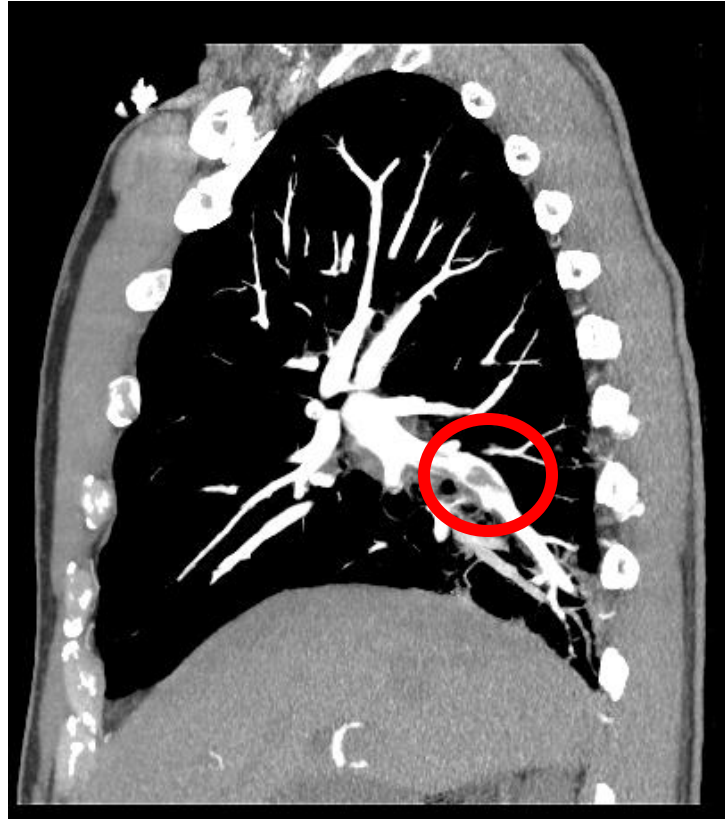


Pulmonary-Vascular Disease

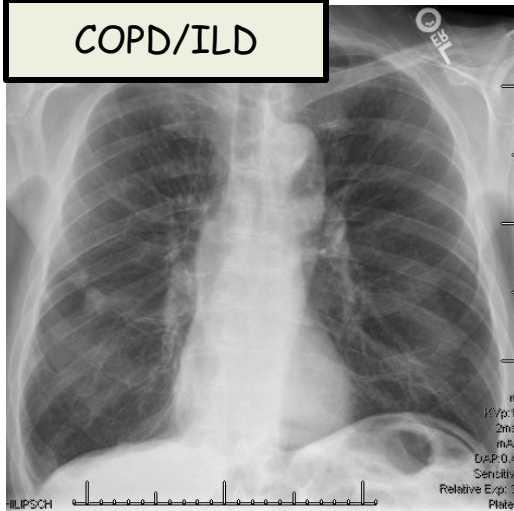


Howard J. Sachs, MD

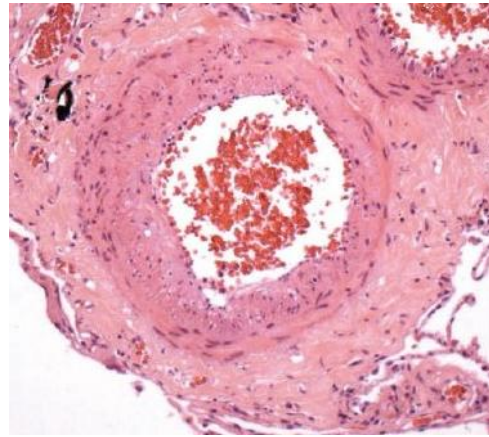
www.12daysinmarch.com

The Disorders

COPD/ILD



Chronic Hypoxia
Vasoconstrictive

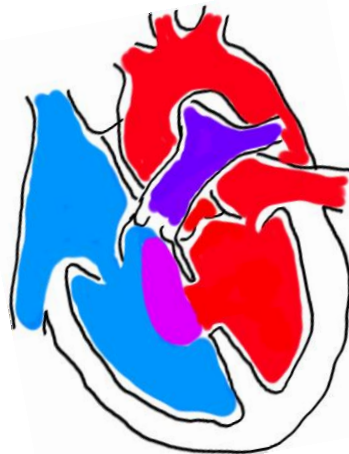


Obliterative
PPH



Obstructive

Hyperkinetic
LEFT → right Shunt



Passive 2nd to LV Failure

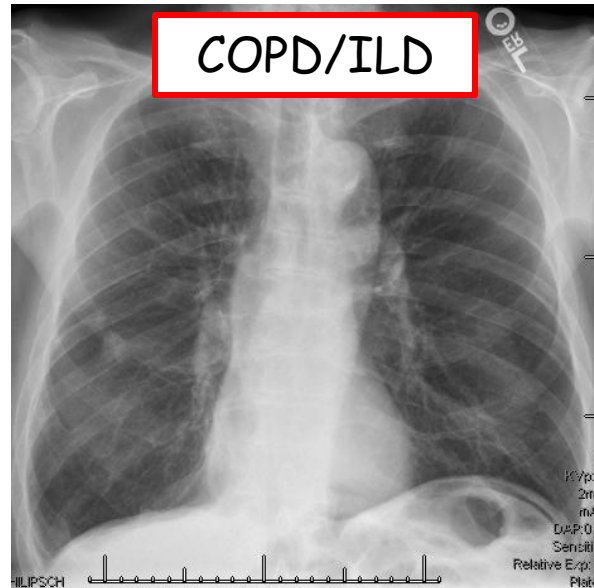
Chronic Hypoxic → Vasoconstriction

Key Point: Unlike hypoxia in other tissues, pulmonary hypoxia causes vasoconstriction (not vasodilation)



Low PaO_2

↑ Pulmonary Resistance

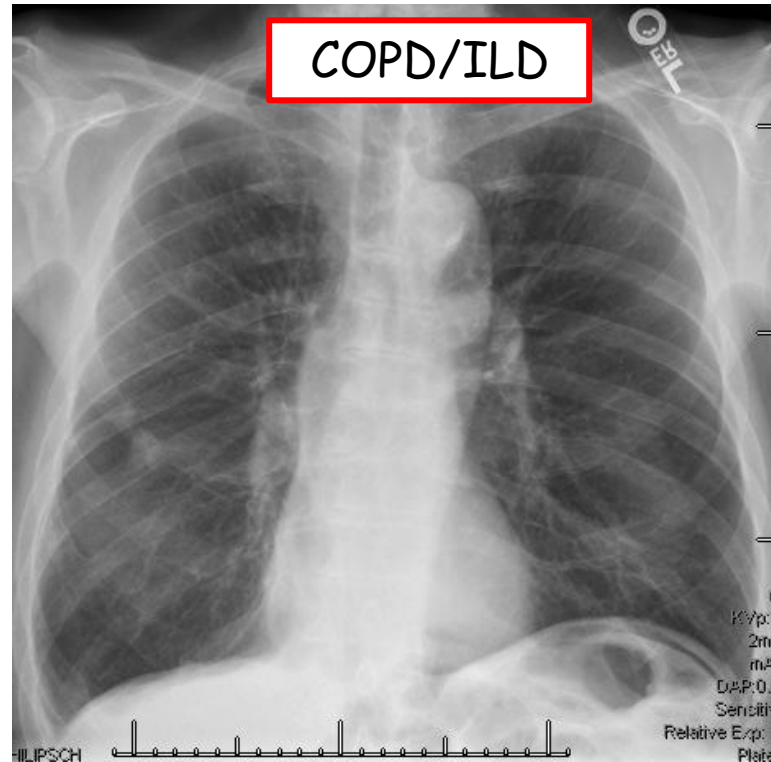


COPD/ILD



High PCO_2

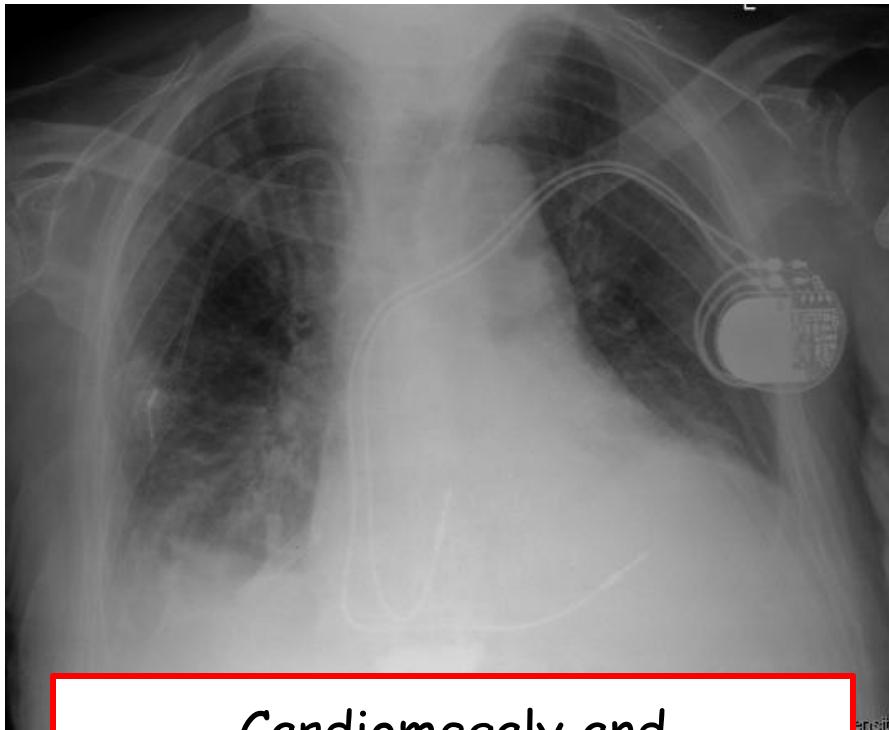
Chronic Hypoxic → Vasoconstriction



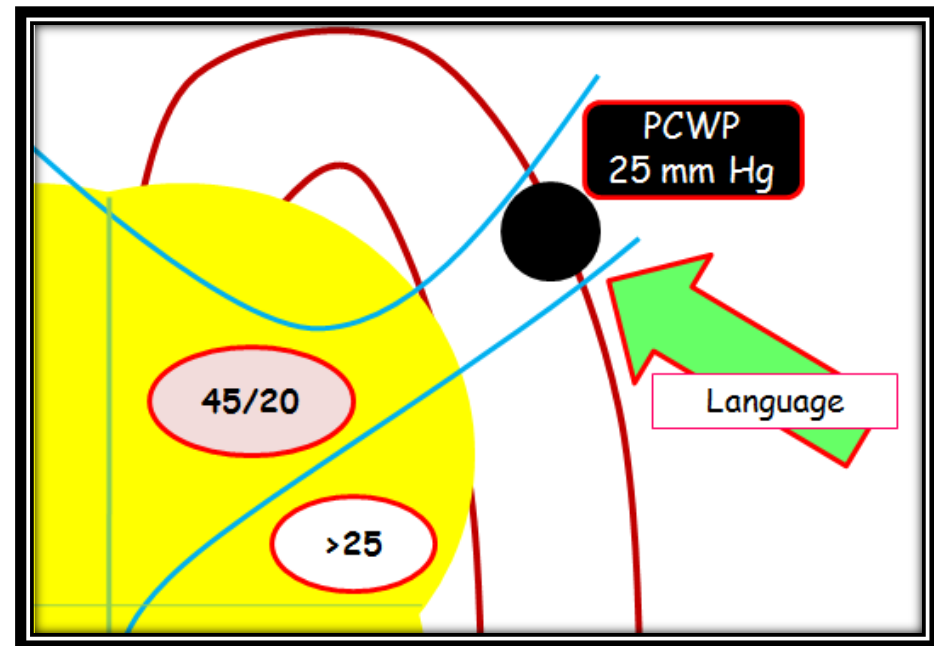
Pulmonary HTN/Cor Pulmonale secondary to parenchymal destruction as well as hypoxic vasoconstriction.

Pulmonary HTN 2° to Cardiac Disease

LV Failure causes Pulmonary Venous HTN

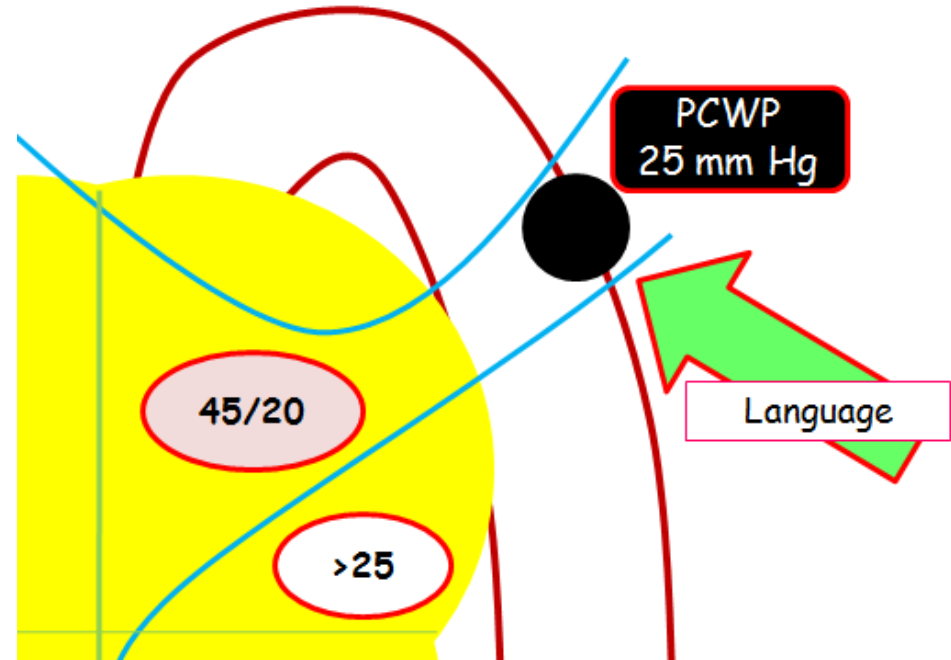
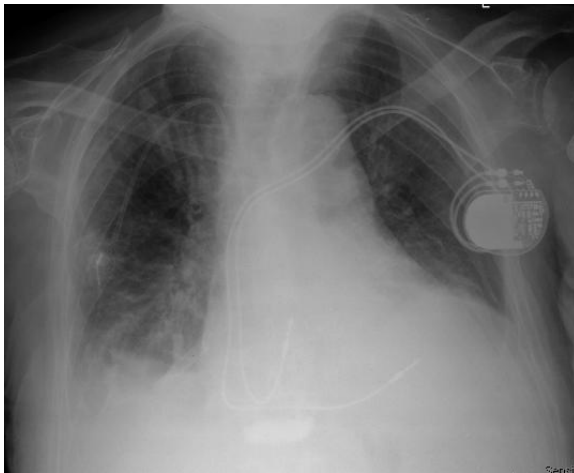


Cardiomegaly and
Transudative Pleural Effusion



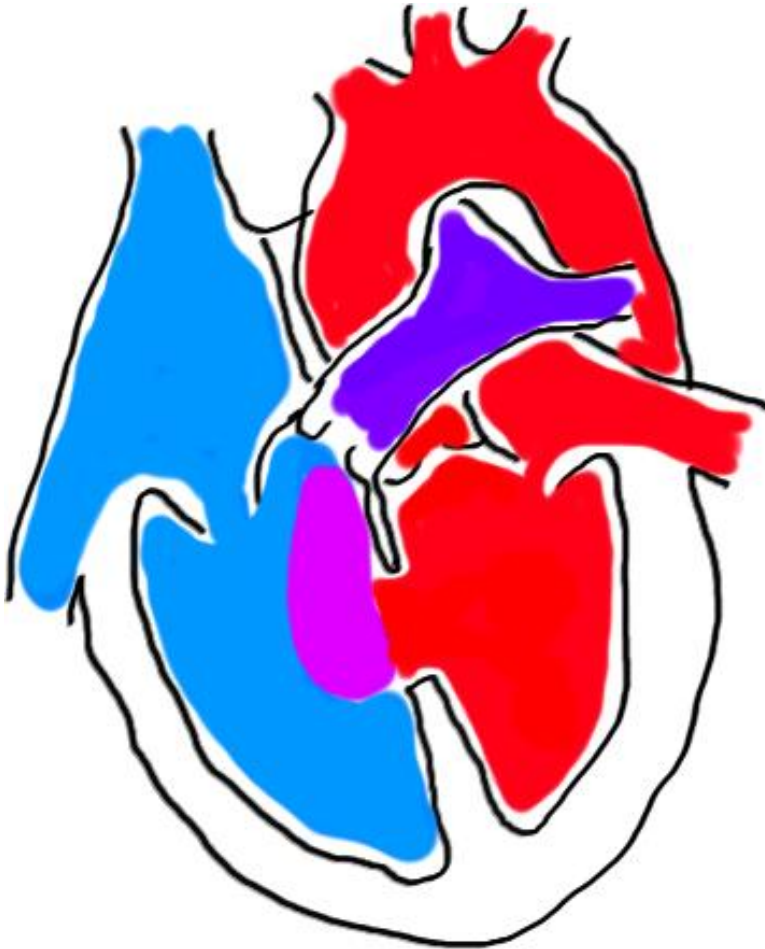
Pulmonary HTN 2° to Cardiac Disease

LV Failure



- High left sided pressures → High right sided pressures
- Most common cause of **right** CHF is **left** CHF
- Not considered Cor Pulmonale
- **NBME isn't subtle about CHF (rales, S3)**
- More importantly to know that normal PCWP excludes left sided disease as etiology

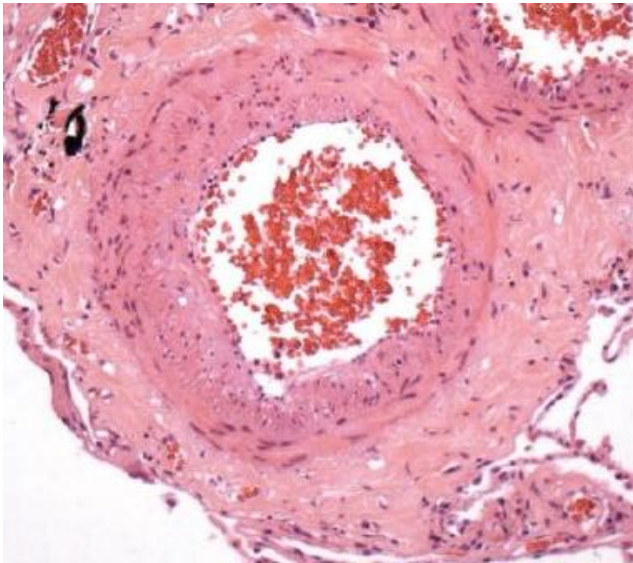
Pulmonary HTN 2° to Cardiac Disease



Left → Right Shunt

- Increased volume, pressure
- Not considered a cause of Cor Pulmonale
- Discussed in Cardiology Section

The Disorders



Obliterative/PPH



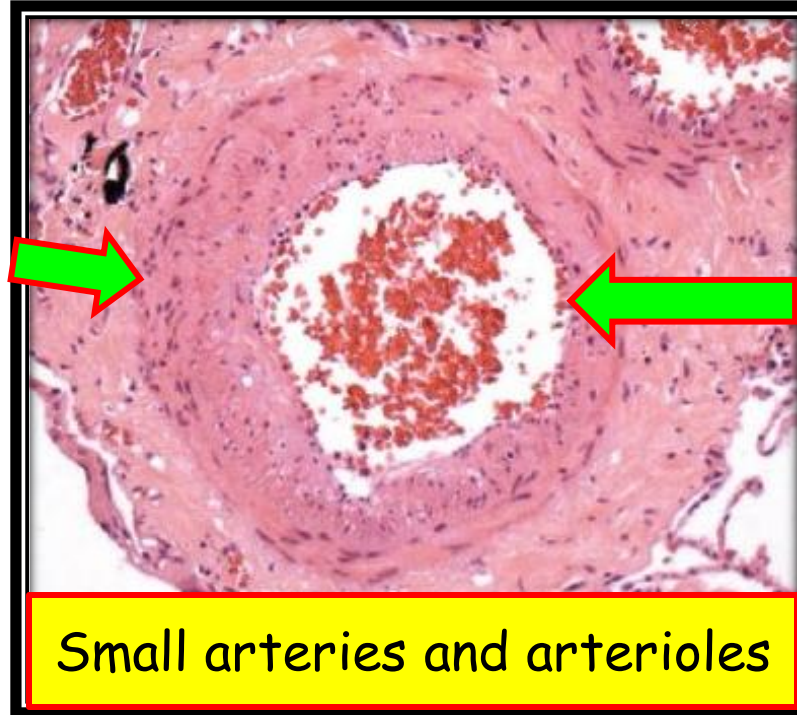
Obstructive

Primary Pulmonary (Arterial) HTN

If you understand the pathology...

Intimal
Hyperplasia

Media
Hypertrophy



Lumen
Obliteration

Small arteries and arterioles

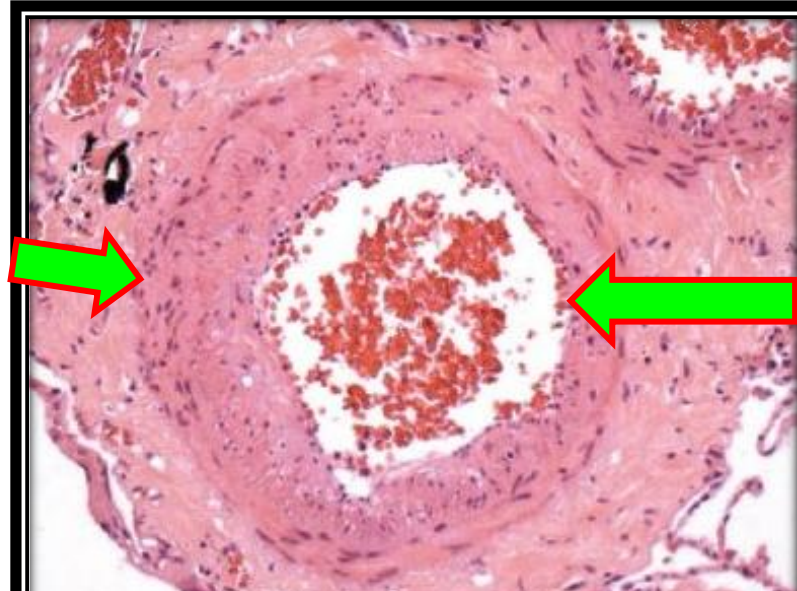
Primary Pulmonary (Arterial) HTN

If you understand the pathology...

Intimal
Hyperplasia

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Proliferative
Arteriopathy



Lumen
Obliteration

Occlusive
Arteriopathy

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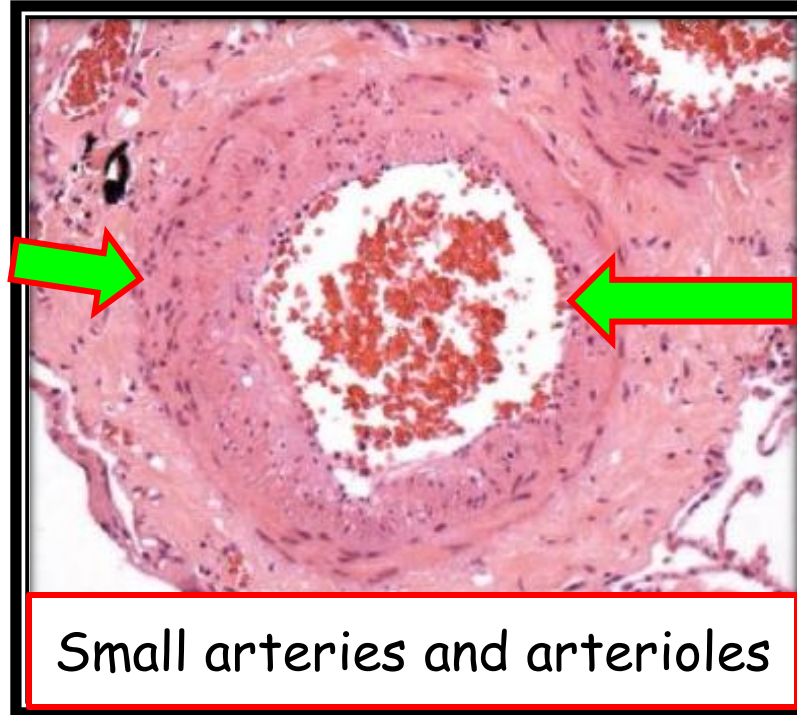
Primary Pulmonary (Arterial) HTN

If you understand the pathology...

Intimal
Hyperplasia

Media
Hypertrophy

Proliferative
Arteriopathy



Lumen
Obliteration

Occlusive
Arteriopathy

Small arteries and arterioles

- Who gets this and what is the cause?
- What's the natural history?
- This is the boards...how does rx underscore the pathophysiology?

Primary Pulmonary (Arterial) HTN

- Who gets it?
 - Idiopathic, Familial or Associated with other diseases (**diffuse systemic sclerosis**).
 - Familial dominates on USMLE as in, 'mother died at 35 now daughter has similar syndrome.'

Primary Pulmonary (Arterial) HTN

- Who gets it?
 - Idiopathic, Familial or Associated with other diseases (systemic sclerosis).
 - Familial dominates on USMLE as in, 'mother died at 35 now daughter has similar syndrome.'
- Why does it occur?
 - BMPR2 mutation: family of $TGF-\beta$. Leads to a bad cascade:

$TGF-\beta$

Primary Pulmonary (Arterial) HTN

- Who gets it?
 - Idiopathic, Familial or Associated with other diseases (systemic sclerosis).
 - Familial dominates on USMLE as in, 'mother died at 35 now daughter has similar syndrome.'
- Why does it occur?
 - BMPR2 mutation: family of **TGF- β** . Leads to a bad cascade:
 - Smooth mm proliferation
 - \downarrow Vasodilation (\downarrow NO, prostacyclin)
 - \uparrow Endothelin (\rightarrow vasoconstriction)
 - \uparrow Fibrosis/Thrombosis

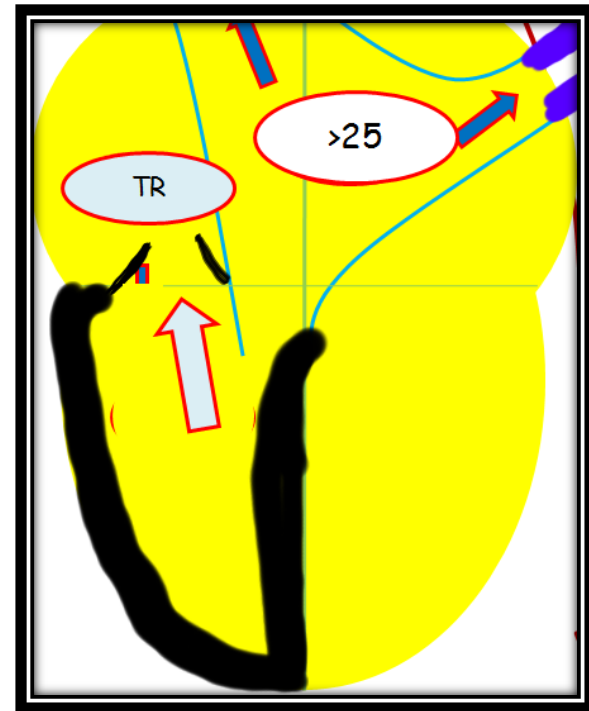
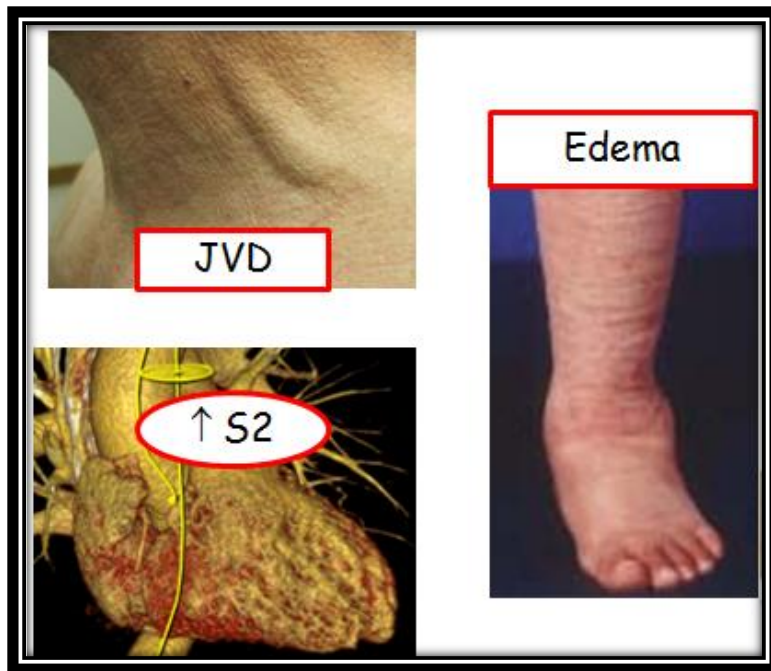
Primary Pulmonary (Arterial) HTN

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Rx

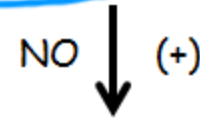
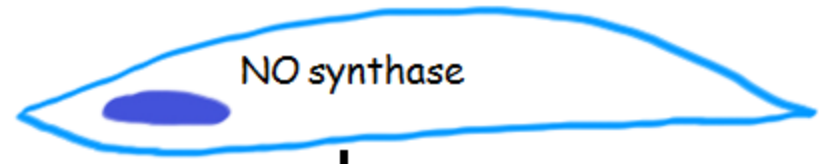
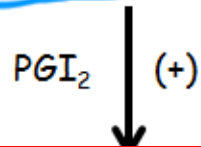
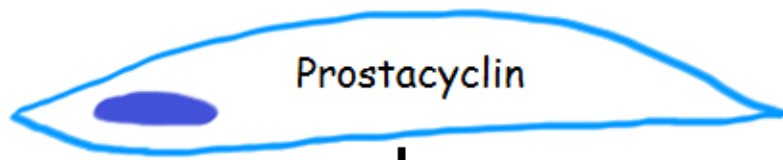
Primary Pulmonary (Arterial) HTN

What's the Natural History?



Death from Cor Pulmonale

Vascular endothelium



Vasodilate

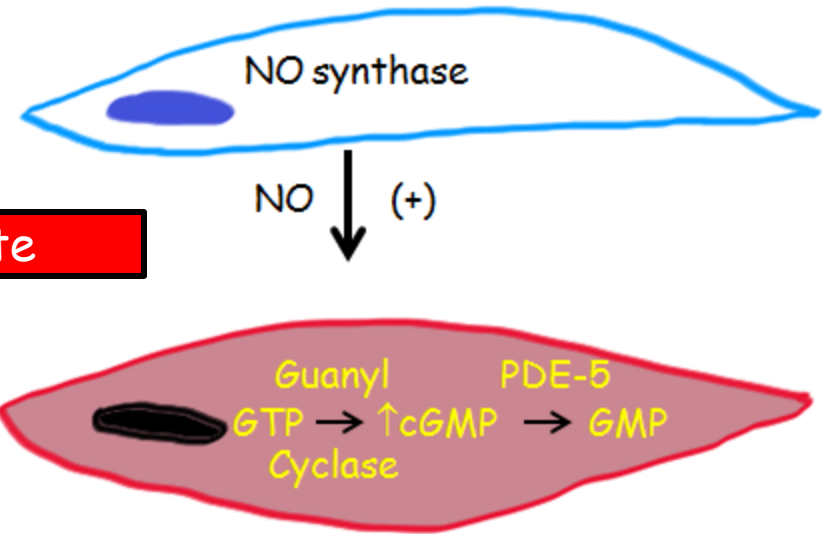
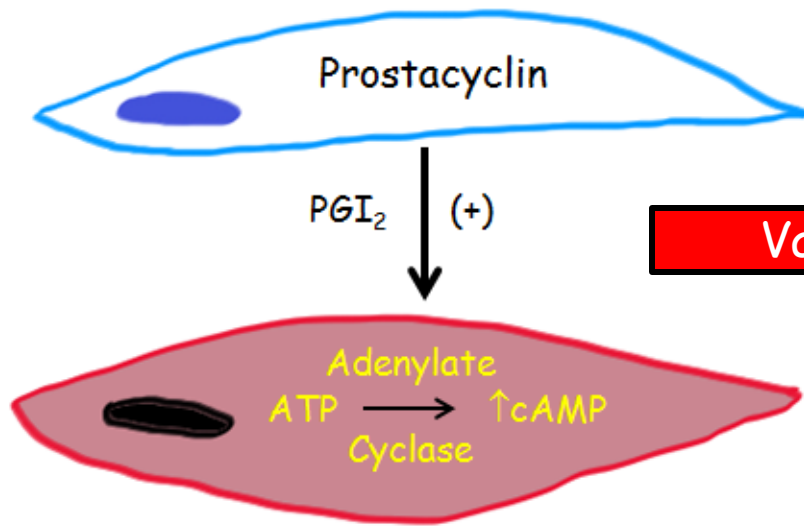
This is the boards:
What therapeutics underscore the pathophysiology?

Vascular smooth muscle

ET-1



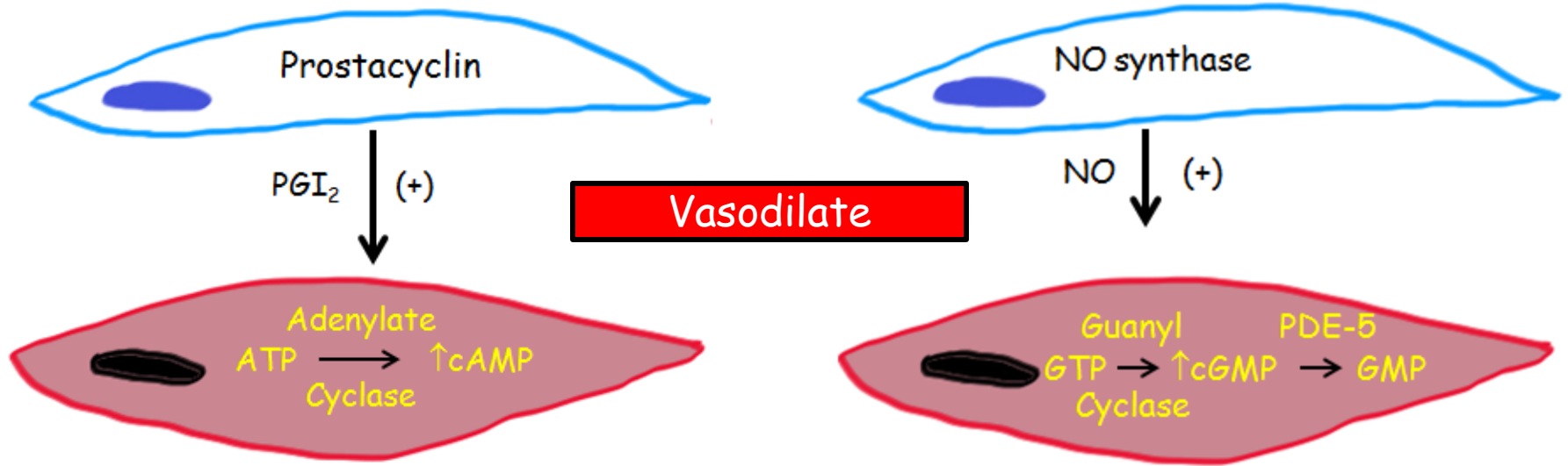
Vascular endothelium



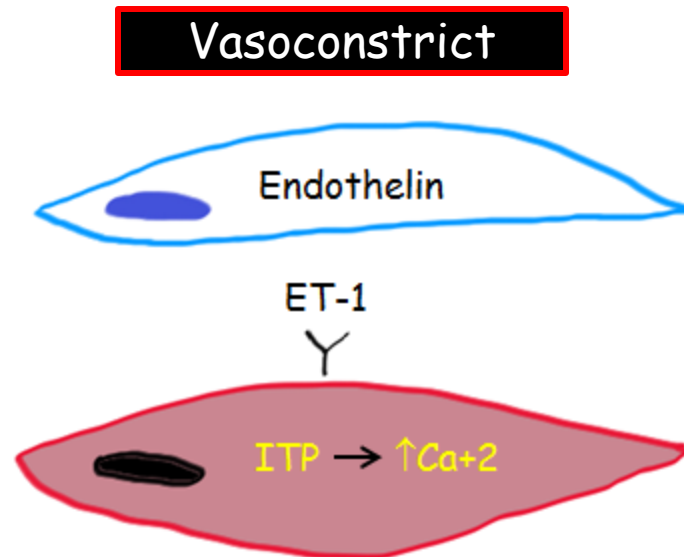
Vasodilate

Vascular smooth mm cell

Vascular endothelium

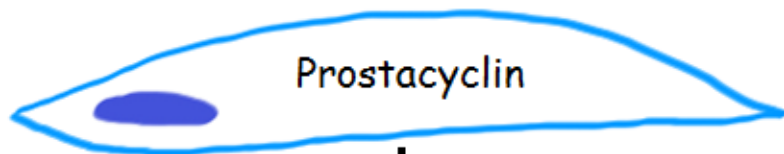


Vascular smooth mm cell

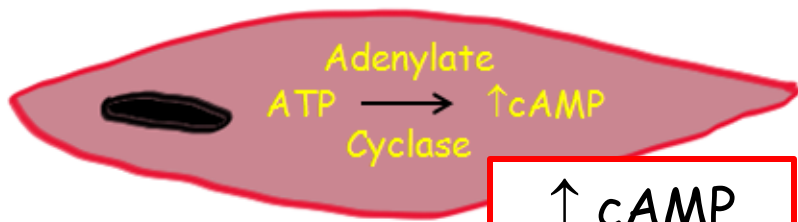


Vasodilators

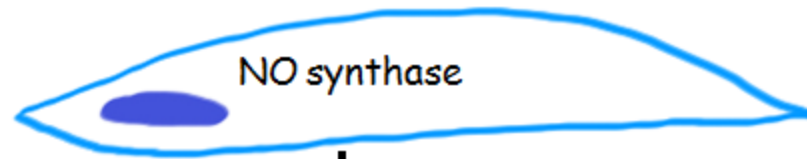
Vascular endothelium



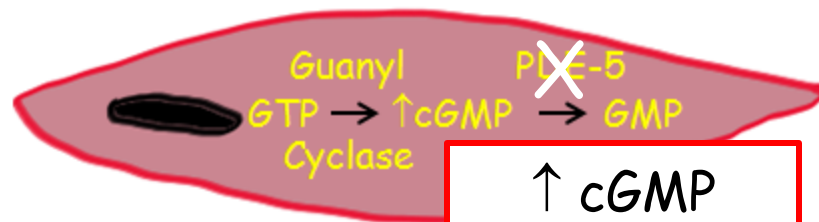
Prostanoids:
Epoprostenol, Iloprost



↑ cAMP



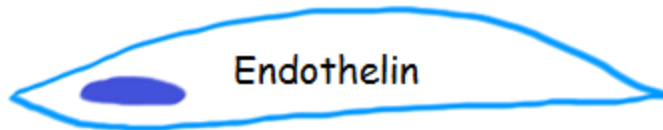
PDE-5 Inhibitors:
Sildenafil



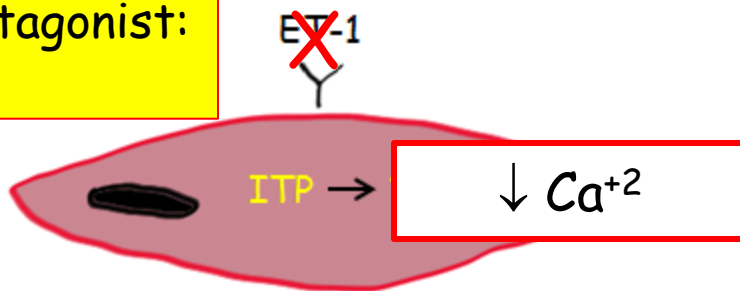
↑ cGMP

Vascular smooth mm cell

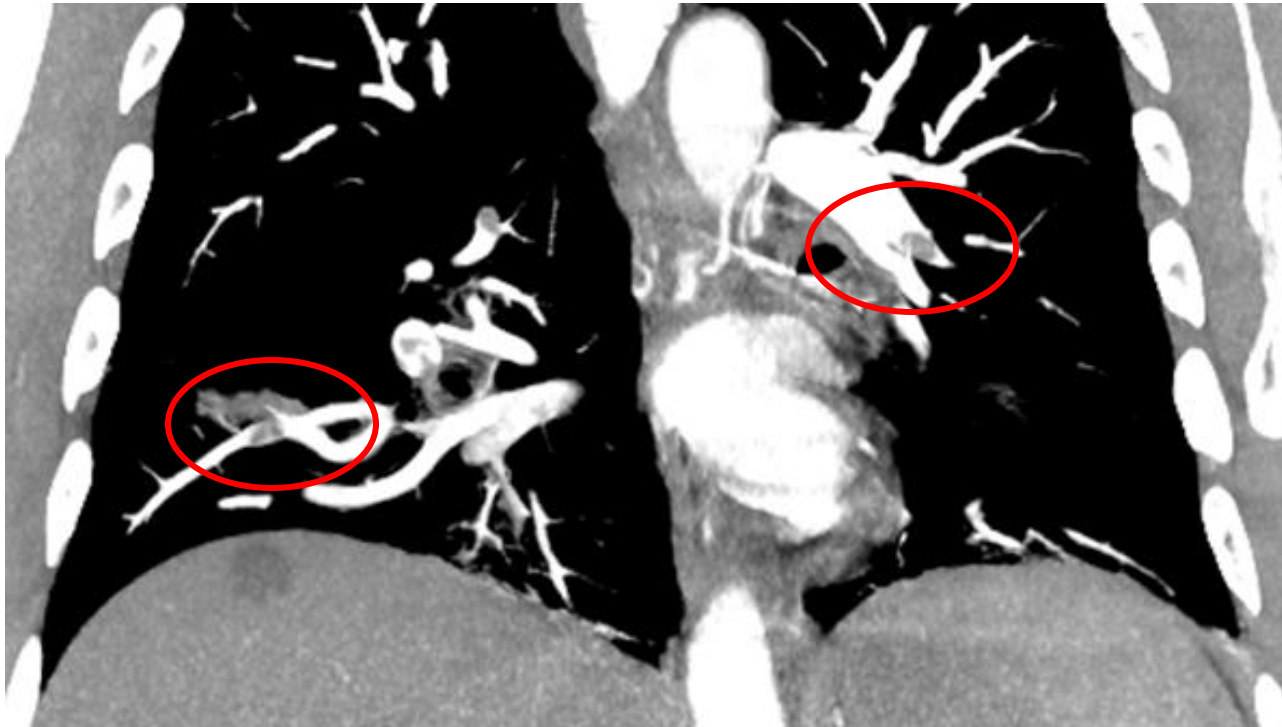
~~Vasoconstrict~~



Endothelin Receptor Antagonist:
Bosentan



The Disorders



Obstructive: Thromboembolic

Obstructive: Thromboembolic

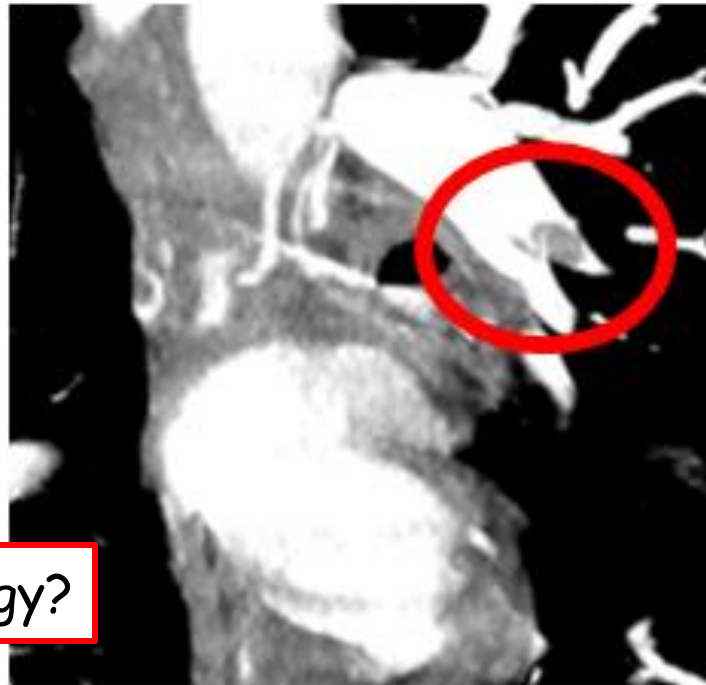
Who's at risk?

Signs and
Symptoms?

Diagnostics?

Pathophysiology?

Therapeutics →
AC



Obstructive: Thromboembolic

Who's at risk?

Signs and
Symptoms?

Diagnostics?

Pathophysiology?

Therapeutics →
AC



What
embolizes?

- Thrombus
- Fat
- Amnion
- Air
- Tumor
- Cholesterol

Obstructive: Thromboembolic

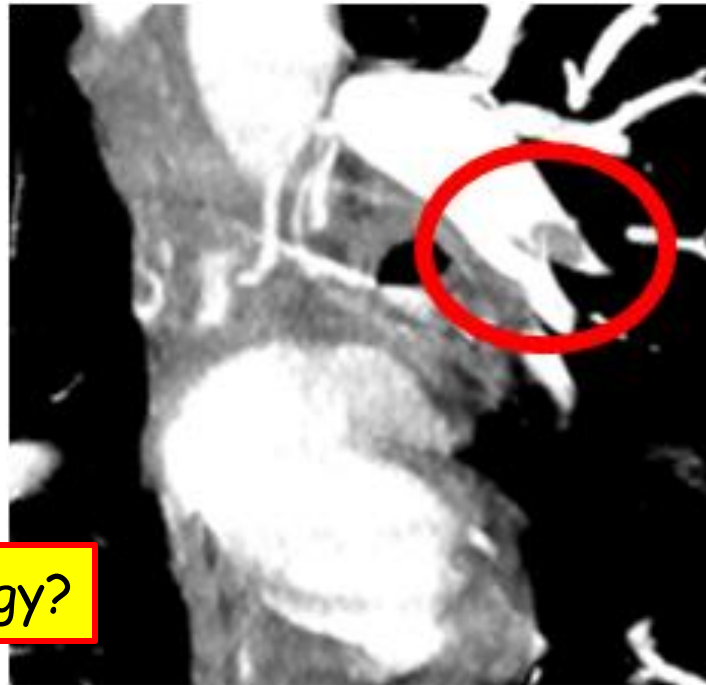
Who's at risk?

Signs and
Symptoms?

Diagnostics?

Pathophysiology?

Therapeutics →
AC



What
embolizes?

- Thrombus
- Fat
- Amnion
- Air
- Tumor
- Cholesterol

Who is at Risk?

- Virchow's Triad
 - Stasis
 - Endothelial injury
 - Thrombophilia

Who is at Risk?

- Virchow's Triad
 - Stasis
 - Postoperative any procedure; hospitalized for any reason
 - Trucker, Long Drive, Air Flight

Who is at Risk?

- Virchow's Triad
 - Stasis
 - Postoperative any procedure; hospitalized for any reason
 - Trucker, Long Drive, Air Flight
 - Endothelial injury
 - Prior Clot
 - Thrombophilia
 - Oral Contraceptive Pills (OCPs)
 - Neoplasia: Pancreas (migratory thrombophlebitis); Polycythemia vera (Budd-Chiari); Renal cell carcinoma (renal vein thrombosis)
 - Inheritable Conditions (Factor V, II; Protein C,S; ATIII, APLA)

What signs and symptoms will be present?

- Symptom
 - SOB, pleurisy, hemoptysis/cough
 - **Calf pain/swelling** (migratory)
 - Symptom related to occult malignancy: weight loss, pain in midepigastrium radiating to midback, hematuria, HA/dizzy, itch.
- Signs
 - Leg swelling, redness, discomfort (Homan's sign)
 - Tachypnea, tachycardia

What signs and symptoms will be present?

Favorite Question(s) from Risk Factors and Signs/Symptoms:

1. Patient with s/s PE. Likely site or cause?
Deep Venous Thrombosis (DVT) means a **Deep Vein** as in **femoral vein**
2. Patient with transient and recurrent thrombophlebitis. Likely dx?
Neoplasm (Pancreas)
3. Trucker drives cross country and develops leg swelling. Develops aphasia/hemiplegia. Likely dx?
Patent Foramen Ovale (PFO or ASD)

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
- Nuclear Ventilation Perfusion Scan
- CT Angiogram
- D-dimer

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)

- Typical Value: 7.48 - 30 (pCO₂) - 60 (pO₂) - 22 (HCO₃⁻)

↑ ↑ ↓ ↓

Alkalosis Hyperventilation Hypoxemia Acute Metabolic Compensation

Respiratory Alkalosis

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)

- Typical Value: 7.48 - 30 (pCO₂) - 60 (pO₂) - 22 (HCO₃⁻)

↑ ↑ ↓ ↓

Alkalosis Hyperventilation Hypoxemia **Acute** Metabolic Compensation

Respiratory Alkalosis

Compensation is always in the 'same direction'

If PCO₂ decreases, the kidney compensates by decreasing HCO₃ reabsorption

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)

- Typical Value: 7.48 - 30 ($p\text{CO}_2$) - 60 ($p\text{O}_2$) - 22 (HCO_3^-)

↑ ↑ ↓ ↓

Alkalosis Hyperventilation Hypoxemia Acute Metabolic Compensation

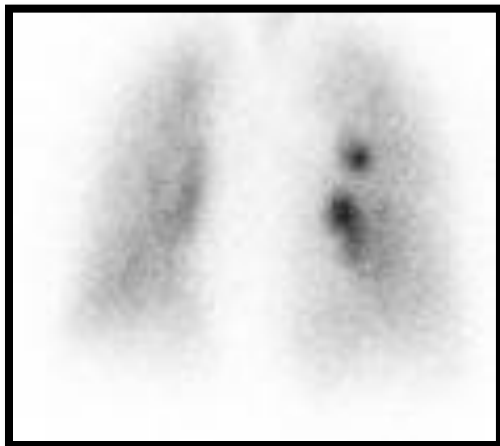
Respiratory Alkalosis

What is the basis for the hypoxemia?

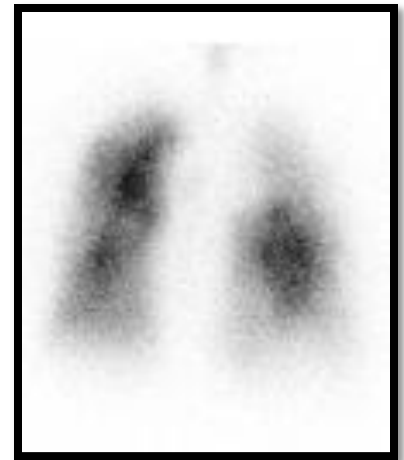
Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
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- ↑ ↑ ↓ ↓
- Alkalosis Hyperventilation Hypoxemia Acute Metabolic Compensation
- Respiratory Alkalosis

What is the basis for the hypoxemia?



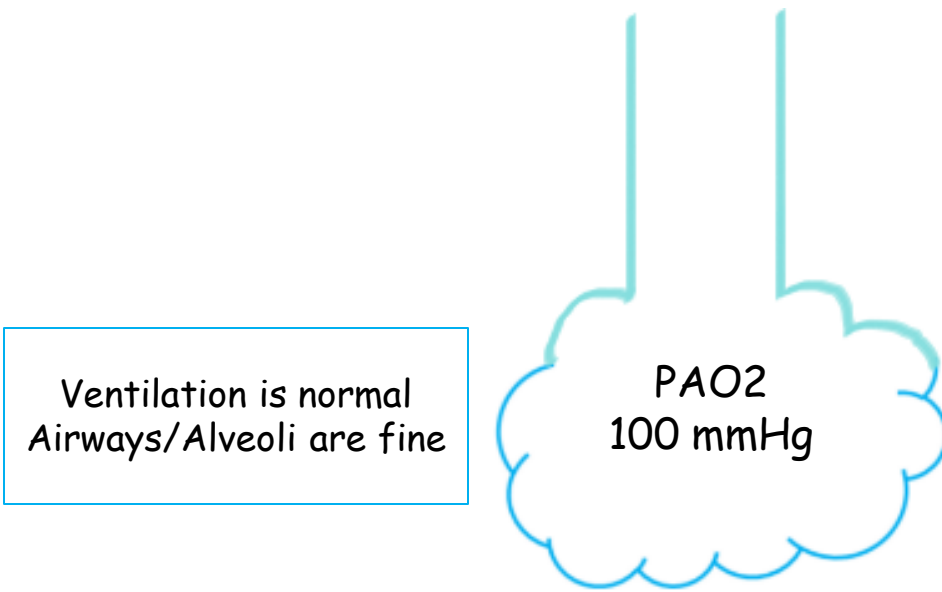
V-Q Mismatch
(Ventilation-Perfusion)



V-Q Mismatch

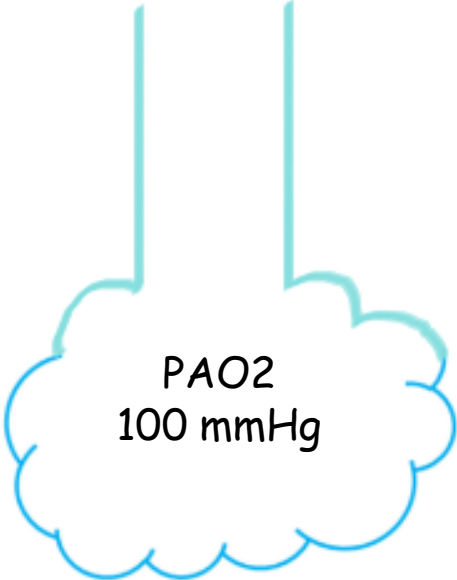
Ventilation is normal
Airways/Alveoli are fine

PAO₂
100 mmHg



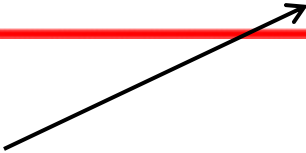
V-Q Mismatch

Ventilation is normal
Airways/Alveoli are fine



Clot

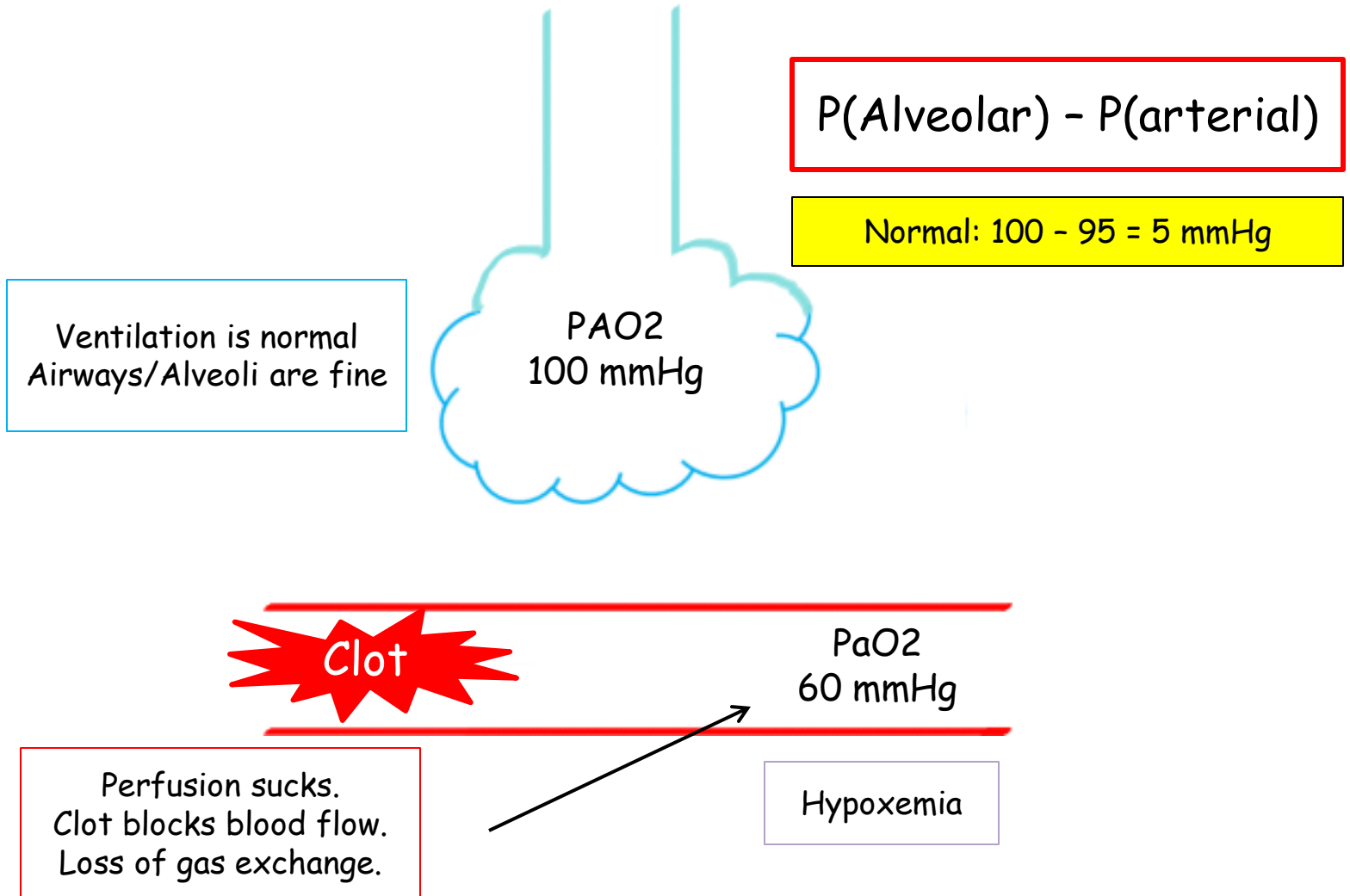
Perfusion sucks.
Clot blocks blood flow.
Loss of gas exchange.



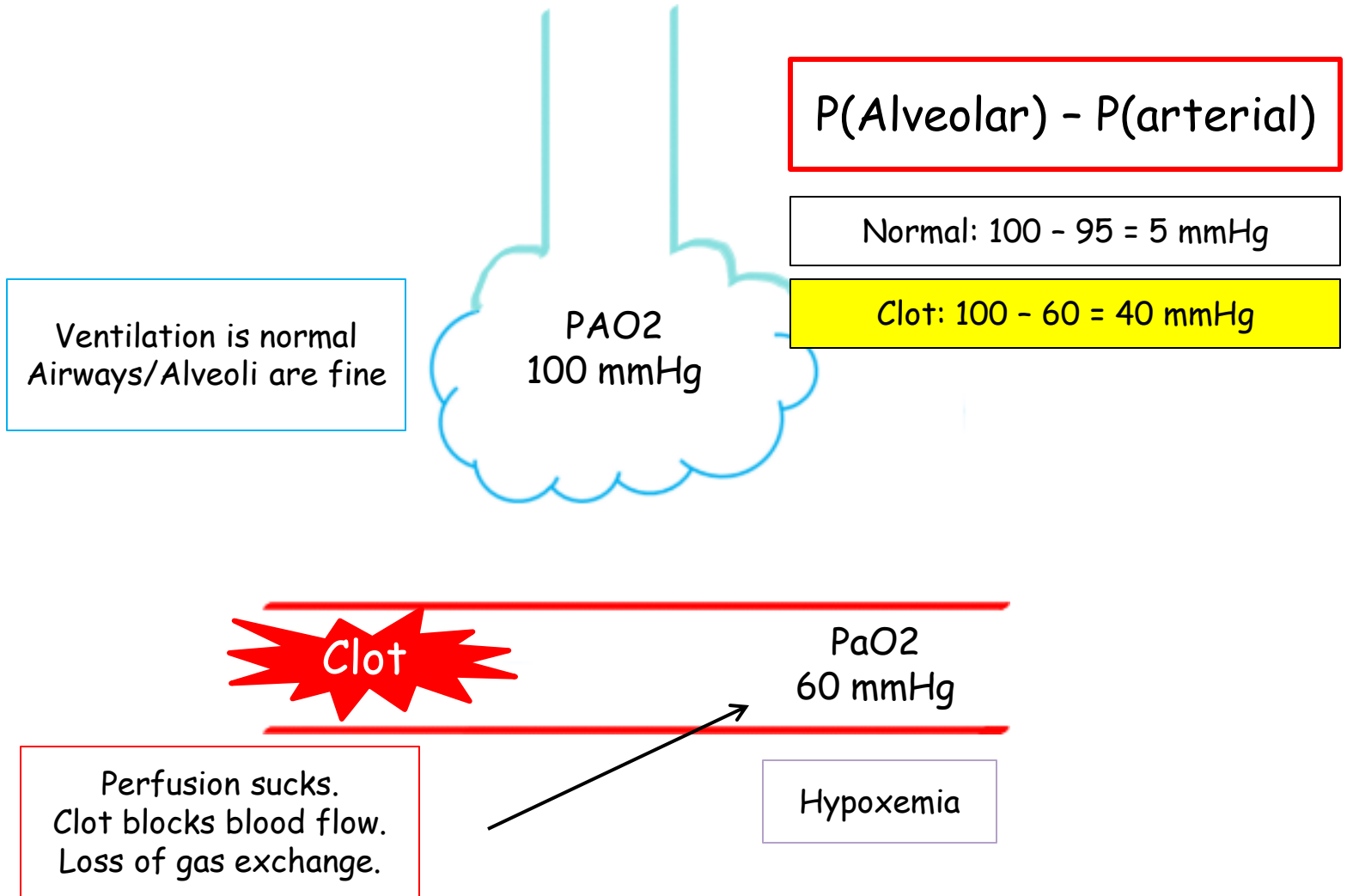
PaO₂
60 mmHg

Hypoxemia

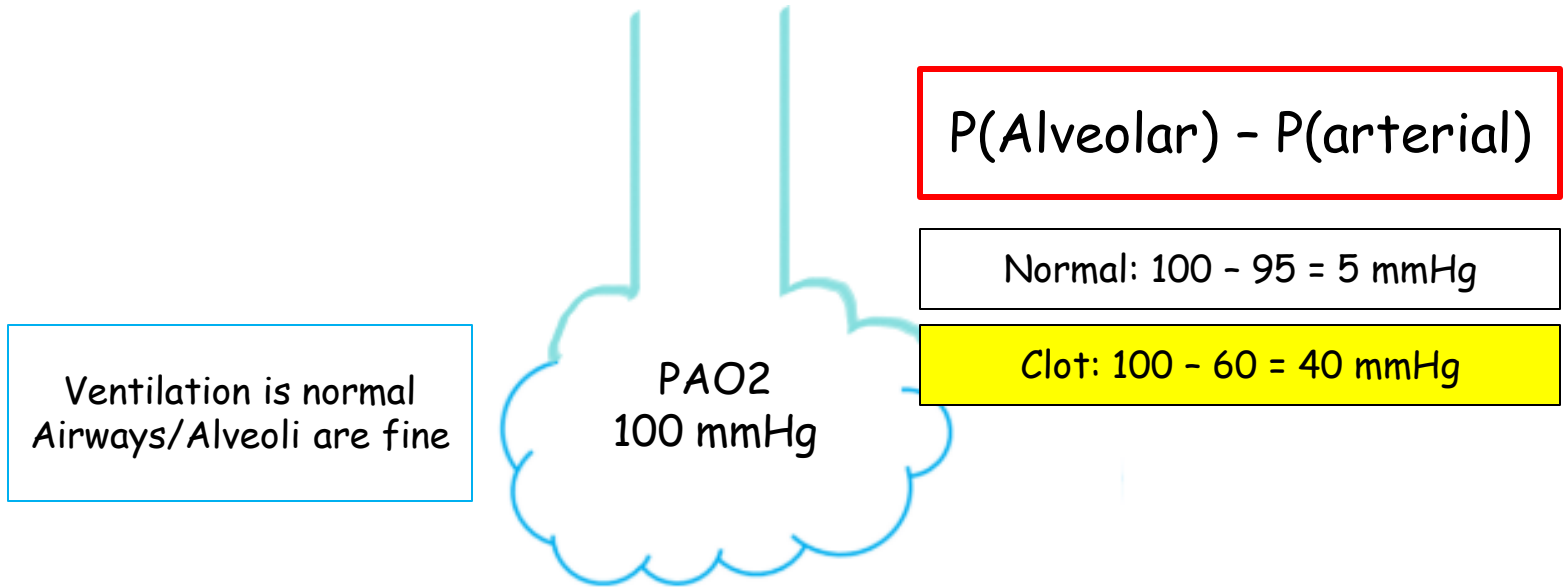
Derivative: Widened A-a Gradient



Derivative: Widened A-a Gradient



Derivative: Widened A-a Gradient



The A-a gradient is used to categorize causes of hypoxemia

Derivative: Widened A-a Gradient

Dead Space

Ventilating a region that lacks blood flow

PAO₂
100 mmHg

P(Alveolar) - P(arterial)

Normal: $100 - 95 = 5$ mmHg

Clot: $100 - 60 = 40$ mmHg

Clot

Derivative: Widened A-a Gradient

Dalton's Law
of Partial Pressures

PAO₂
100 mmHg

P(Alveolar) - P(arterial)

Normal: $100 - 95 = 5$ mmHg

Clot: $100 - 60 = 40$ mmHg

Clot

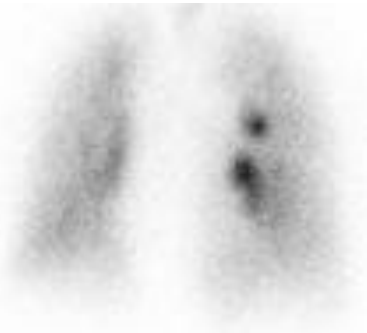
PaO₂
70 mmHg



FYI...

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
- Nuclear Ventilation Perfusion Scan (V-Q Scans)
- CT Angiogram
- D-dimer



Ventilation:
Breath in radiolabeled gas

Assess for Defects
(V-Q Mismatch)



Perfusion:
Inject radiolabeled tracer

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
- Nuclear Ventilation Perfusion Scan

Indicated if IV contrast allergy or renal failure



Ventilation:
Breath in radiolabeled gas

Assess for Defects
(V-Q Mismatch)



Perfusion:
Inject radiolabeled tracer

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
- Nuclear Ventilation Perfusion Scan

Indicated for PE, asthma, allergy or renal failure

Dead space

Assess for Defects
(V-Q Mismatch)

Ventilation:
Breathe in radiolabeled gas

Perfusion:
Inject radiolabeled tracer

Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
- Nuclear Ventilation Perfusion Scan
- CT Angiogram
- D-dimer

Be prepared to see either autopsy or CT angiogram pointing to a clot.

As always, the graphic will be difficult BUT the vignette gives ample information to determine the diagnosis.

But then they ask the derivative (i.e. where did the clot come from, what was the underlying cause, etc?)

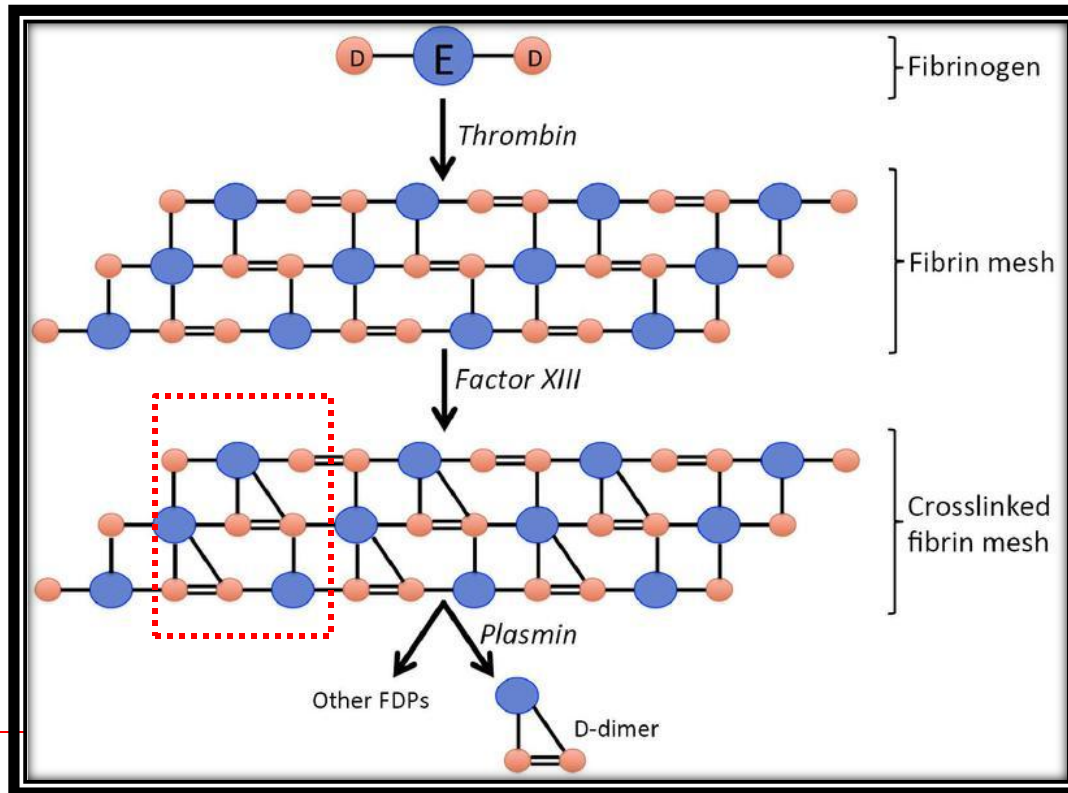


Diagnostic Studies with Pathophysiology Subtheme

- Arterial Blood Gas analysis (ABG)
- Nuclear Ventilation Perfusion Scan
- CT Angiogram
- D-dimer
 - What is it?
 - How is it used?
 - Key Derivative: d-dimer v fibrin degradation (split) products FDP)?

D-dimer

- What is it?
 - Breakdown product of **cross linked fibrin**. 'Cross linked' implies fibrin monomers that have been stabilized by activated factor XIII.

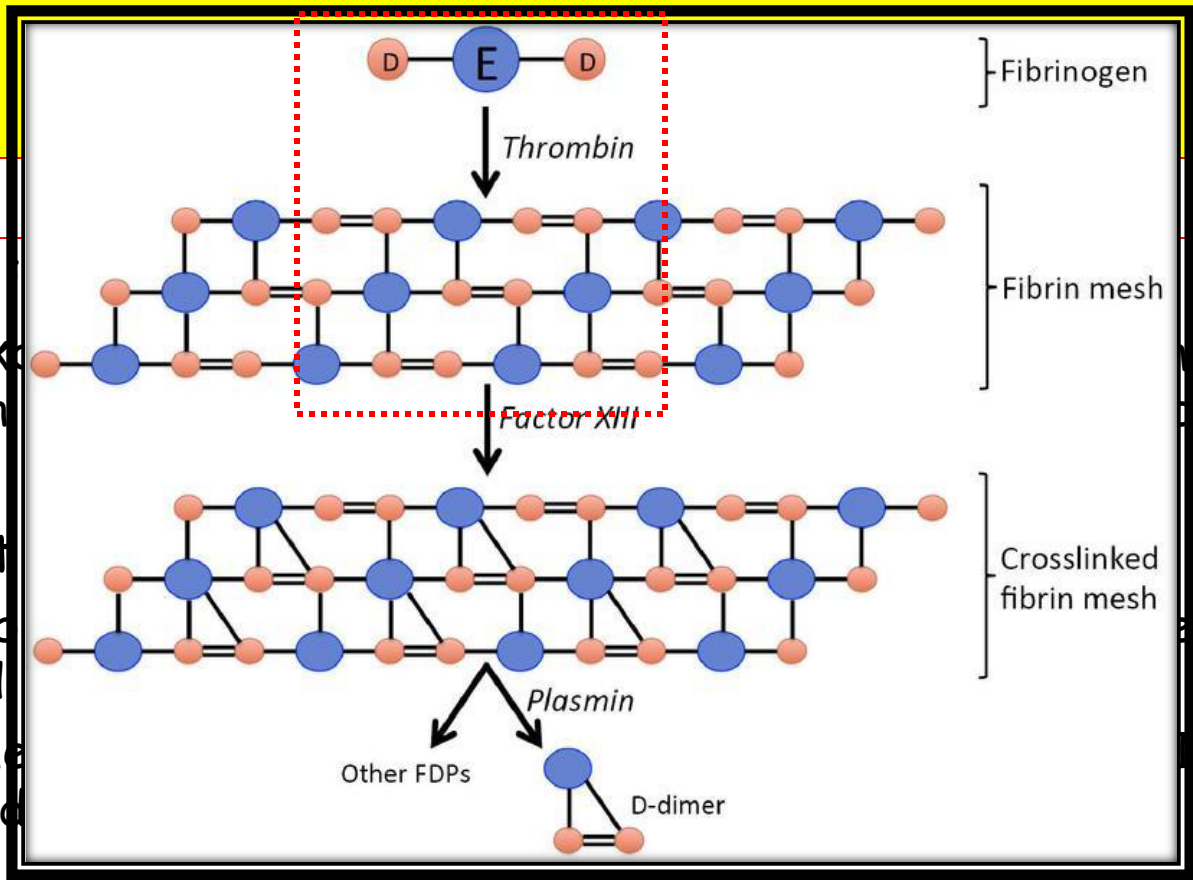


D-dimer

- What is it?
 - Breakdown product of cross linked fibrin. 'Cross linked' implies fibrin monomers that have been stabilized by activated factor XIII.
- How is it used?
 - As a breakdown product of blood clots (thrombus), elevated values would imply presence of clot.
 - As the test lacks specificity, it is best used when **NEGATIVE** to exclude the presence of clot.

D-dimer

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 - Fibrin split products are even less specific than d-dimer. They can be derived from circulating fibrinogen (even in absence of clot).
 - D-dimer, therefore, is more specific for clots than FDP.



- What is
 - Breakdown of fibrin
- How is it
 - As a blood clot would
 - As the blood is excluded

applies to Factor XIII.

and values

VE to

- Key Derivative: d-dimer v fibrin degradation (split) products?
 - Fibrin split products are even less specific than d-dimer. They can be derived from circulating fibrinogen (even in absence of clot).
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Fat Embolism

Who's at risk?

Signs and
Symptoms?

Diagnostics?

Pathophysiology?

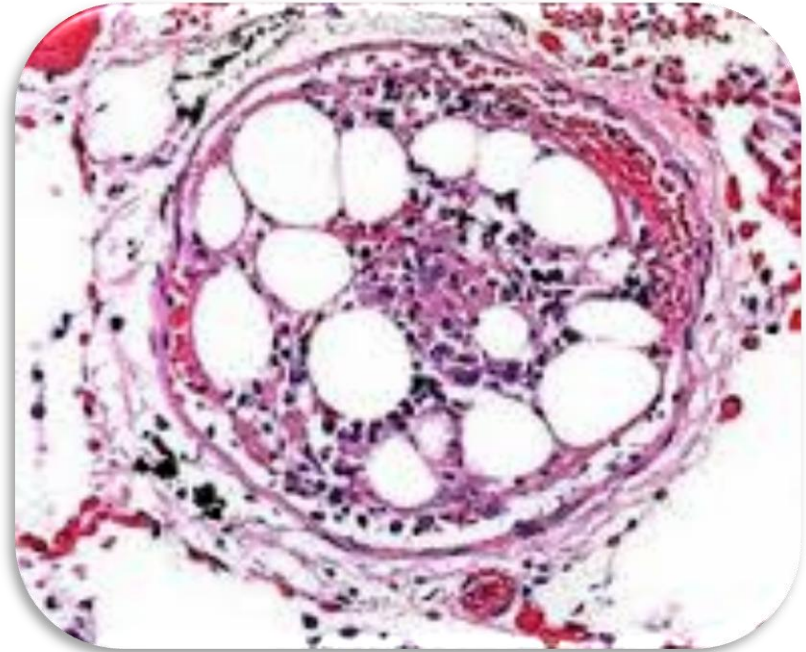
Therapeutics?



What
embolizes?

- Thrombus
- Fat
- Amnion
- Air
- Tumor
- Cholesterol

Fat Embolism



- **Key Concepts**

- After long bone injury
- Typically, 3rd day
- Confusion, SOB, **petechial rash** (on upper chest; low platelets due to adhering to fat globules)
- Histology reveals fat globules in pulmonary arterioles
- **Can cause ARDS (FFA cause toxic injury)**

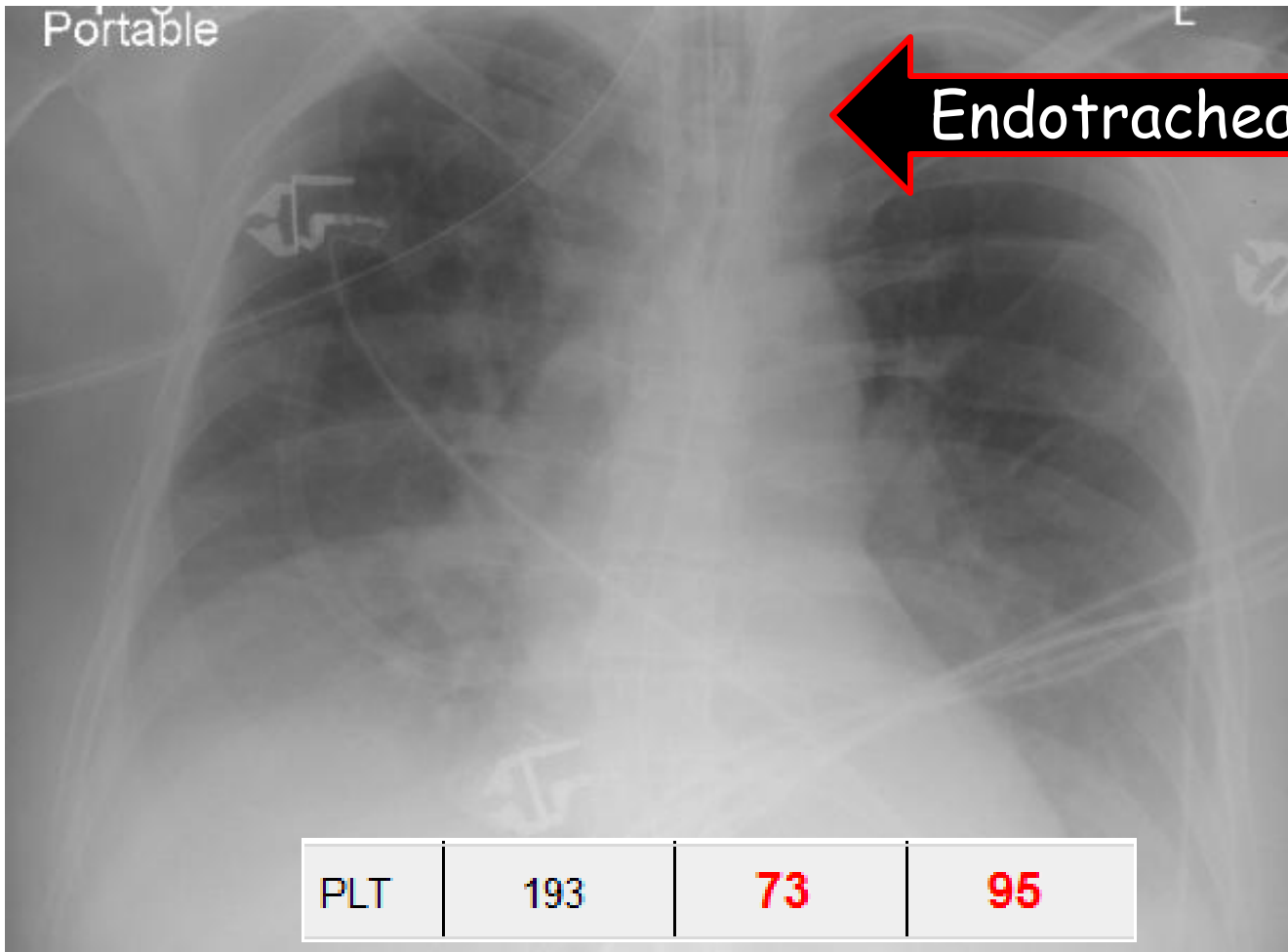
Fat Embolism

- Key Concepts

- After long bone injury; Typically, 3rd day
- Confusion, SOB, petechial rash (on upper chest; low platelets due to adhering to fat globules)
- Histology reveals fat globules in pulmonary arterioles
- Can cause ARDS (FFA cause toxic injury)

Your Mission:

1. Distinguish from pulmonary embolism (platelets and rash)
2. Know the pathology: fat globules in arterioles
3. Understand the fat globules belong on our bellies, not in our circulation → ARDS



Fracture patient on Day 4
of hospitalization



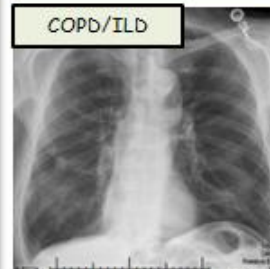
Pulmonary Vascular Disorders

Part I:
General Principles
Differential Diagnoses
Basic Physiology/Diagnostics

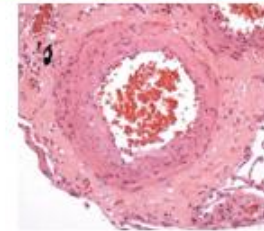
Part II (The Disorders):
Primary Pulmonary Hypertension
Thromboembolic Disease

Pulmonary HTN

Pulmonary Artery > 25 mmHg (normal ~ 12)



Chronic Hypoxia
Vasoconstrictive

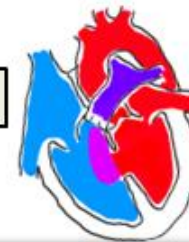


Obliterative
PPH



Obstructive

Hyperkinetic
LEFT → right Shunt



Passive 2nd to LV Failure

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