Pulmonary Hypertension

Ali khaddam, MD,MRCP
Cardiology Department
Damascus University

How Common is It?

- Pulmonary Hypertension → Relatively Common
- Pulmonary ***Arterial*** Hypertension → Relatively Uncommon

What is the Difference?

- Pulmonary Hypertension = A general term used to describe elevated pressure in the pulmonary vascular bed, not describing where the "lesion" is.

- Pulmonary Arterial Hypertension = A term that describes elevated pressure in the pulmonary vasculature, limited to the arteries/arterioles, and due to an intrinsic abnormality in the pulmonary arterial bed.

Definition of PAH by WHO

- Required:
  - Mean PAP ≥ 25 mm Hg at rest or 35 mmHg with exercise
  - PCWP ≤ 15 mm Hg
- Should be present:
  - PVR ≥ 3 Wood Units (240 dynes.sec.cm-5)

Classification of PH

- The current classification system groups together forms of pulmonary hypertension based on similarities in their pathophysiologies and responses to treatment.
- Important to classify patients correctly to ensure therapeutic choices are appropriate.

Group 1 -- PAH

- IPAH
- Familial
- Associated with PAH
  - Connective Tissue Disease (Scleroderma, SLE, MCTD, DM/PM, RA)
  - Congenital Heart Disease
  - Portal hypertension (5-7% of patients)
  - HIV (0.5% of patients)
  - Drugs/toxins (aminorex-, dexfenfluramine-, or fenfluramine-containing products, cocaine, methamphetamine)
  - Other: thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, myeloproliferative disorders, splenectomy
- Associated with venous/capillary involvement
  - Pulmonary veno-occlusive disease (elevated mPAP, normal PCWP, evidence of pulmonary vascular congestion)
  - Pulmonary capillary hemangiomatosis
- PPHN

Groups 2-5 -- PH

- Group 2: Pulmonary hypertension with left heart disease
  - Left-sided ventricular or atrial disease
  - Left-sided valvular disease
- Group 3: Pulmonary hypertension associated with lung disease and/or hypoxemia
  - Chronic obstructive lung disease
  - Interstitial lung disease
  - Sleep-disordered breathing
  - Alveolar hypoventilation disorders
  - Chronic exposure to high altitude
  - Developmental abnormalities
- Group 4: Pulmonary hypertension due to chronic thrombo-embolic disease
  - Thromboembolic obstruction of proximal pulmonary arteries
  - Thromboembolic obstruction of distal pulmonary arteries
- Group 5: Miscellaneous
  - Sarcoidosis, histiocytosis X, lymphangiomyomatosis, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis)

Symptoms of PAH

- Dyspnea 60%
- Fatigue 19%
- Near syncope/syncope 13%
- Chest pain 7%
- Palpitations 5%
- LE edema 3%

WHO functional classification

- Class I: No limitation in physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
- Class II: Slight limitation in physical activity. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
- Class III: Marked limitation in physical activity. Less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
- Class IV: Inability to perform any physical activity without symptoms. Signs of right heart failure. Dyspnea and/or fatigue may be present at rest. Syncope.

Reasons to Suspect PAH

- Unexplained dyspnea despite multiple diagnostic tests .
- Typical symptoms .
- Co-morbid conditions :
  - CREST, liver disease, HIV, sickle cell
  - Family history of PAH
  - History of stimulant/anorexigen use

Physical Examination

- Cardiovascular findings:
  - Large a wave in the jugular venous pulse;
  - Prominent v waves in the jugular venous pulse
  - Left parasternal (right ventricular) heave;
  - Systolic pulsation in the second left intercostal space
  - Fourth heart sound of right ventricular origin
  - Third heart sound of right ventricular origin
  - High-pitched early diastolic murmur of pulmonic regurgitation,
  - Holosystolic murmur of tricuspid regurgitation
  - Signs of right ventricular failure (hepatomegaly, edema, and ascites)
  - Cyanosis
- Patients whose PAH is associated with another illness often have clinical features of that disease.

Physical exam clues

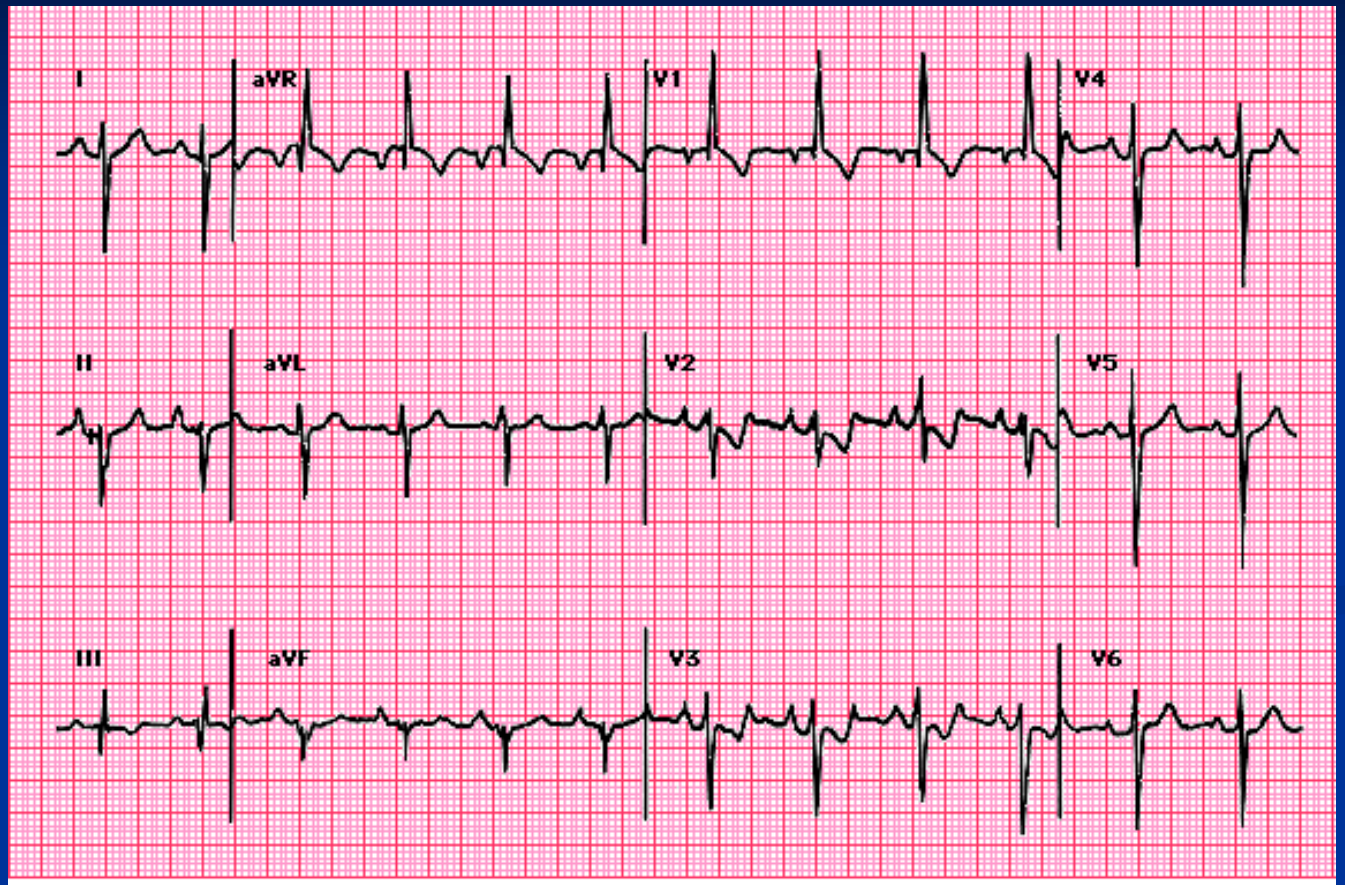
- Telengectasias
- Calcinosis
- Raynaud's
- Palmar erythema/stigmata of liver dz
- JVD
- RV heave
- Murmur TR, VSD/ASD
- Loud P2 (can hear 2nd heart sound clearly at apex)
- Clubbing
- LE edema

Diagnostic Work-up

- Labs
  - Autoimmune serologies
  - Markers of liver synthetic function
  - HIV serologies when dictated by history
- EKG
  - Not sensitive enough to be a screen but can help guide diagnosis workup
    - RVH 87% of PH
    - RAD 79% of PH
    - RAE: p wave > 2.5 mm in II, III, aVF

ECG

- Highly specific but not very sensitive.
- Right axis deviation
- Right atrial and right ventricular enlargement.
- Right bundle branch block
- ST and T wave changes in the anterior precordial leads.



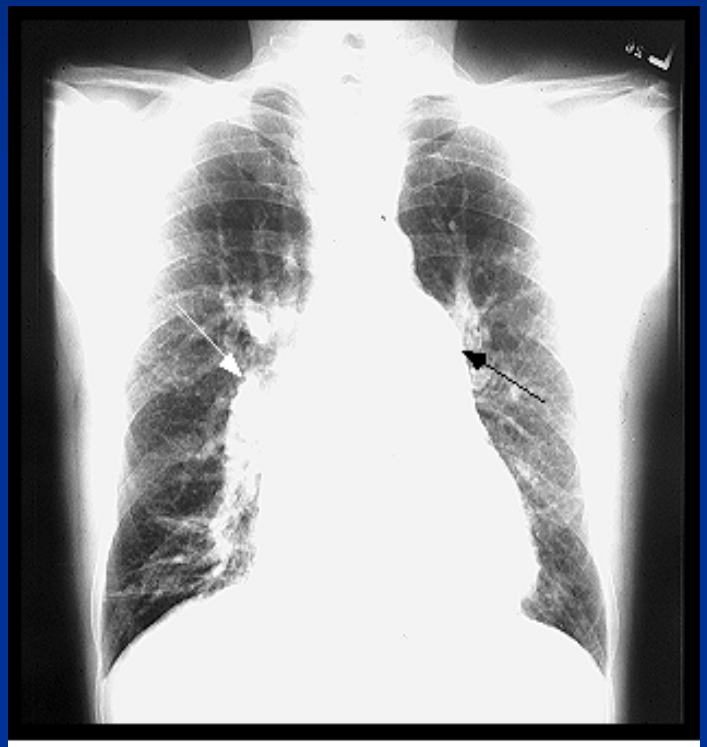
Right ventricular hypertrophy Right ventricular hypertrophy due, in this case, to primary pulmonary hypertension. The characteristic features include marked right axis deviation (+210° which is equal to −150°), tall R wave in V1 (as part of a qR complex), delayed precordial transition zone with prominent S waves in leads V5 and V6, inverted T waves and ST depression in V1 to V3 consistent with right ventricular "strain", and peaked P waves in lead II consistent with concomitant right atrial enlargement. Courtesy of Ary Goldberger, MD.

Diagnostic Work-up

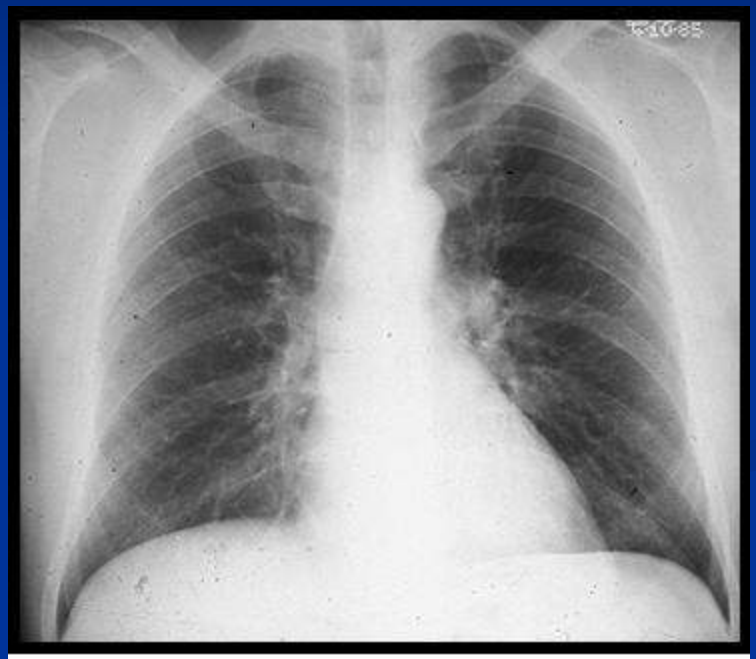
- Chest x-ray
  - Not sensitive enough to screen
  - Attenuated peripheral vasculature
  - Enlarged PAs (especially right)
- Echocardiogram
  - Order for screening when clinical suspicion exists
  - Order for standard interval screening in selected groups:
    - Family of those with IPAH
    - Scleroderma spectrum
    - CHD pts
    - Pre-liver transplant

CXR-PA view

Enlargement of the main pulmonary artery and its major branches, with marked tapering of peripheral arteries .



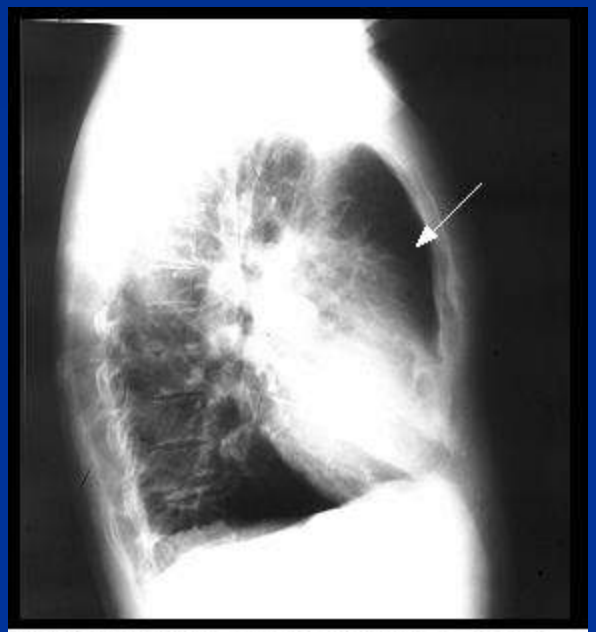
Pulmonary artery hypertension Chest radiograph in PA view showing enlarged pulmonary arteries (arrows) due to pulmonary hypertension induced by anomalous pulmonary venous drainage. Courtesy of Sven Paulin, MD.



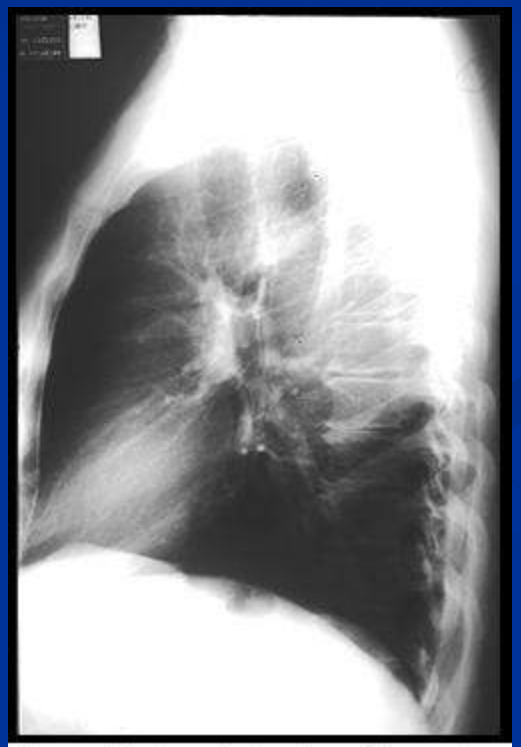
Normal chest film Posteroanterior view of a normal chest radiograph. Courtesy of Carol M Black, MD.

CXR-lateral view

Encroachment of the retrosternal air space -- right ventricular enlargement/hypertrophy

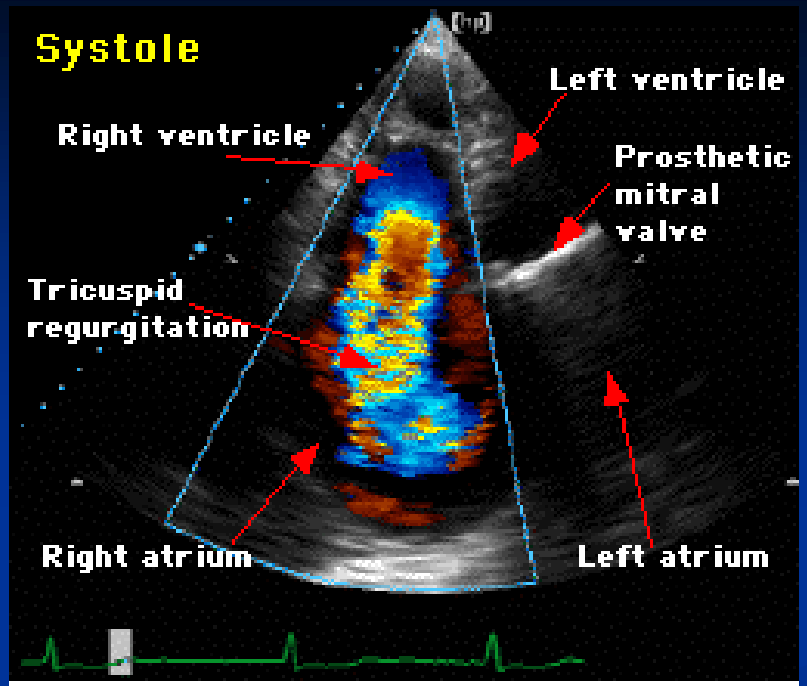


Pulmonary artery hypertension Chest radiograph in lateral view showing decreased retrosternal space (arrow) due to right ventricular enlargement in pulmonary hypertension. Courtesy of Sven Paulin, MD.



Normal lateral chest radiograph Courtesy of Steven Weinberger, MD.

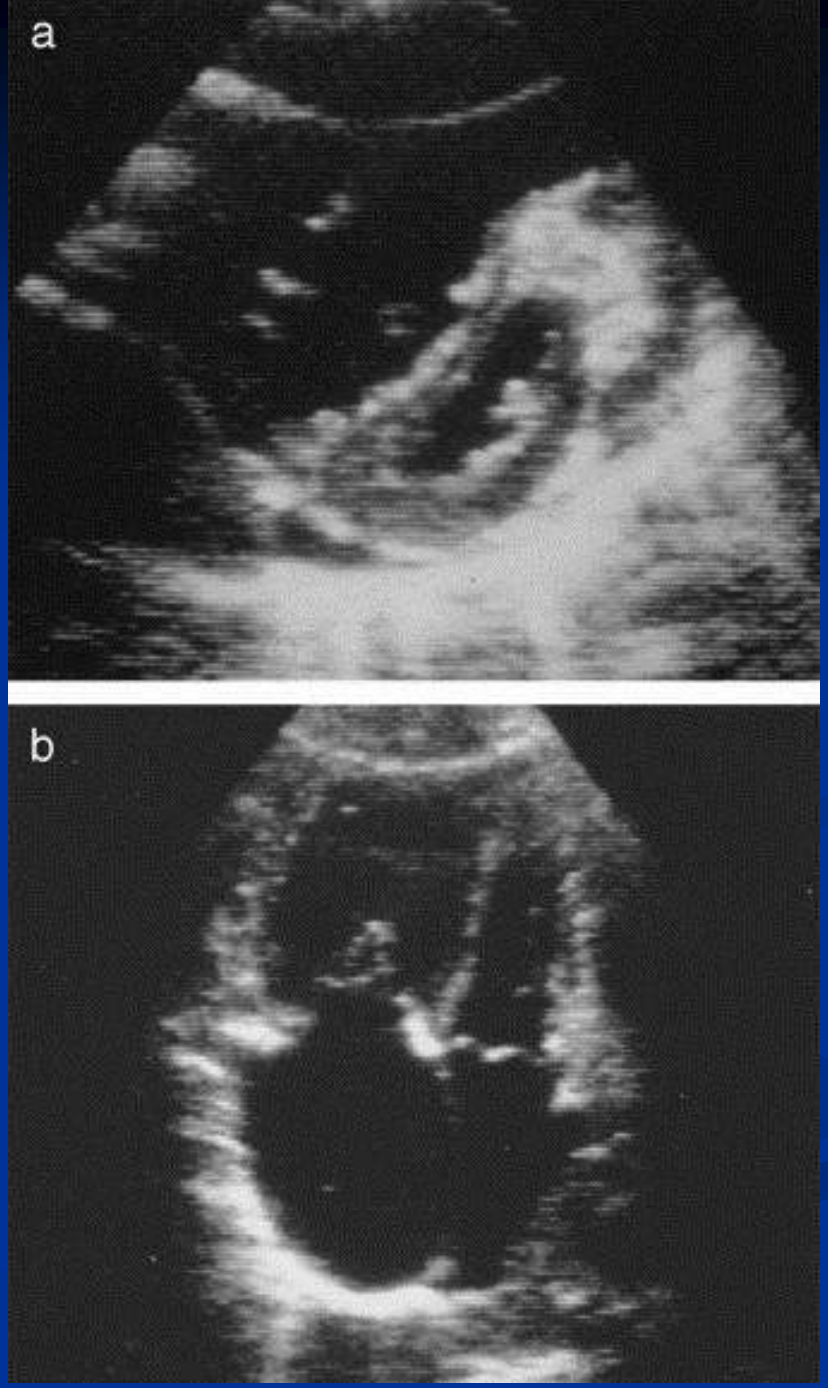
Doppler Echocardiogram



Tricuspid regurgitation The four chamber view from a 2-D echocardiogram with color flow Doppler shows significant tricuspid regurgitation with a dilated right atrium. There is a prosthetic mitral valve suggesting that the etiology for tricuspid regurgitation is pulmonary hypertension resulting from previous mitral valve disease. (Courtesy of Thomas Binder, MD. University of Vienna).

Echocardiogram

Right atrial and ventricular enlargement and flattening of the intraventricular septum -- parasternal short axis view (a) and four chamber view (b).



Echocardiogram Findings

- Increased sPAP or TR jet
- Right atrial and ventricular hypertrophy
- Flattening of interventricular septum
- Small LV dimension
- Dilated PA
- Pericardial effusion

Always Rule out CTEPH

- Must be excluded in every case of PAH
- V/Q scan is preferred screening test, not PE protocol CT (this is best for acute emboli).
- In chronic thromboembolic disease, at least one (and more commonly, several) segmental or larger mismatched ventilation-perfusion defects are present.
- Formal angiography will be done before surgical procedure if V/Q positive

Right Heart Cath

- Essential for firm diagnosis:
  - Helps to not dx people with PAH that do not have it!
  - Evaluate for septal defects
  - Shed light on the issue of diastolic dysfunction
  - Assess severity and response to CCB

Treatment

- **General measures**

  Physical activity; Diuretics; Supplemental oxygen

  Digoxin; Anticoagulation
- **Specific treatment**

  1. Calcium channel blockers: nifedipine and diltiazem
  2. Prostacylin analogues: Epoprostenol
  3. Endothelin receptor antagonists: Bosentan
  4. Phosphodiesterase-5 inhibitors: sildenafil
- **Interventional and surgical therapy**: atrial septostomy,Lung or heart-lung transplantation

General measures:

- Avoid pregnancy
  - Contraception imperative
  - Maternal mortality 30%
- Immunizations for respiratory illnesses

  Influenza & pneumonia vaccinations
- Minimize valsalva maneuvers—increase risk of syncope
  - Cough, constipation, heavy lifting, etc

Diuretics

- Principally to treat edema from right heart failure
- May need to combine classes

  -Thiazide and loop diuretics
- Patients often require large doses of diuretics

Coumadin

- Studies only show benefit in IPAH patients, based on improved survival.
- Other PAH groups not as clear, use in them considered expert opinion.
- Generally, keep INR 2.0-2.5.
- Thought to lessen in-situ thrombosis

Oxygen

- Minimize added insult of hypoxic vasoconstriction
- Keep oxygen saturation ≥90%
  - May be impossible with large right to left shunt

PAH-Specific Therapies

- Calcium channel blockers (diltiazem, nifidipine)
- Endothelin receptor antagonists (ERAs)—**bosentan**,
- Phosphodiesterase (type 5) inhibitors (PDE 5-I)--**sildenafil**
- Prostanoids

Summary

- Make sure to differentiate PAH from PH
- Determine etiology of PAH as best as possible
- Refer early to specialist if you find it
- Don't treat without a RHC

Pulmonary Embolism

Dr. Ali Khaddam MD, MRCP
Cardiology Department
Damascus University

PE

- **Epidemiology**
  - Five million cases of venous thrombosis each year
  - 10% of these will have a PE
  - 10% will die
  - Incidence of 700 per 1 million
  - Correct diagnosis is made in only 10-30% of cases
  - Up to 60% of autopsies will show some evidence of past PE

PE

- **Epidemiology**
  - 90-95% of pulmonary emboli originate in the deep venous system of the lower extremities
  - Other rare locations include
    - Uterine and prostatic veins
    - Upper extremities
    - Renal veins
    - Right side of the heart

Risk Factors

- CHF
- Malignancy
- Obesity
- Estrogen/OCP
- Pregnancy (esp post partum)
- Lower ext injury
- Coagulopathy
- Venous Stasis
- Prior DVT
- Age > 70
- Prolonged Bed Rest
- Surgery requiring > 30 minutes general anesthesia
- Orthopedic Surgery

Virchow's Triad

- Rudolf Virchow postulated more than a century ago that a triad of factors predisposed to venous thrombosis
  - **Local trauma to the vessel wall**
  - **Hypercoagulability**
  - **Stasis of blood flow**
- It is now felt that pts who suffer a PE have an underlying predisposition that remains silent until an acquired stressor occurs

PE

- When venous emboli become dislodged from their site of origin, they embolize to the pulmonary arterial circulation or, paradoxically to the arterial circulation through a patent foramen ovale
  - About 50% of pts with pelvic or proximal leg deep venous thrombosis have PE
  - Isolated calf or upper extremity venous thrombosis pose a lower risk for PE

Pathophysiology

- Increased pulmonary vascular resistance
- Impaired gas exchange
- Alveolar hyperventilation
- Increased airway resistance
- Decreased pulmonary compliance

Right Ventricular Dysfunction

- Progressive right heart failure is the usual immediate cause of death from PE
- As pulmonary vascular resistance increases, right ventricular wall tension rises and perpetuates further right ventricle dilation and dysfunction
- Interventricular septum bulges into and compresses the normal left ventricle

Clinical Syndromes

- Pts with massive PE present with systemic arterial hypotension and evidence of peripheral thrombosis
- Pts with moderate PE will have right ventricular hypokinesis on echocardiogram but normal systemic arterial pressure
- Pts with small to moderate PE have both normal right heart function and normal systemic arterial pressure

Diagnosis

- Thrombotic Pulmonary Embolism
- Nonthrombotic Pulmonary Embolism
  - Fat Embolism
  - Amniotic Fluid Embolism
  - IVDA (Talc, cotton, etc)

Symptoms and signs of PE

Small – moderate PE

- Dyspnea
- Chest pain
- Cough/hemoptysis
- diaphoresis
- Tachypnea
- Tachycardia
- Hypoxemia
- Rales
- Wheezing
- Mild fever

Massive PE

- Cyanosis
- Anxiety
- Restlessness
- Confusion
- hypotension

Diagnosis

- **H&P**
- Always ask about prior DVT, or PE
  - Family History of thromboembolism
  - Dyspnea is the most frequent symptom of PE
  - Tachypnea is the most frequent physical finding

Symptom list

- 73% Dyspnea
- 66% Pleuritc Pain
- 43% Cough
- 33% Leg Swelling
- 30% Leg Pain
- 15% Hemoptysis
- 12% Palpitations
- 10% Wheezing
- 5% Angina-Like pain

- 2% mortality In pts without hypotension
- 30% mortality When there is shock
- 70% mortality If cardiopulmonary arrest occurs

Differential Diagnosis

- PE is known as "the great masquerader"
- USA, MI
- Pneumonia, bronchitis
- CHF
- Asthma
- Costochondritis, Rib Fx,
- Pneumothorax
- **PE can coexist with other illnesses!!**

Estimation of Pretest Clinical Probability of Pulmonary Embolism

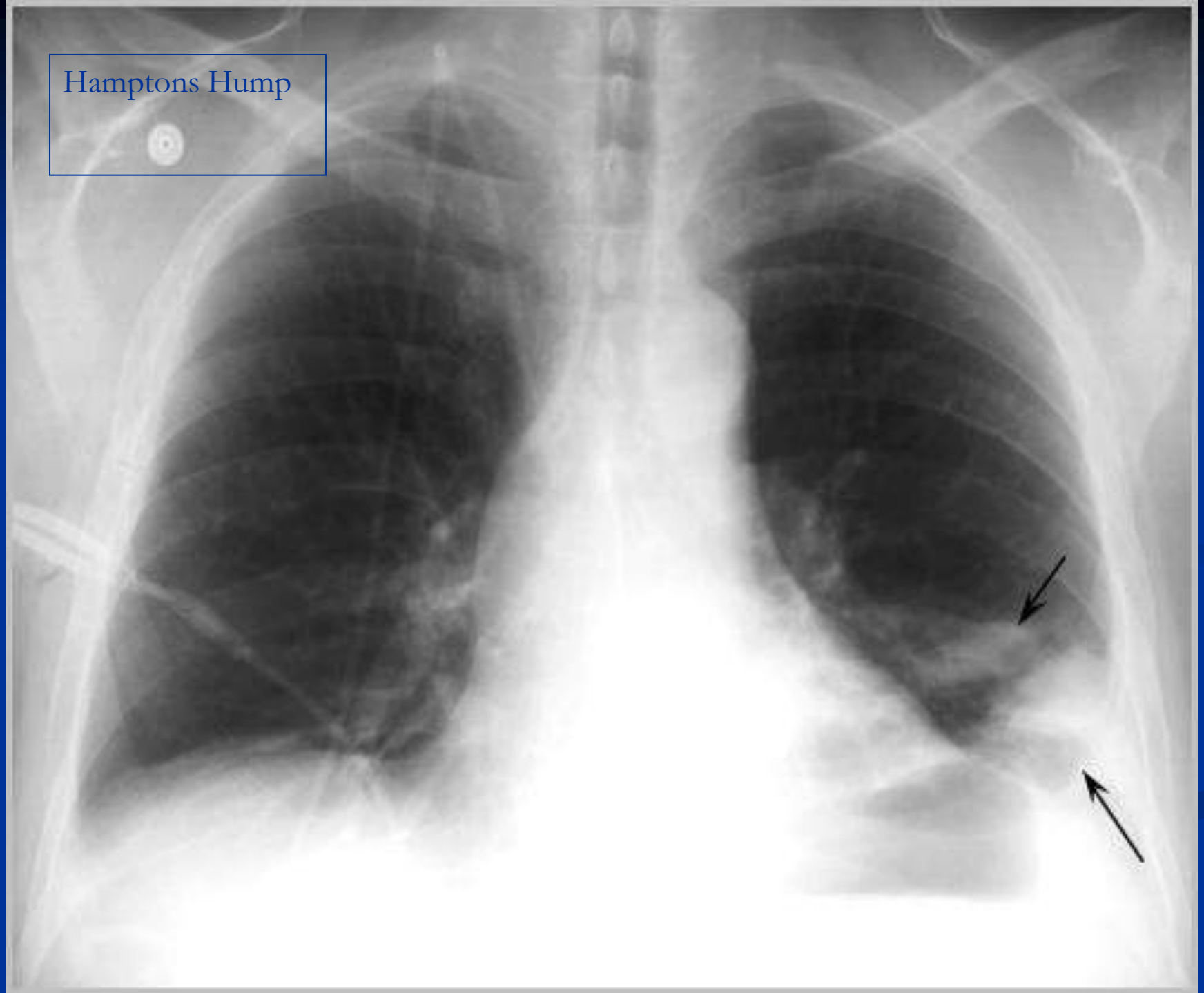
- **Low-probability** (unlikely)
  1. Symptoms incompatible with pulmonary embolism or compatible symptoms that can be explained by an alternative process, such as pneumonia, pneumothorax, or pulmonary edema
  2. No radiographic or ECG abnormalities compatible with pulmonary embolism, or findings that can be explained by an alternative diagnosis
  3. Absence of risk factors for venous thromboembolism
- **Intermediate-probability** (possible/probable)
  1. Symptoms compatible with pulmonary embolism, but no associated radiographic or ECG findings
  2. Constellation of findings not consistent with low or high clinical probability
- **High-probability** (very likely)
  1. Symptoms compatible with pulmonary embolism (sudden-onset dyspnea, pleuritic chest pain, tachypnea, or syncope), not explained otherwise
  2. Radiographic or ECG findings compatible with pulmonary embolism,
  3. Presence of risk factors for venous thromboembolism

Diagnosis

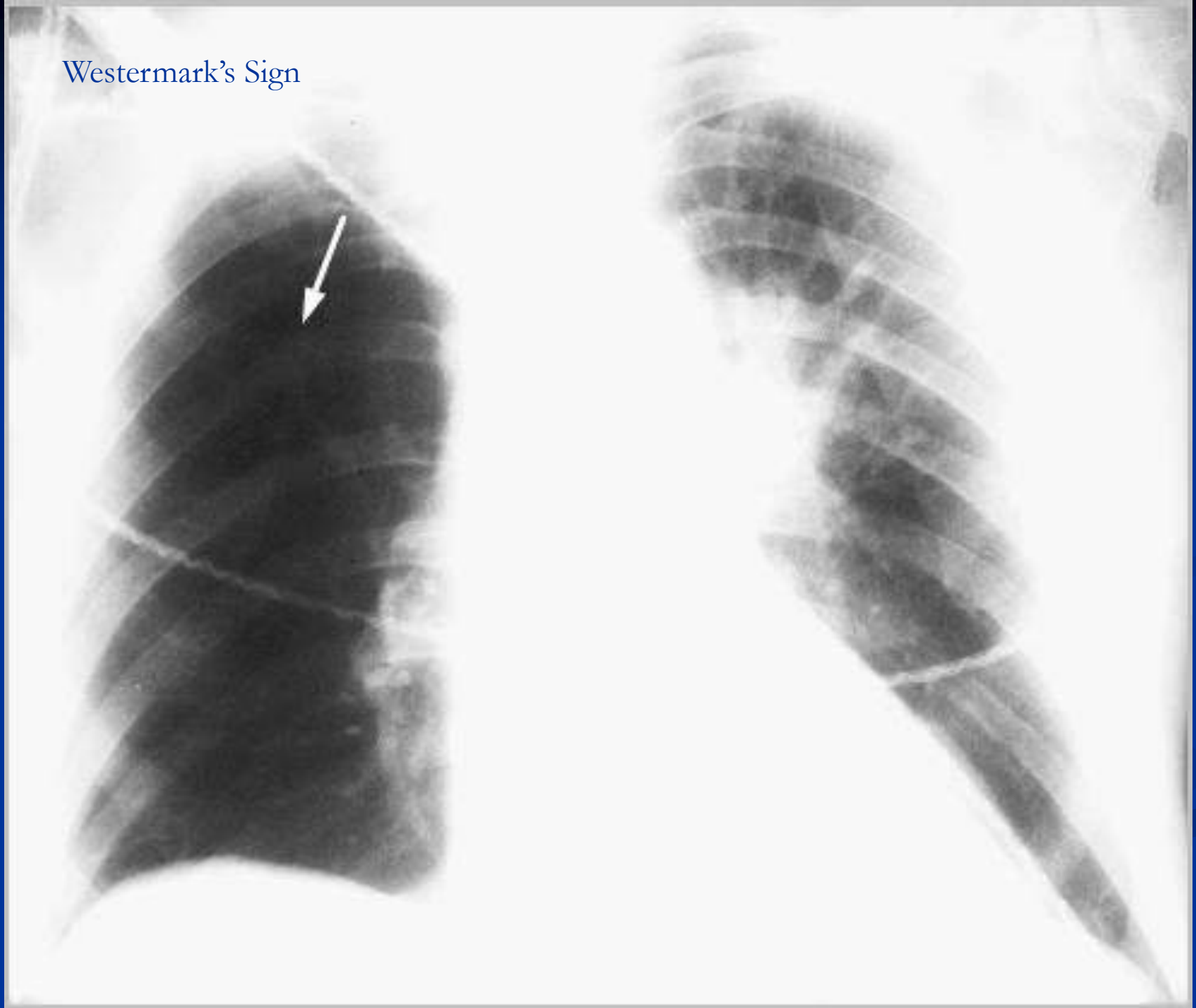
- **Serum Studies**
  - **D-dimer**
    - Elevated in more than 90% of pts with PE
    - Reflects breakdown of plasmin and endogenous thrombolysis
    - Not specific: Can also be elevated in MI, sepsis, or almost any systemic illness
    - Negative predictive value
  - ABG-contrary to classic teaching, arterial blood gases lack diagnostic utility for PE

Diagnosis

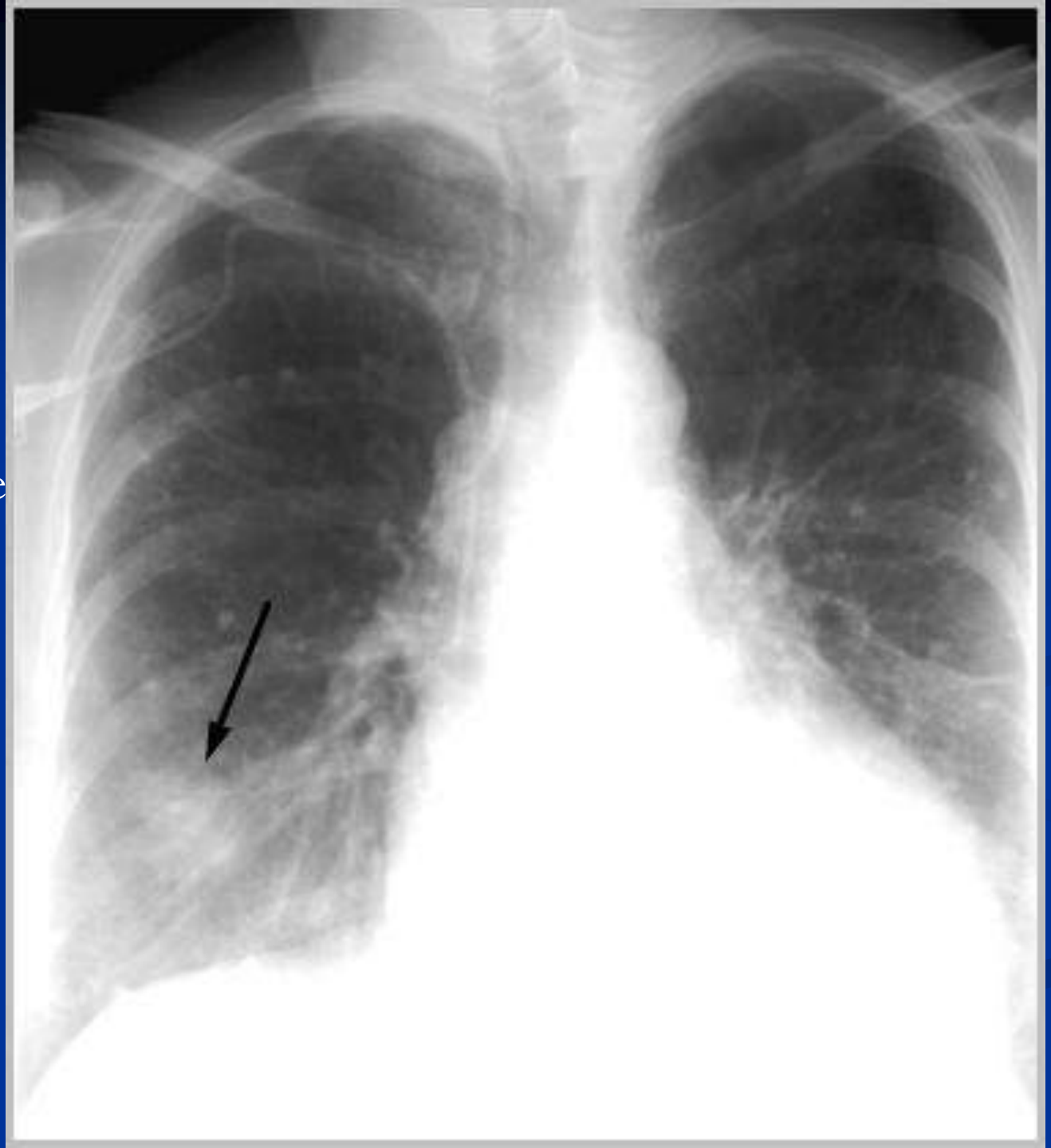
- **CXR**
  - Usually reveals a non specific abnormality.
  - Classic abnormalities include:
    - Westermark's Sign - focal oligemia
    - Hampton's Hump - wedge shaped density
      Enlarged Right Descending Pulmonary Artery


Hamptons Hump

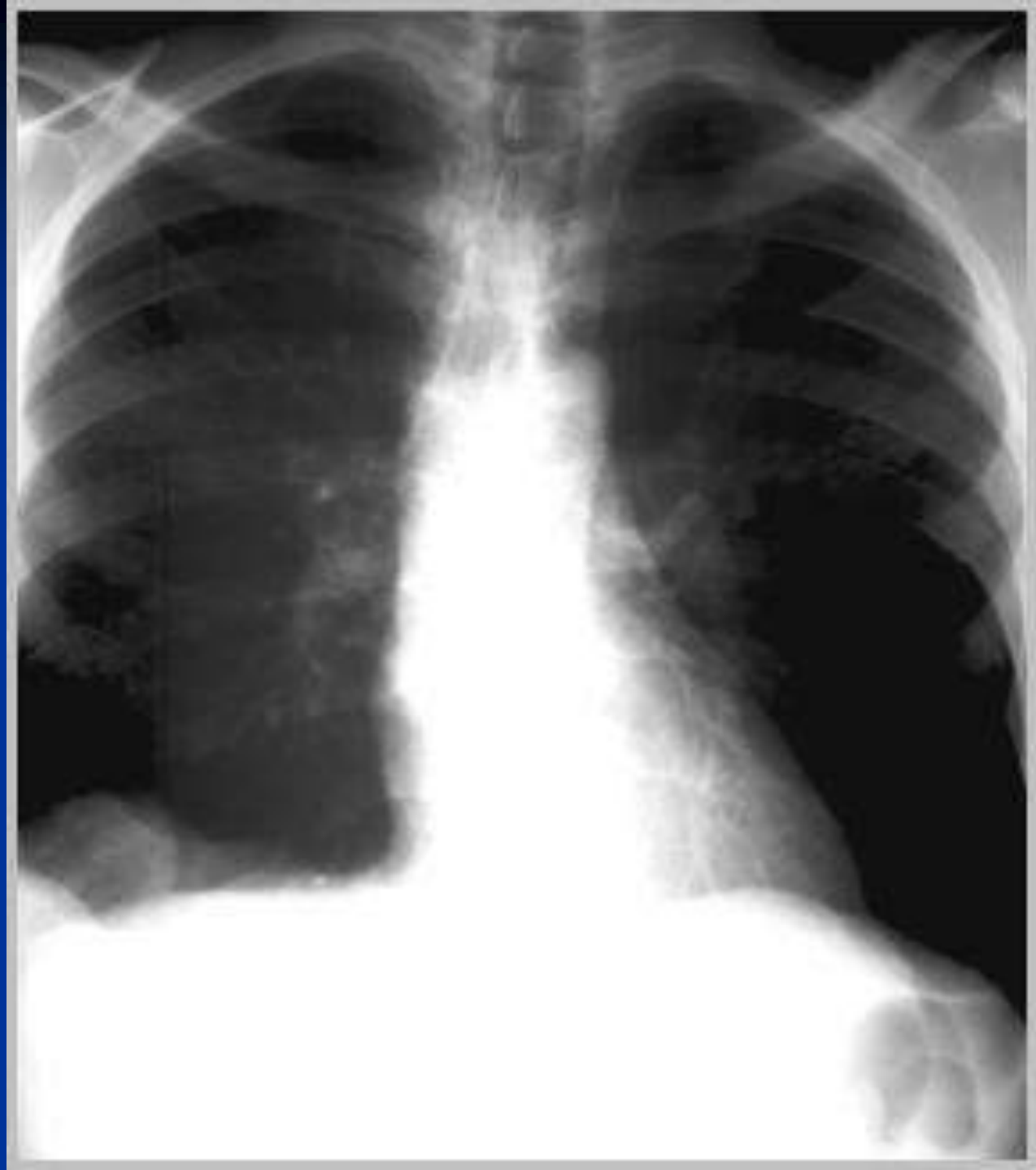
Westermark's Sign



PE which appears like a mass.



PE with effusion
and elevated diaphragm



Venous Ultrasonography

- About 1/3 of pts will have no imaging evidence of DVT
  - Clot may have already embolized
  - Clot present in the pelvic veins (U/S usually inadequate)

* Work up for PE should continue even if doppler (-) in a pt in whom you have a high clinical suspicion

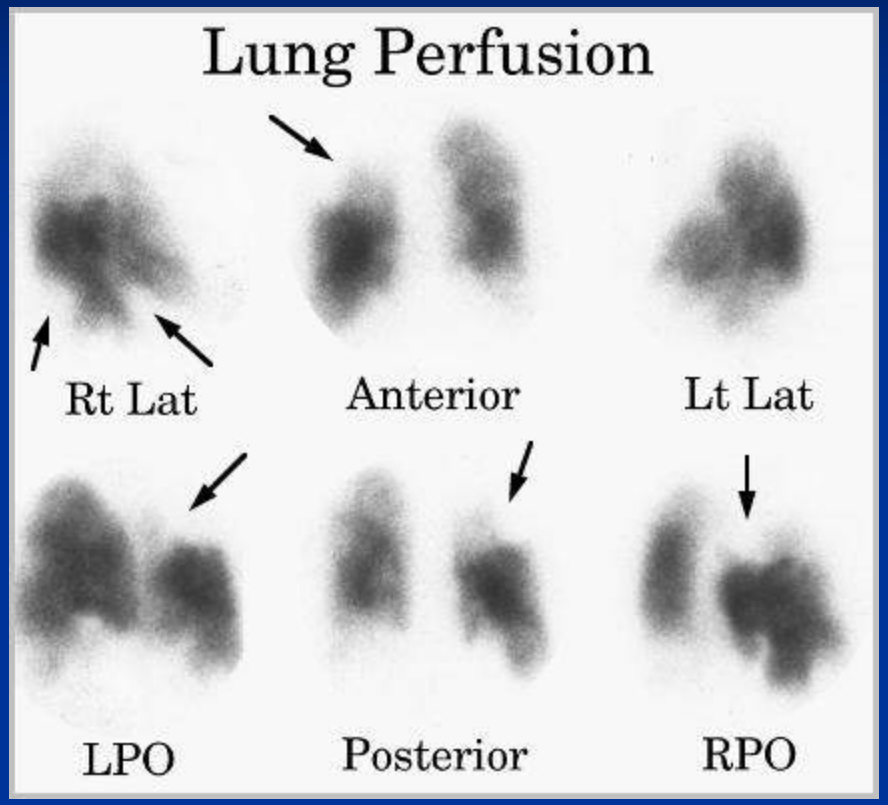
V/Q Scan

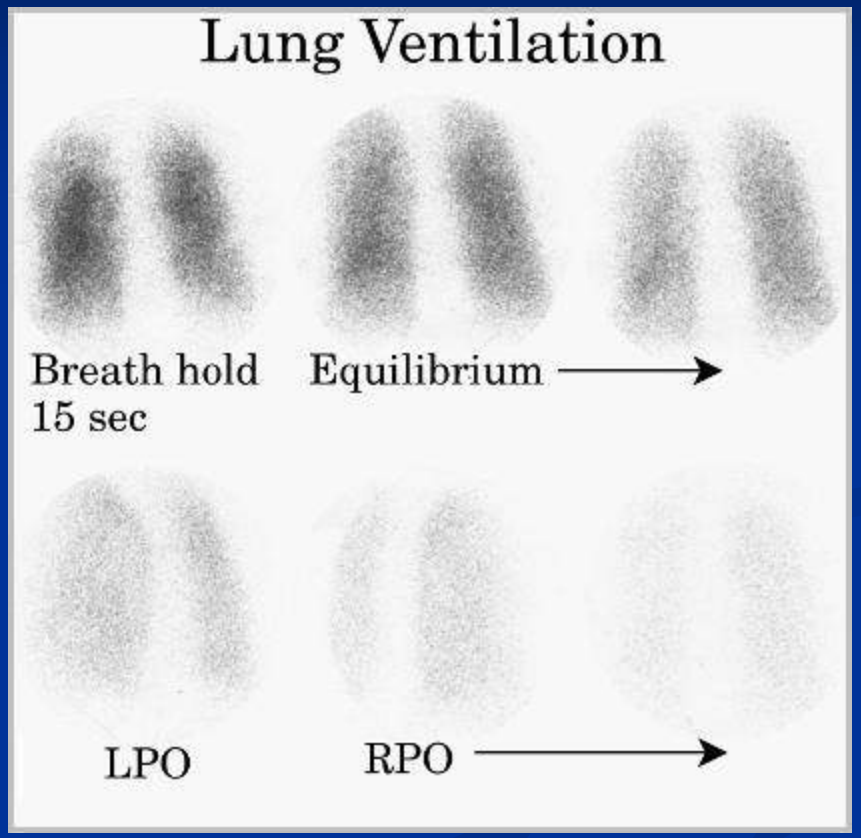
- Historically, the principal imaging test for the diagnosis of PE
  - A perfusion defect indicates absent or decreased blood flow
  - Ventilation scan obtained with radiolabeled gases
  - A high probability scan is defined as two or more segmental perfusion defects in presence of normal ventilation scan

V/Q Scan

- Useful if the results are normal or near normal, or if there is a high probability for PE
  - As many as 40% of pts with high clinical suspicion for PE and low probability scans have a PE on angiogram

High Probability V/Q Scan





Pulmonary Angiogram

- Most specific test available for diagnosis of PE
- Can detect emboli as small as 1-2 mm
- Most useful when the clinical likelihood of PE differs substantially from the lung scan result or when the lung scan is intermediate probability

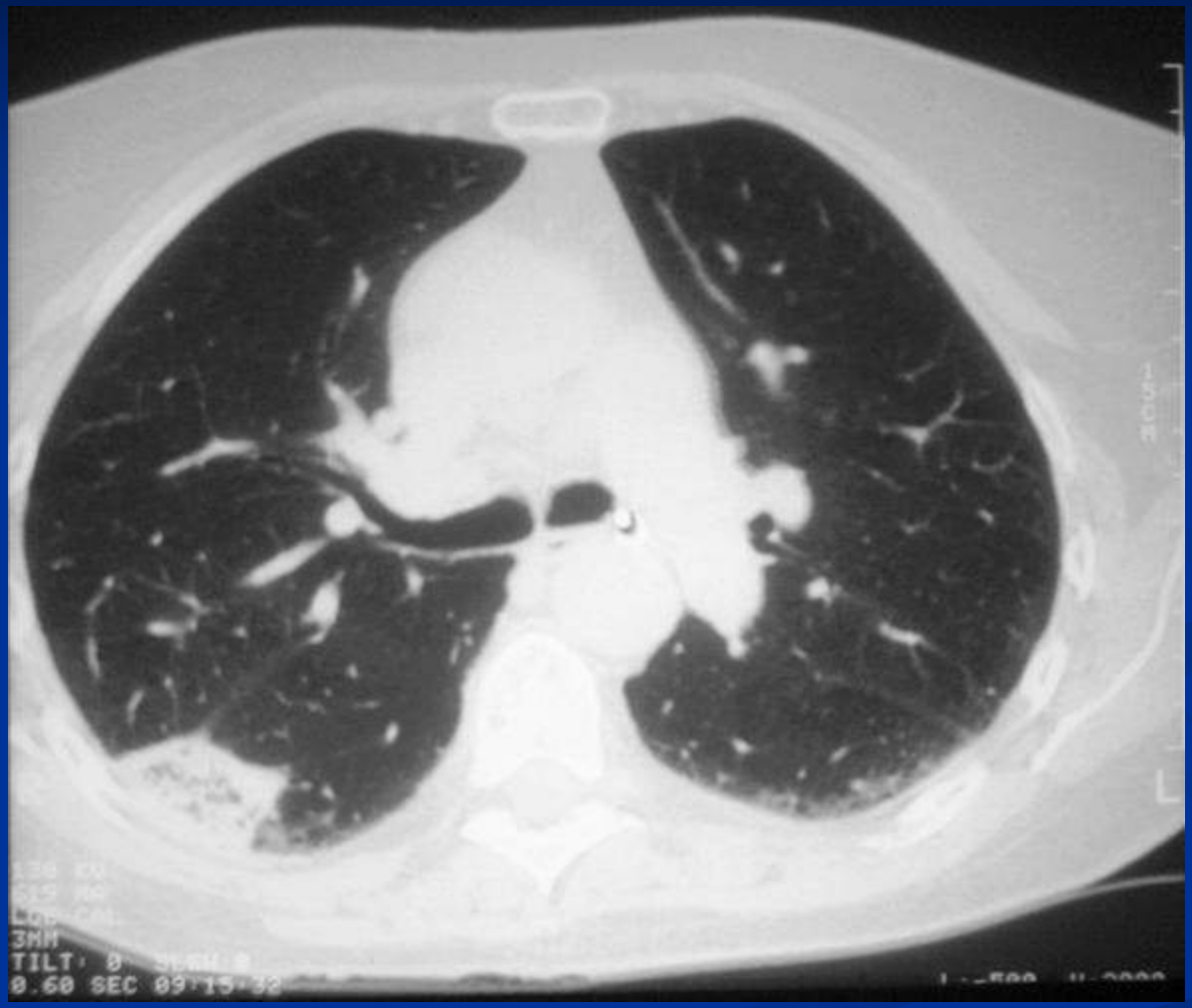
Echocardiogram

- Useful for rapid triage of pts
- Assess right and left ventricular function
- Diagnostic of PE if hemodynamics by echo are consistent with clinical history

Spiral CT Scan

- Identifies proximal PE (which are the ones usually hemodynamically important)
- Not as accurate with peripheral PE

CT revealing pulmonary infarct



Treatment

- **Begin treatment with either unfractionated heparin or LMWH, then switch to warfarin** (Prevents additional thrombus formation and permits endogenous fibrinolytic mechanisms to lyse clot that has already been formed, **Does NOT directly dissolve thrombus that already exists)**

Treatment

- Pain Relief
- Oxygen
- Dobutamine for pts with right heart failure and cardiogenic shock
- Volume loading is not advised because increased right ventricular dilation can lead to further reductions in left ventricular outflow

Treatment

- Thrombolysis

  1. Hemodynamically compromised by PE – definitie indication

  2. Pulmonary hypertension or right ventricular dysfunction detected by echocardiography, pulmonary arterial catheterization, or new ECG evidence of right heart stain. (controversial)

- Embolectomy
  - Reserved for pts at high risk for death and those at risk for recurrent PE despite adequate anticoagulation, contraindication for thrombolytics

Adjunctive Therapy

- **Duration of Anticoagulation**
  - Dependent upon the clinical situation
    - Cancer, and Obesity most likely will need indefinite treatment
    - For other pts with isolated calf vein thrombosis (3 mos), proximal leg DVT (6 mos) and PE (1yr)
- **Inferior Vena Cava Filter**
    - When anticoagulation cannot be undertaken
    - Recurrent thrombosis despite anticoagulation

Conclusion

- PE is often a misdiagnosed clinical disorder.
- Rapid identification and appropriate treatment may often prevent unnecessary morbidity and mortality.

" Live as if you were to die tomorrow , learn as if you were to live forever "

- Gandhi

" Go for it and give your best. Even if the destination is not reached, the knowledge will never be wasted."