Pulmonary Thromboembolism

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OUTLINE

- Understand the historical context of pulmonary emboli
- Comprehend the pathophysiology and know some common risk factors
- Be aware of the clinical features of PE and have a basic understanding of various diagnostic test
- Gain a therapeutic approach to the treatment of PE and discuss a simplified method in the work-up of PE

Definition

- 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

Epidemiology

- A Common disorder and potentially deadly
  - Five million cases of venous thrombosis each year
  - 10% of these will have a PE
  - 10% will die: Untreated mortality rate of 20% - 30%
  - Highest incidence in hospitalized patients
- A hard diagnosis to make
  - Correct diagnosis is made in only 10-30% of cases
  - Up to 60% of autopsies will show some evidence of past PE
  - Plummets to 5% with timely intervention

Emboli origination

- 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 3 months post partum)
- Lower ext injury
- Previous thrombophlebitis
- Coagulopathy
- Venous Stasis
- Prior DVT
- Age > 70
- Prolonged Bed Rest
- Immobilization
- Surgery requiring > 30 minutes general anesthesia
- Orthopedic Surgery
- Stroke

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 a acquired stressor occurs

Impairment in coagulant regulation

- Factor V Leiden mutation
- Protein C deficiency
- Protein S deficiency
- Antithrombin deficiency
- Prothrombin gene mutation A20210
- Anticardiolipin antibodies
- Lupus anticoagulant
- Hyperhomocystinemia

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 Presentation

- The Classic Triad:
  - **Hemoptysis, Dyspnea, Pleuritic Pain**
  - Not very common!
  - Occurs in less than 20% of patients with documented PE
- Three Clinical Presentations
  - Pulmonary Infarction
  - Submassive Embolism
  - Massive Embolism

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
  - Pulmonary Infarction usually indicates a small PE, but is very painful, because it lodges near the innervation of the pleural nerves

Symptoms

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

Presentation is often "atypical"

Signs and symptoms are frequently vague and nonspecific and rarely "classic"

Signs

with Angiographically Proven PE

Sign	Percent
Tachypnea > 20/min	92
Rales	58
Accentuated S2	53
Tachycardia >100/min	44
Fever > 37.8	43
Diaphoresis	36
S3 or S4 gallop	34
Thrombophebitis	32
Lower extremity edema	24

Who do we work up?

- Pretest Probability
- Definition: “The probability of the target disorder (PE) before a diagnostic test result is known”.
- Used to decide how to proceed with diagnostic testing and final disposition

Diagnostic tests

- Laboratory Analysis
  - CBC, ESR, Hgb/Hct,
  - D-Dimer
  - ABG's
- Imaging Studies
  - CXR
  - V/Q Scans
  - Spiral Chest CT
  - Pulmonary Angiography
  - Echocardiograpy
- Ancillary Testing
  - EKG
  - Pulse Oximetry

D-dimer

- Fibrin split product
- Reflects breakdown of plasmin and endogenous thrombolysis
- Elevated in more than 90% of pts with PE
- Not specific: Can also be elevated in MI, sepsis, or almost any systemic illness (False Positives)
- Negative predictive value: 93-100%

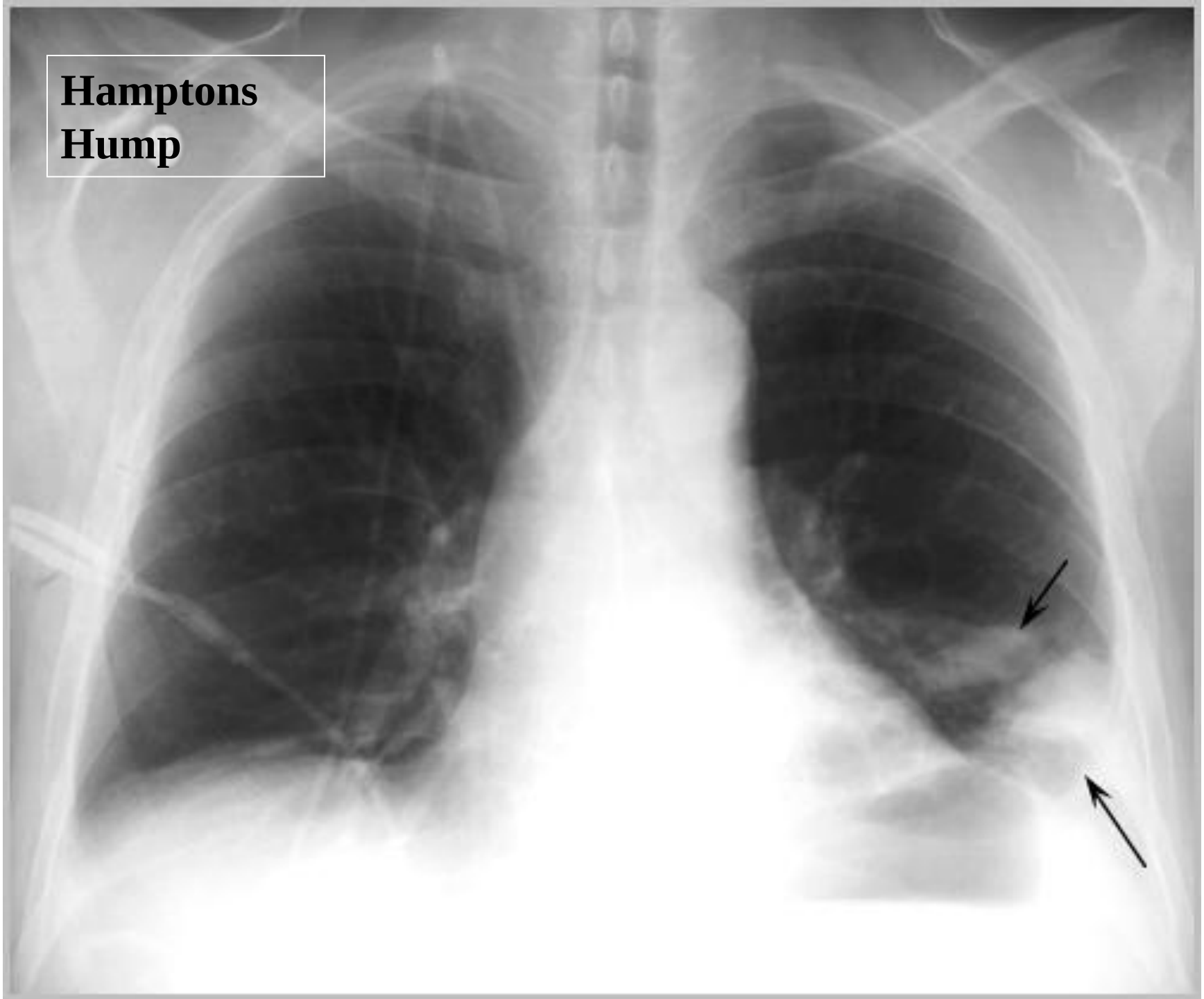
ABG/Pulse Oximetry

- Arterial blood gases lack diagnostic utility for PE

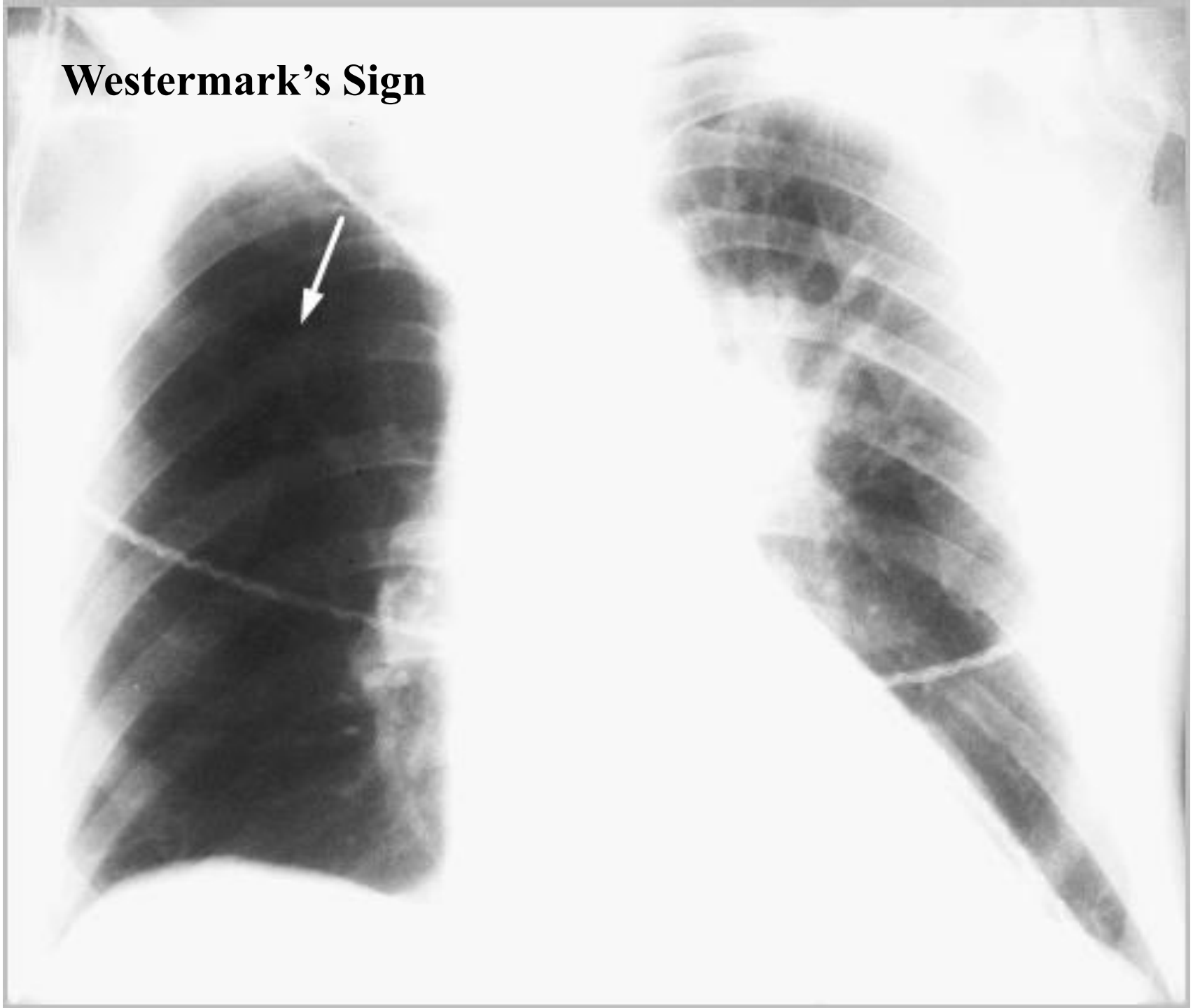
- A-a Gradient
  - Alveolar arterial oxygen gradient
  - A better measure of gas exchange than the pO2
  - 148-1.2(PaCO2) - PaO2
  - Gradient > 15-20 is considered abnormal.
  - Done at Room air
  - Nonspecific and insensitive in ruling out PE

CXR

- Usually reveals a non specific abnormality
  - Nonspecific and insensitive
  - 14% normal
- Classic abnormalities include:
  - Westermark's Sign - focal oligemia
  - Hampton's Hump - wedge shaped density
  - Enlarged Right Descending Pulmonary Artery (Palla's sign)


Hamptons
Hump

Westermark's Sign

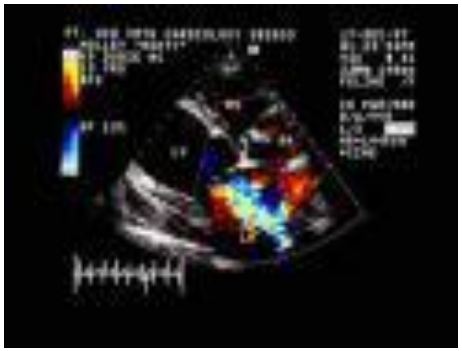


Venous Ultrasonography

- Relies on loss of vein compressibility as the primary criterion
- 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)
  - Workup for PE should continue even if dopplers (-) in a pt in which you have a high clinical suspicion

Echocardiography

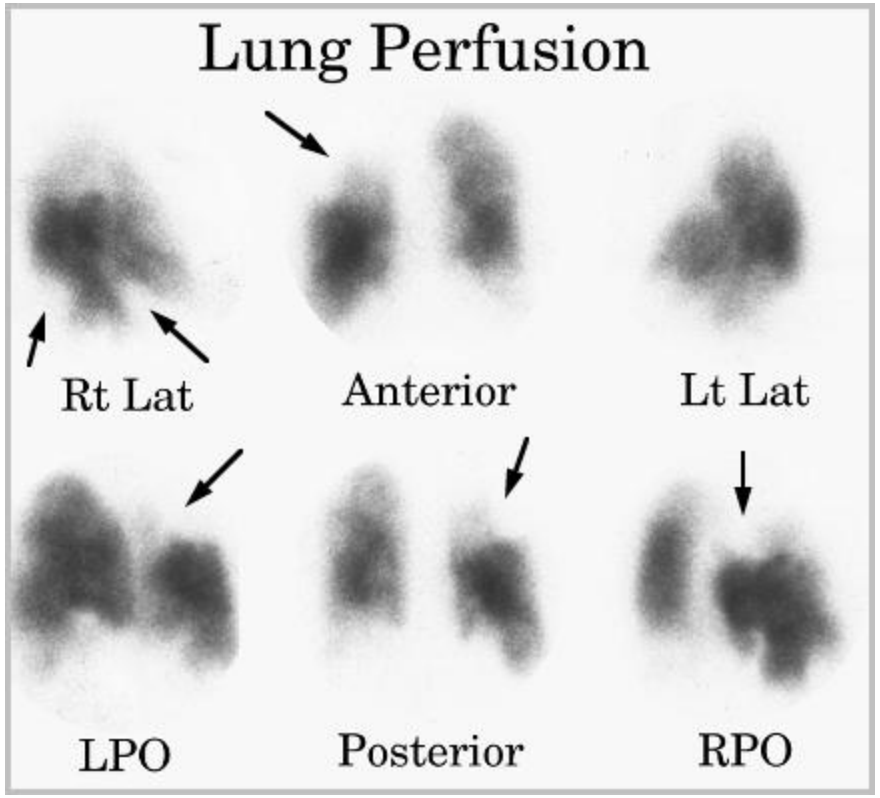
- Consider in every patient with a documented pulmonary embolism
  - EKG maybe helpful in demonstrating right heart strain
- Early fibrinolysis can reduce mortality 50%!

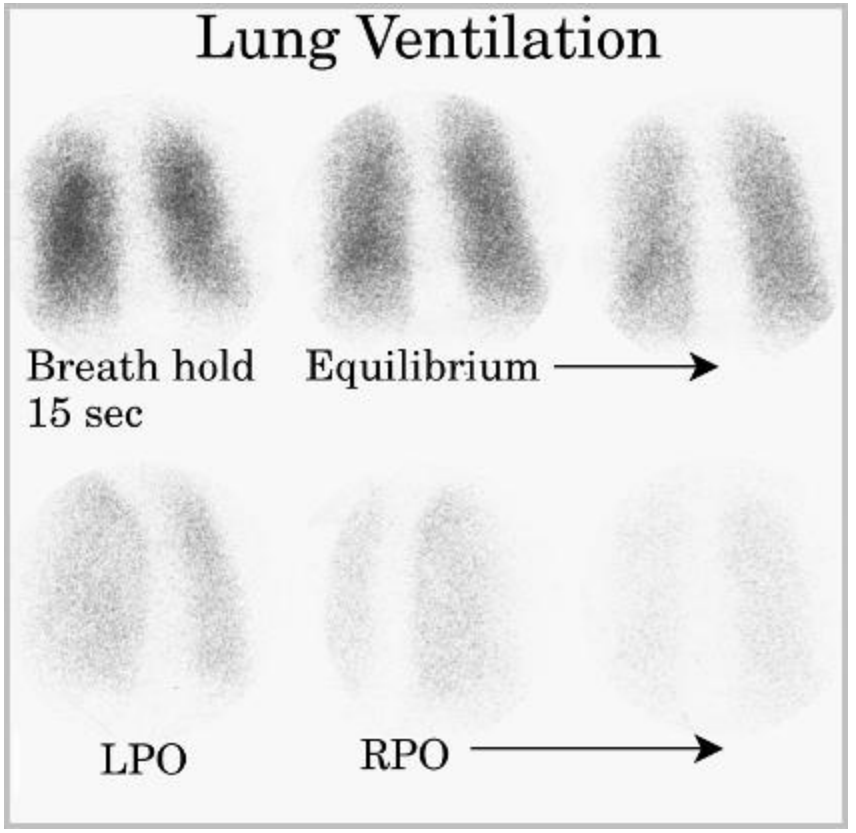


V/Q Scan

- 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 nl ventilation scan
- Relatively noninvasive and preferred in pregnancy
- sadly most often nondiagnostic
- Interpretation of results:
  - High probability → Treat for PE
  - Normal Scan → If low pre-test, your done
  - Everything else → Purse another study (CT, Angio)

High Probability V/Q Scan





Pulmonary Angiogram

- “Gold Standard”
- Most specific test available for diagnosis of PE
- Can detect emboli as small as 1-2 mm
- Positive result is a “cutoff” of flow or intraluminal filling defect

- “Court of Last Resort”

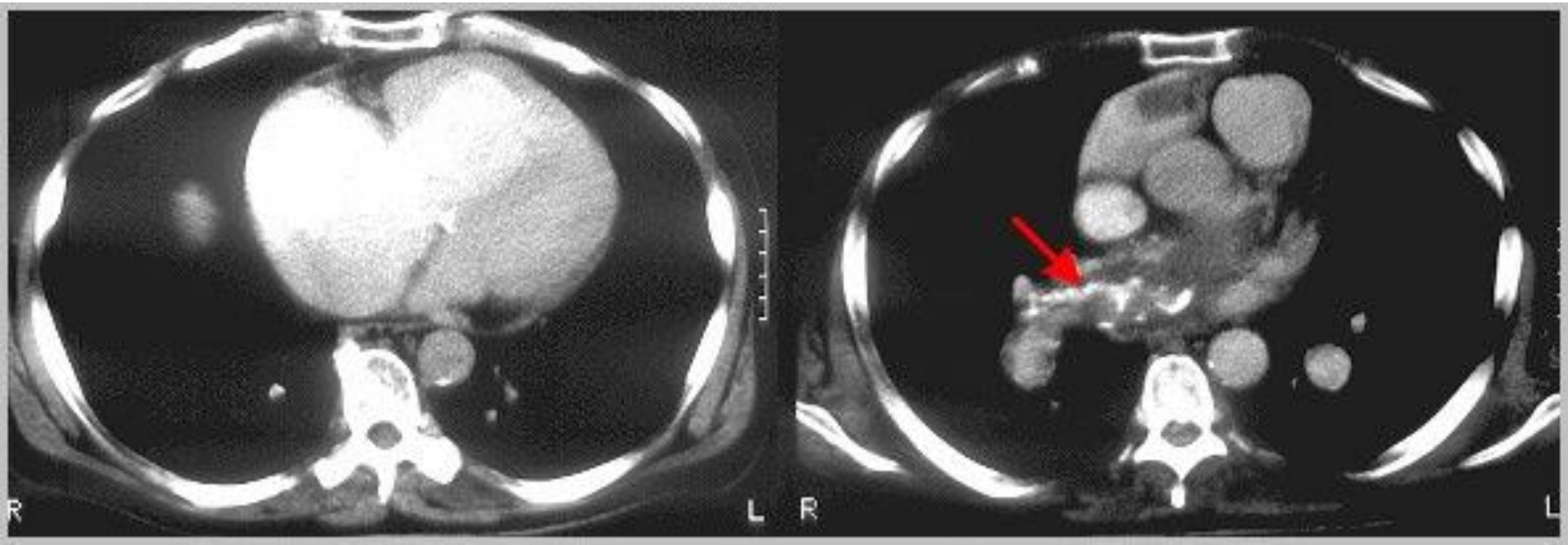
Echocardiogram

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

- Most Common Findings:
  - Tachycardia or nonspecific ST/T-wave changes
- Acute cor pulmonale or right strain patterns
  - Tall peaked T-waves in lead II (P pulmonale)
  - Right axis deviation
  - RBBB
  - S1-Q3-T3 (occurs in only 20% of PE patients)

CT Scan

- Noninvasive and Rapid
- Risk to patients with borderline renal function
- Identifies proximal PE--Hard to detect subsegmental pulmonary emboli
- CTPA: currently gold standard and initial test of choice



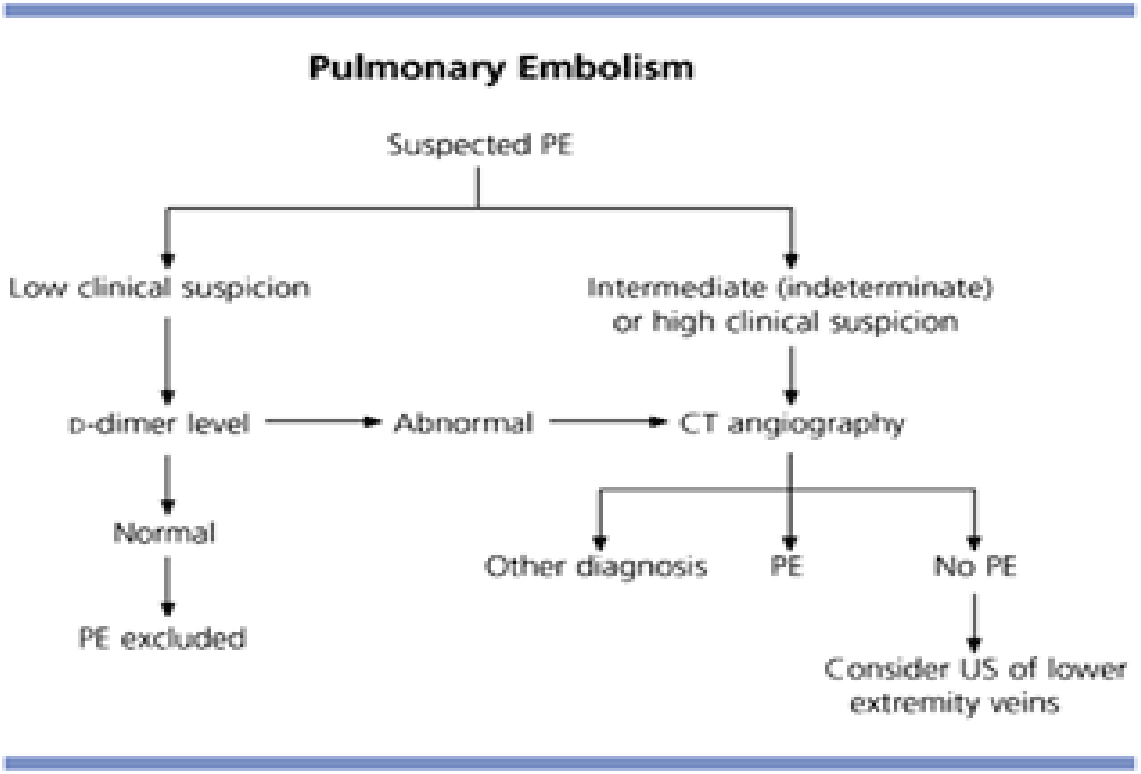
Diagnosis

- 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
  - Dyspnea, syncope, hypotension, or cyanosis suggest a massive PE
  - Pleuritic CP, cough, or hemoptysis

A Simplified Algorithm

- Pre-test probability
- D-dimer (VIDAS-DD)
- CT angiography

Low Pre-test, D-dimer (-), patient had < 1.7% 90 day PE occurrence in a Mayo Clinic Study



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

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**
  - **Dosing**
    - Unfractionated: 80 units/kg bolus, 18 units/kg/hr
    - LMWH: 1 mg/kg Q 12 or 1.5mg/kg Q D
- Warfarin for at least 3 months, INR 2-3

Treatment

- Pain Relief
- Supplemental 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
  - Hemodynamically compromised by PE – definitie indication
  - Pulmonary hypertension or right ventricular dysfunction detected by echocardiography, pulmonary arterial catheterization, or new electrocardiographic evidence of right heart strain. (controversial)
- Embolectomy
  - Reserved for pts at high risk for death and those at risk for recurrent PE despite adequate anticoagulation, contraindication for thrombolytics
  - Carries a 40% operative mortality;Alternative is Transvenous Catheter Embolectomy

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 (1 year)
- Inferior Vena Caval Filter
    - When anticoagulation cannot be undertaken
    - Recurrent thrombosis despite anticoagulation

Summary

- PE is a potentially deadly and common event which may present in various ways.
- Rapid identification and appropriate treatment may often prevent unnecessary morbidity and mortality.
- Consider PE in any patient with an unexplainable cause of dyspnea, pleuritic chest pain, or findings of tachycardia, tachpnea, or hypoxemia.
- Qualitative D-Dimers have NPV of 93-99%.
- Heparin remains the mainstay of therapy with the initiation of Warfarin to follow.
- Simplified Algorithm: (Pretest probability, D-Dimer, +/- CT angio), then disposition.

Questions

- What are the risk factors for PE?
- Please describe the definition and the key points of the diagnosis of acute PE.
- What is massive PE and the principle for the treatment?
- Please describe the anticoagulation therapy and the follow-up plan.

Further readings

- Samuel Z. Goldhaber. 256 Deep Venous Thrombosis and Pulmonary Thromboembolism. In: 17th Harrison's Principle of Internal Medicine. PP 1651-1657.
- Agnelli G, Becattini C. Acute pulmonary embolism. N Engl J Med 2010;363(3):266-74.
- Spurzem JR, Geraci SA. Outpatient management of patients following pulmonary embolism. Am J Med 2010;123(11):987-90.

Thank you !

Questions are welcome ☺

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Estimation of Pretest Clinical Probability of Pulmonary Embolism
Pretest Clinical Probability Clinical Findings

- **Low-probability**
  (unlikely)1. Symptoms incompatible with pulmonary embolism or compatible symptoms (see below; high-probability section) that can be explained by an alternative process, such as pneumonia, pneumothorax, or pulmonary edema
  2. No radiographic or electrocardiographic 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 electrocardiographic 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 electrocardiographic findings compatible with pulmonary embolism, or widened alveolar-arterial oxygen gradient, not explained otherwise
  3. Presence of risk factors for venous thromboembolism