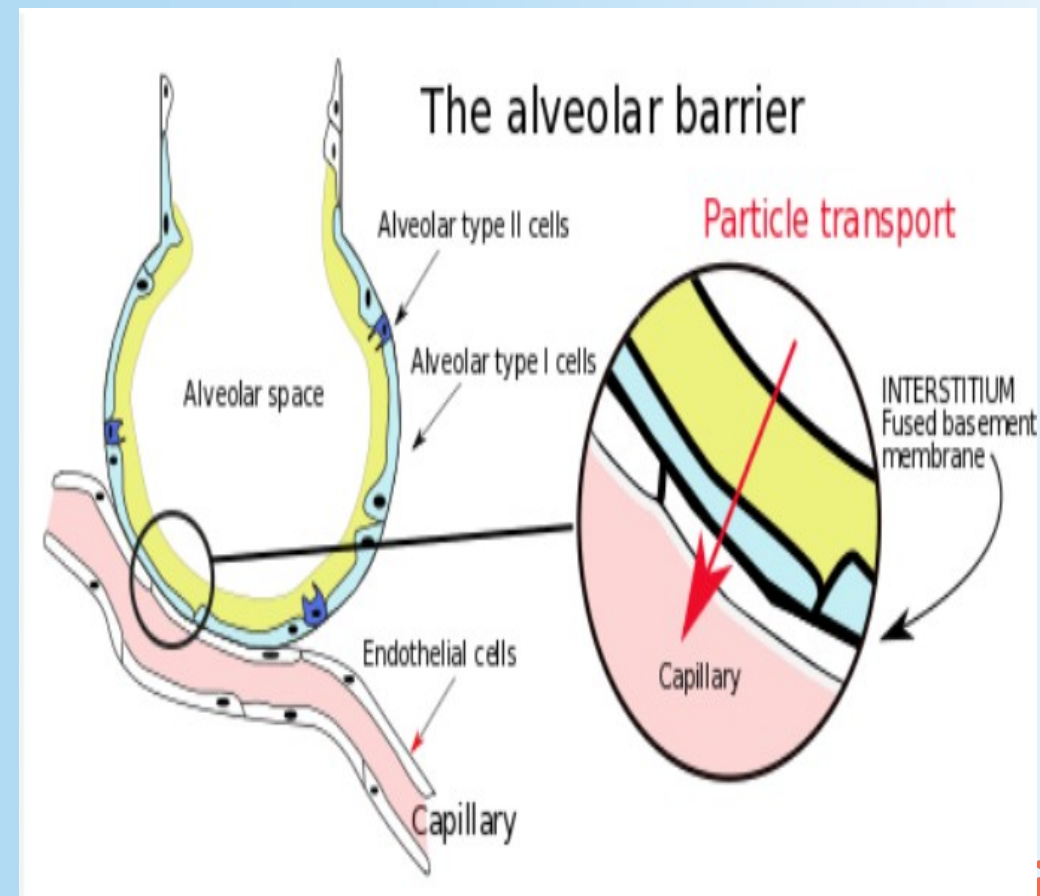
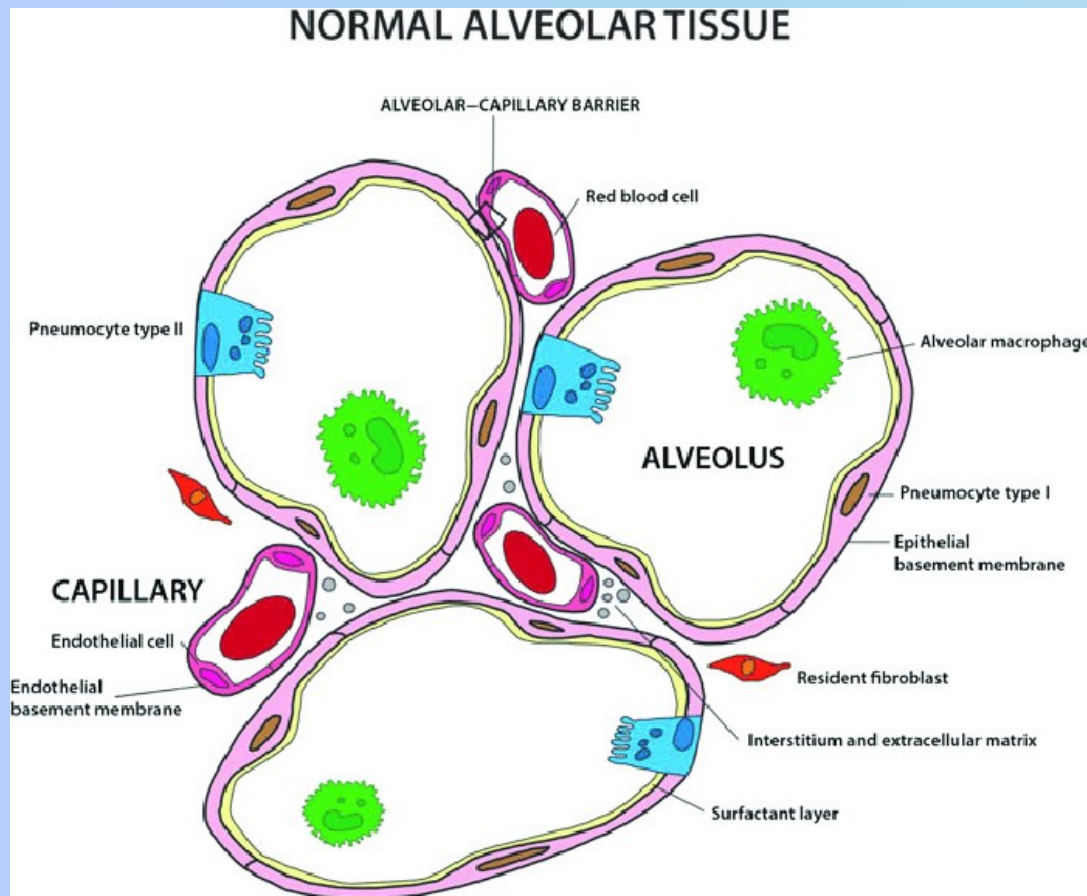


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Respiratory Failure

Respiratory Failure: Failure of the lungs to exchange gases well enough to maintain homeostasis

**Type I: Hypoxemic
Respiratory Failure**

$\text{PaO}_2 < 60\text{mm Hg}$

Acute: Develops in
Minutes to hours

Chronic: Develops
over days or longer

**Type II: Hypercapnic
Respiratory Failure**

$\text{PaCO}_2 > 50\text{mm Hg}$

Acute: Develops in
Minutes to hours

Chronic: Develops over
days or longer

Hypoxemic Respiratory Failure (HRF)

May be caused by V/Q mismatch, Shunting, Diffusion Impairment or Reduced Inspired Oxygen

V/Q mismatch

- Most common cause of HRF
- Diseases that cause low V/Q ratios may lead to HRF
 - **COPD**- Obstruction of airways causes poor ventilation → low V/Q ratio
 - **Asthma**- Characterized by bronchoconstriction, impairing ventilation
 - **Pneumonia**- Lung infection that fills alveoli with fluid, pus, debris
 - **ARDS**- Inflammatory infiltration of lungs decrease ventilation

Hypoxemic Respiratory Failure (HRF)

May be caused by V/Q mismatch, Shunting, Diffusion Impairment or Reduced Inspired Oxygen

Shunting ($V/Q=0$)

- Extreme V/Q mismatch where blood bypasses gas exchange
 - **Heart Shunting**- Congenital heart defects that cause right-to-left shunting.
 - **Severe Pneumonia**- Cellular debris, pus, fluid eliminate alveolar ventilation
 - **ARDS**- Inflammatory infiltration of lungs cause atelectasis eliminate ventilation

Hypoxemic Respiratory Failure (HRF)

May be caused by V/Q mismatch, Shunting, Diffusion Impairment or Reduced Inspired Oxygen

Diffusion Impairment

- A thickened or reduced-surface-area alveolar-capillary membrane (ACM) limits gas exchange
 - **Idiopathic Pulmonary Fibrosis**- Fibrosis of pulmonary interstitium thicken the ACM
 - **ARDS**- Proteinaceous fluid thickens ACM
 - **Pulmonary Emphysema**- Characterized by alveolar wall destruction → Reduce SA of ACM

Hypoxemic Respiratory Failure (HRF)

May be caused by V/Q mismatch, Shunting, Diffusion Impairment or Reduced Inspired Oxygen

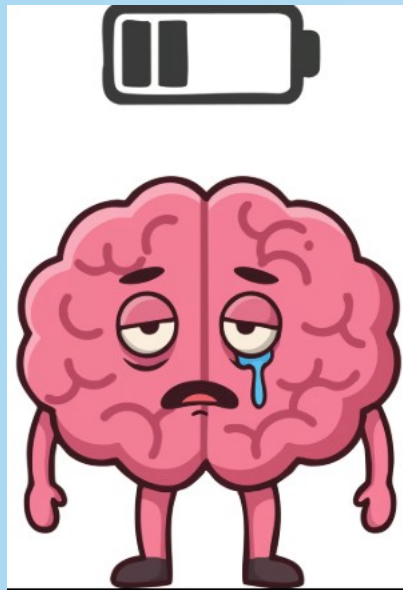
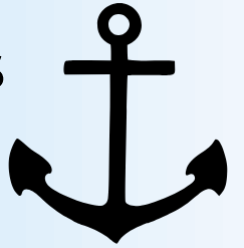
Reduced Inspired Oxygen

- Environmental hypoxia, such as high-altitude exposure
 - Hiking Mount Everest



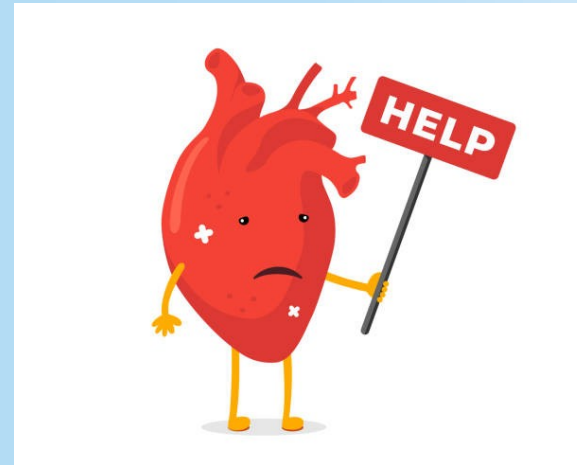
Symptoms of Hypoxemia

- Anchor: The brain doesn't tolerate low oxygen and the body does what it can to maintain homeostasis
- **Brain-** restlessness, confusion, agitation, impaired judgement, memory deficits, lethargy, loss of consciousness



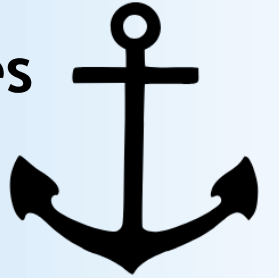
Symptoms of Hypoxemia

- The brain doesn't tolerate low oxygen and the body does what it can to maintain homeostasis
- **Cardiovascular**
 - Early Compensation
 - Tachycardia
 - Severe Hypoxemia
 - Arrhythmia
 - Chronic Hypoxemia
 - Pulmonary Hypertension and Heart Failure (Cor Pulmonale)



Symptoms of Hypoxemia

- Anchor: The brain doesn't tolerate low oxygen and the body does what it can to maintain homeostasis



- **Respiratory**
Tachypnea



Use of Accessory Muscles



Nasal Flaring



Symptoms of Hypoxemia

- Anchor: The brain doesn't tolerate low oxygen and the body does what it can to maintain homeostasis
- **Kidneys**
 - Acute Hypoxemia
 - AKI if severe enough
 - Chronic Hypoxemia
 - Metabolic Acidosis → increased H^+ excretion
 - EPO production → polycythemia



Hypercapnic Respiratory Failure

- Alveolar hypoventilation always underlies hypercapnic respiratory failure

Anchor: “Anything impairing exhalation”



- **CNS depression:** opioid overdose, stroke
- **Neuromuscular disorders:** myasthenia gravis
- **Airway Obstruction:** COPD, asthma, upper airway obstruction
- **Chest Wall abnormalities:** kyphoscoliosis

Symptoms of Hypercapnia

CO₂ is a vasodilator and causes respiratory acidosis!



Neurological: headache, cerebral edema, confusion, drowsiness, coma

Skin: flushed skin

Cardiovascular: Tachycardia and hypertension due to sympathetic activation

Respiratory: Dyspnea, tachypnea



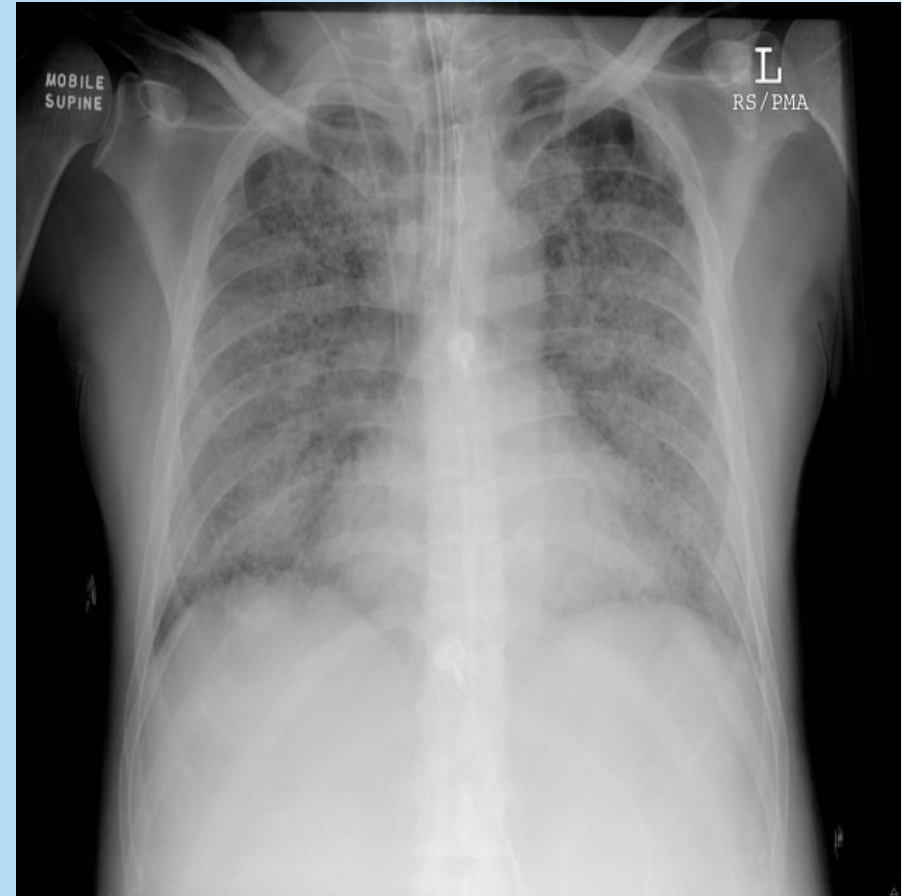
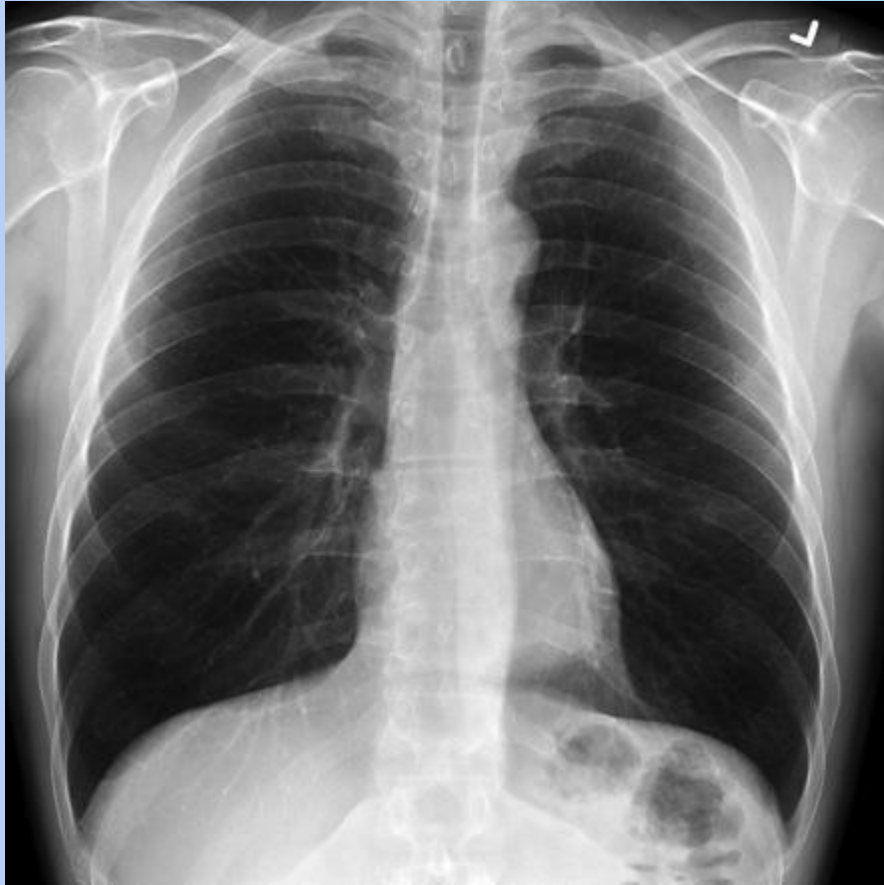
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Acute Respiratory Distress Syndrome

- Acute respiratory distress syndrome (ARDS) is respiratory failure occurring within 1 week of a known clinical insult causing bilateral alveolar injury and hypoxemia.
- Characteristics
 - **Hypoxemia.** ARDS is graded by the degree of hypoxemia
 - **Bilateral Pulmonary Edema in absence of heart failure.**
 - **Increased lung capillary permeability.**
 - **Atelectasis.** Collapsed alveoli which are non functional.
 - **Hyaline alveolar membranes.** Damaged shiny alveolar membranes from hyalin deposition.
 - **Type I Respiratory Failure.**
- Multiple, diverse triggers.

X-ray of ARDS



Exudative Phase (Day 1 to 7)

Trigger event: Systemic or direct injury activates alveolar macrophages

1. Alveolar-Capillary Barrier Breakdown

1. Alveolar macrophages release IL-1, IL-6 and TNF α .
2. Neutrophils recruited to lungs
3. Severe inflammation damages the alveolar capillary barrier



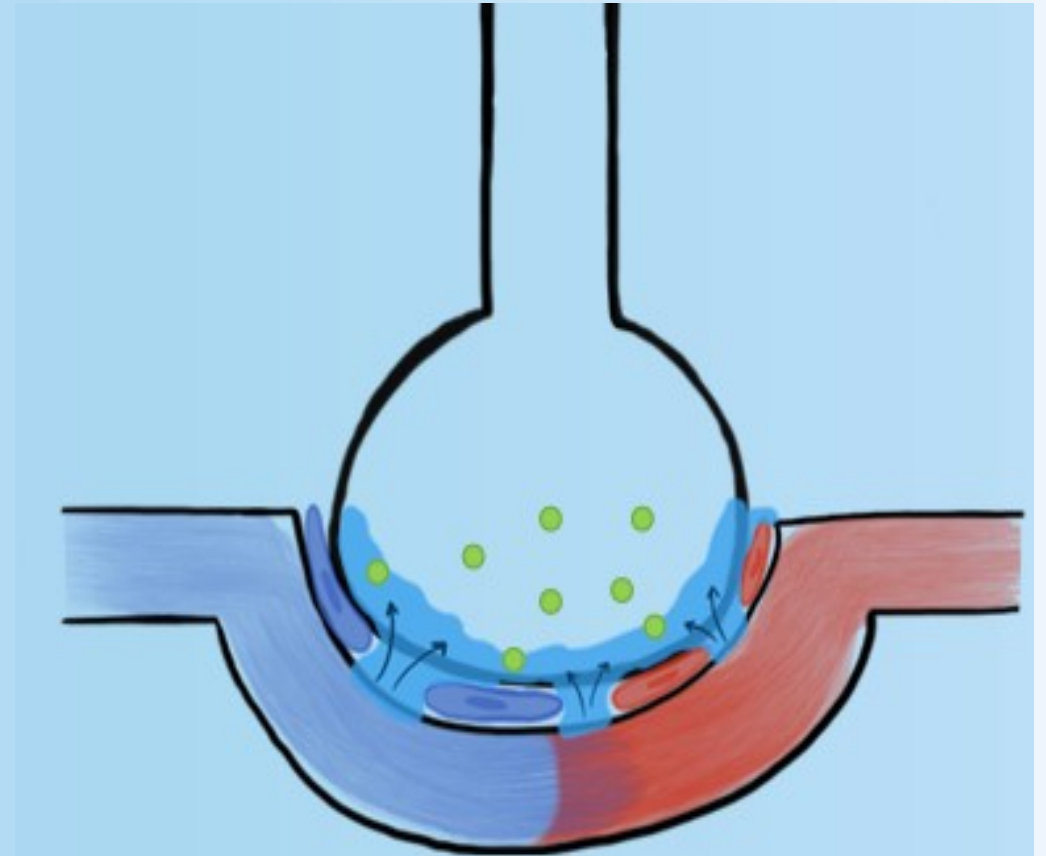
Exudative Phase (Day 1 to 7)

2. Increased Permeability

1. The damaged endothelial cells and Type 1 pneumocytes allow protein-rich fluid (exudate) to leak into the alveolar space

3. Edema Formation

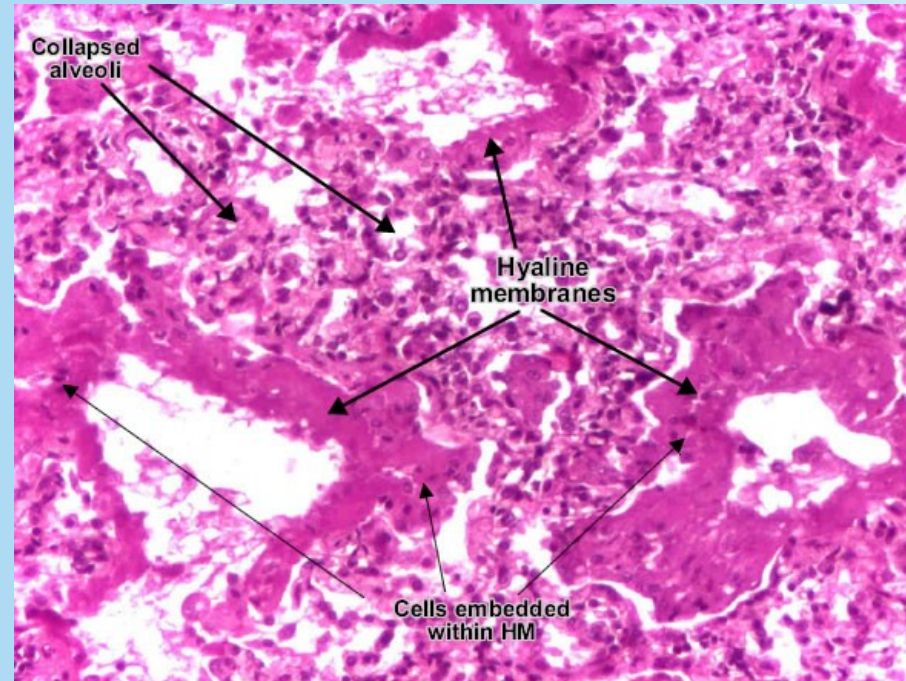
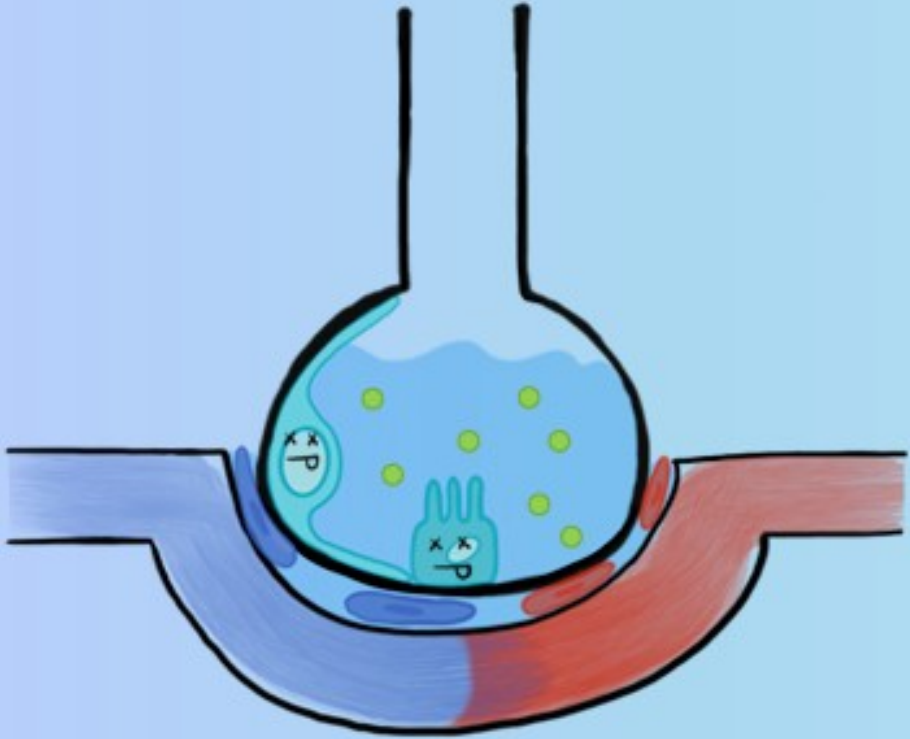
1. Fluid widens the interstitium and enters the alveolus.
2. Surfactant dilution
3. Atelectasis
4. Hypoxemia → Type I Respiratory Failure
5. Decreased V/Q ratio



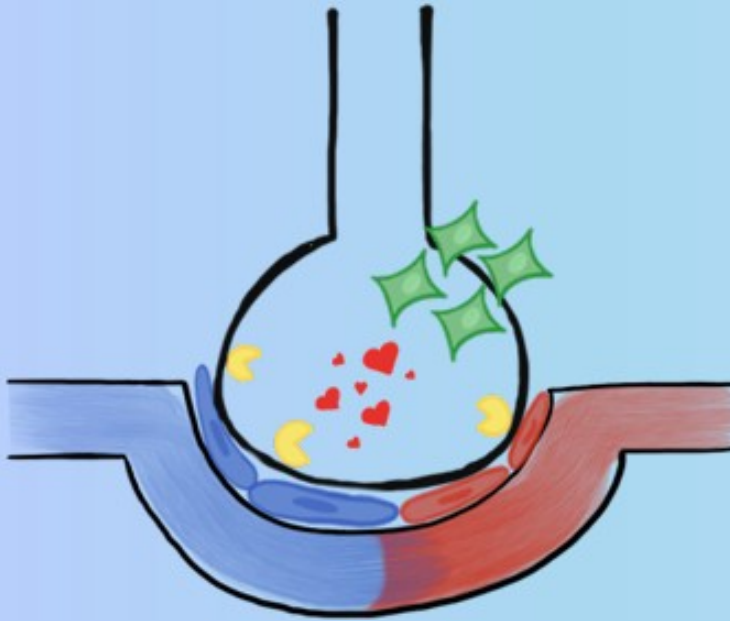
Exudative Phase (Day 1 to 7)

4. Hyaline Membrane Formation.

Leukocytes, proteins (like fibrin), and necrotic debris accumulate and line the alveoli, giving a shiny appearance



Proliferative Phase



1. Repair

1. Type II pneumocytes proliferate to replace damaged type I pneumocytes and produce surfactant to restore alveoli

2. Fibrosis

1. Macrophages release TGF- β
2. TGF- β activates fibroblasts
3. Fibroblasts deposit collagen and extracellular matrix $\rightarrow$ interstitial fibrosis

3. Resolution

1. Anti-inflammatory cytokines resolve inflammation and fibrotic tissue is destroyed.... usually.....

Fibrotic Phase (>21 Days)

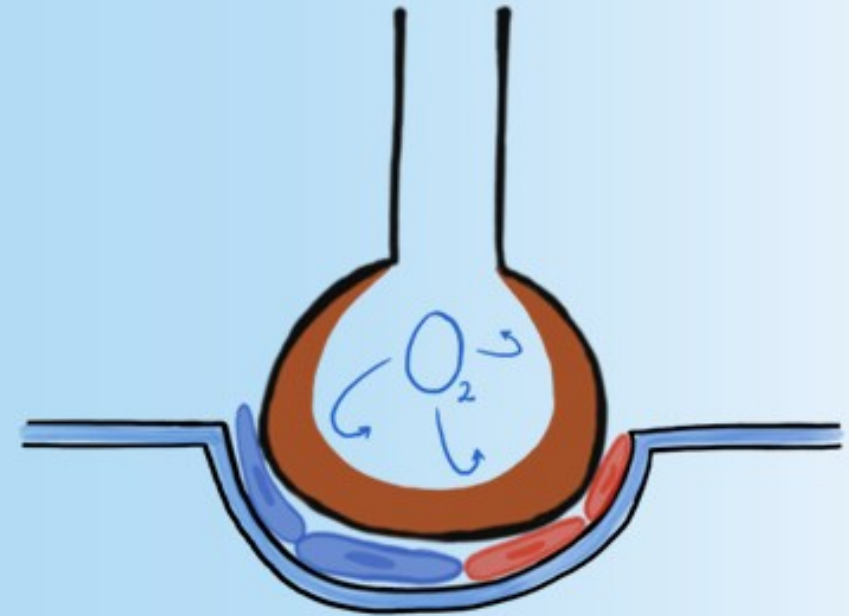
May not occur

1. Chronic Damage

1. Macrophages release TGF- β
2. TGF- β activates fibroblasts
3. Fibroblasts deposit collagen and extracellular matrix $\rightarrow$ interstitial fibrosis

Consequences: Stiffening of lungs and pulmonary capillary obliteration. **Diffusion capacity of lungs limited (DLCO decrease)**

Fibrosis is not always permanent.



High Yield Causes of ARDS

- Anchor: cause ARDS we need an inflammatory or injurious insult to the alveolar-capillary membrane always.
- Pneumonia - most common
- Sepsis
- Aspiration
- Shock
- Trauma
- Smoke Inhalation
- Pancreatitis
- Drug Toxicity
- Transfusion reactions

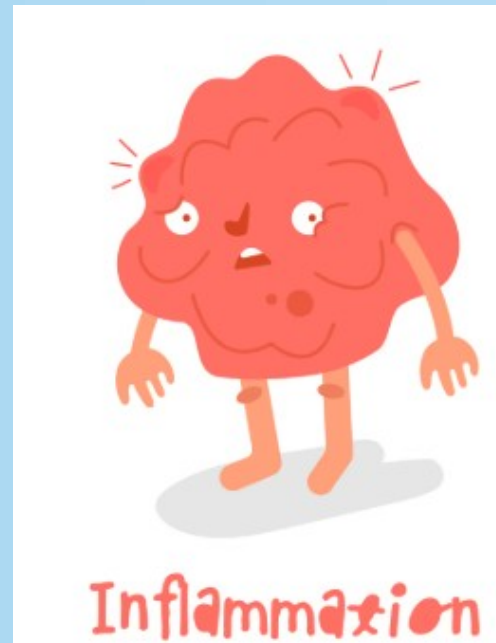


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Pulmonary Hypertension

- Pulmonary hypertension is defined as having mean pulmonary arterial pressure over 20 mm Hg (~14 mm Hg is normal).

The Causes of Pulmonary Hypertension are grouped into 5 groups

Pulmonary Arterial Hypertension (Group 1)

Left Heart Disease Pulmonary Hypertension (Group 2)

Hypoxic Pulmonary Hypertension (Group 3)

Thromboembolic Pulmonary Hypertension (Group 4)

Miscellaneous Pulmonary Hypertension (Group 5)

Pulmonary Arterial Hypertension (Group 1)

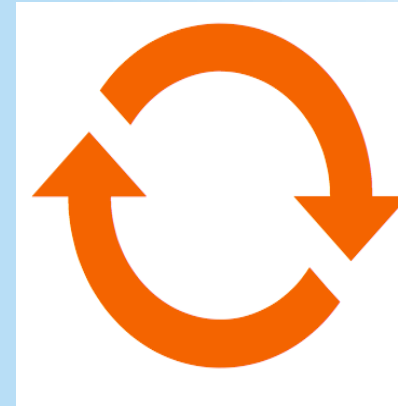
Anchor: Pulmonary Hypertension caused by vascular remodelling except hypoxemic vasoconstriction



- Heritable PH (genetic mutation)
- Idiopathic

Hypertensive Causes

- Chronic Drug use (amphetamine, cocaine via α adrenergic signalling)
- Left-to-right shunting heart defect



Pulmonary Hypertension from Left Heart Disease (Group 2)

Anchor: Any condition on the left heart that increases left atrial pressure



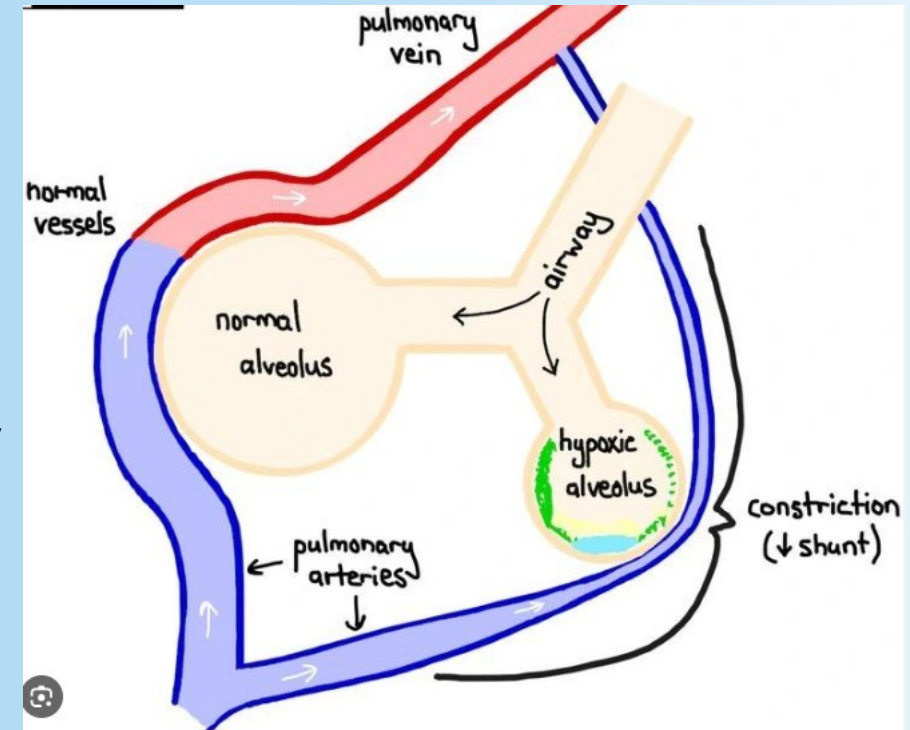
- Systolic and Diastolic heart failure
- Heart Valvular Disease (**mitral valve stenosis**, mitral valve regurgitation aortic stenosis)

Increased Left Atrial Pressure → Backflow into pulmonary veins → Venous congestions → Pulmonary edema + Pulmonary Arterial Hypertension

Pulmonary Hypertension from Hypoxia (Group 3)

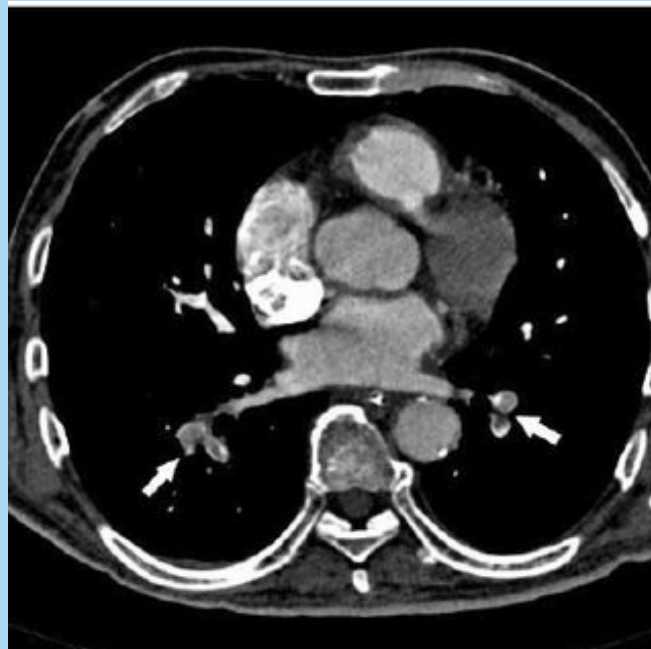
- Recall that the pulmonary arteries constrict when local alveolar PO_2 is low and dilate when the local alveolar PO_2 is high
- HPV becomes maladaptive if hypoventilation is widespread
- Excess hypoventilation → excessive HPV → Increased pulmonary pressures

Ex: COPD, pulmonary fibrosis, sleep apnea



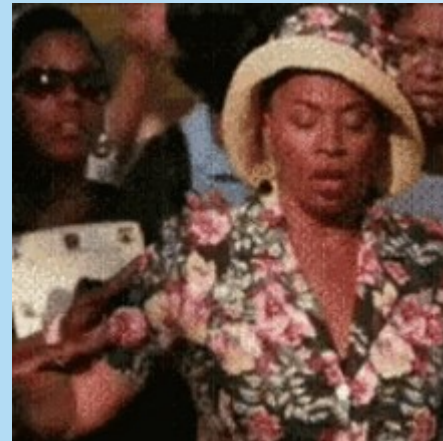
Pulmonary Hypertension from Chronic Thromboembolism (Group 4)

- Persistent or Recurrent thrombi formation in small pulmonary vessels increase vascular resistance, which increase upstream pressures and cause vascular remodelling.



Clinical Manifestations

- Early Signs
 - Exertional dyspnea, fatigue and weakness
- Progressive Signs
 - **Exertional fainting** - Pulmonary resistance is too high → right ventricle cannot increase output → insufficient left atrial preload → lowered cardiac output → lowered cerebral perfusion → syncope
 - Loud S2 from pulmonary pressures



Clinical Manifestations

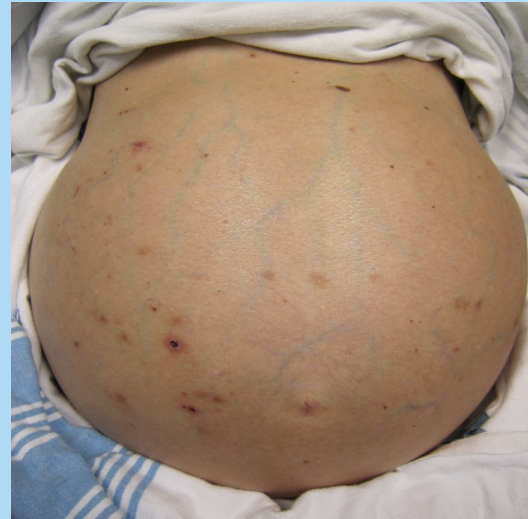
- Right Heart Failure symptoms



JVD



Pitting Edema



Ascites



Hepatomegaly

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Case 1: The Polish Teacher

- A bald, former JUMC Medical Polish teacher presented to the emergency room 3 days ago with sudden epigastric pain radiating to the back and persistent vomiting. Medical history revealed he was lazy, disorganized and would cancel Polish at any opportunity he could get. He had a liking for students from the Southern United States but a dislike for Norwegian students. He drank 8 beers and smoked cigarettes daily for 4 years. Clinical examination revealed a bruise on the right side of his back. Bloodwork revealed elevated WBCs, serum lipases, CRP, glucose. A diagnosis was made and treatment began. However, he grew increasingly dyspneic. Lung auscultation revealed bilateral crackles. SpO2 was 80%. Heart rate increased to 130 BPM. He was put on supplemental oxygen, yet his SpO2 failed to improve.

Questions

- What was the most likely initial diagnosis upon entry to ER?
- What is the most likely cause of the initial disease?
- What is the current diagnosis of the lung condition?
- What likely caused the lung condition and how?
- How do you treat this patient?

Case 2: The Gang Member

- A 28 year old Crip member from Southside Los Angeles was practicing his crip walk in the McDonald's parking lot at 2 in the afternoon when he suddenly collapsed. Bystanders called an ambulance for him and he was brought to the hospital. Medical history revealed that he often felt dizzy while exercising, but he ignored it because of a desire for the “cleanest walk in the set”. Lung auscultation revealed bilateral crackles and decreased breath sounds. Heart auscultation revealed a loud and snappy S2 followed by a low-pitched diastolic murmur best heard at the apex. When sent back to the waiting room, he began practicing his “walk” but collapsed yet again after 4 minutes.

Questions

- What is the most likely heart pathology? Why?
- What is the most likely lung pathology? Why?
- Why is the patient fainting?