Pulmonary Vascular Diseases

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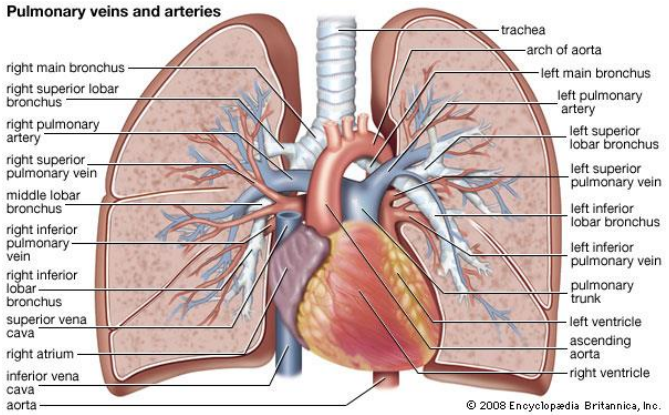
Pulmonary Circulatuion

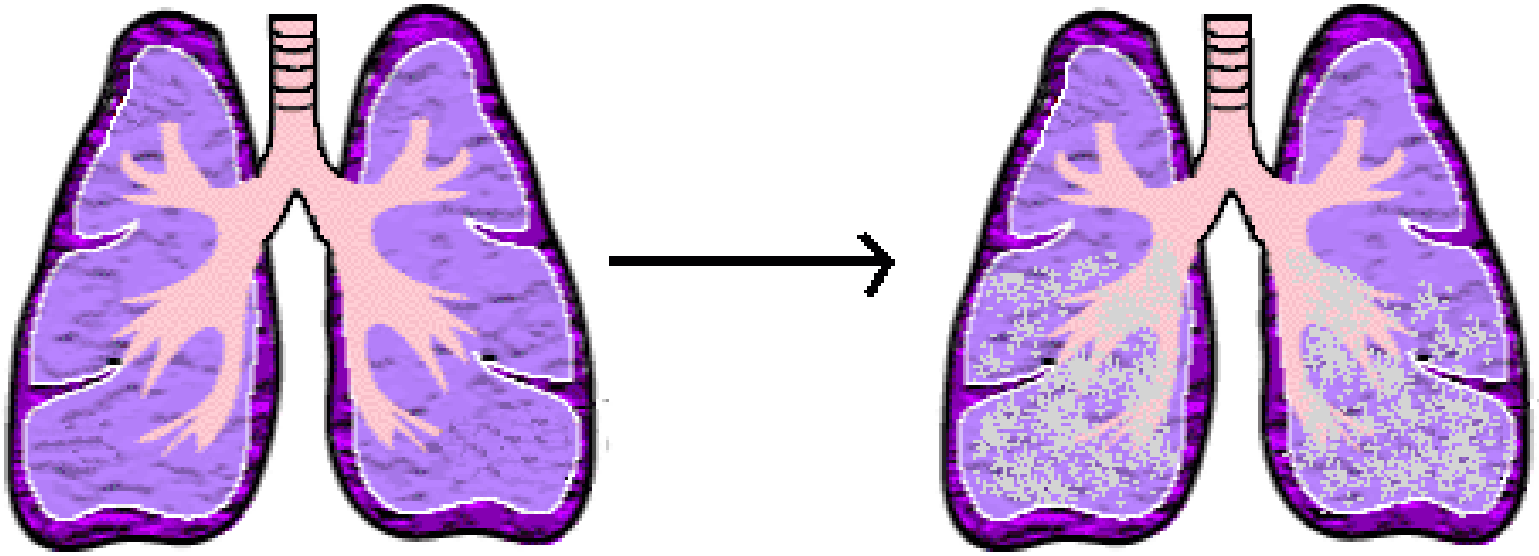
- Dual supply
  - Pulmonary arteries
  - Bronchial arteries
- Low pressure system
- Pulmonary artery receives entire cardiac output (a filter)



Low pressure system….

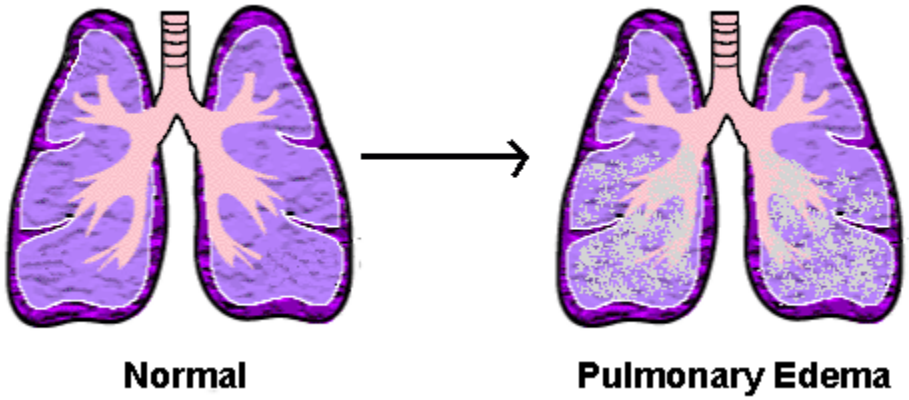
- Thin walled vessels
- Low incidence of atherosclerosis

Pulmonary oedema



Pulmonary Oedema

- Accumulation of fluid in the lung
  - Interstitium
  - Alveolar spaces
- Causes a restrictive pattern of disease



Pulmonary Oedema (causes)

1. Haemodynamic (↑ hydrostatic pressure)
2. Due to cellular injury
   i. Alveolar lining cells
   ii. Alveolar endothelium

   Localised – pneumonia

   Generalised – adult respiratory distress syndrome (ARDS)

Increased pulmonary venous pressure

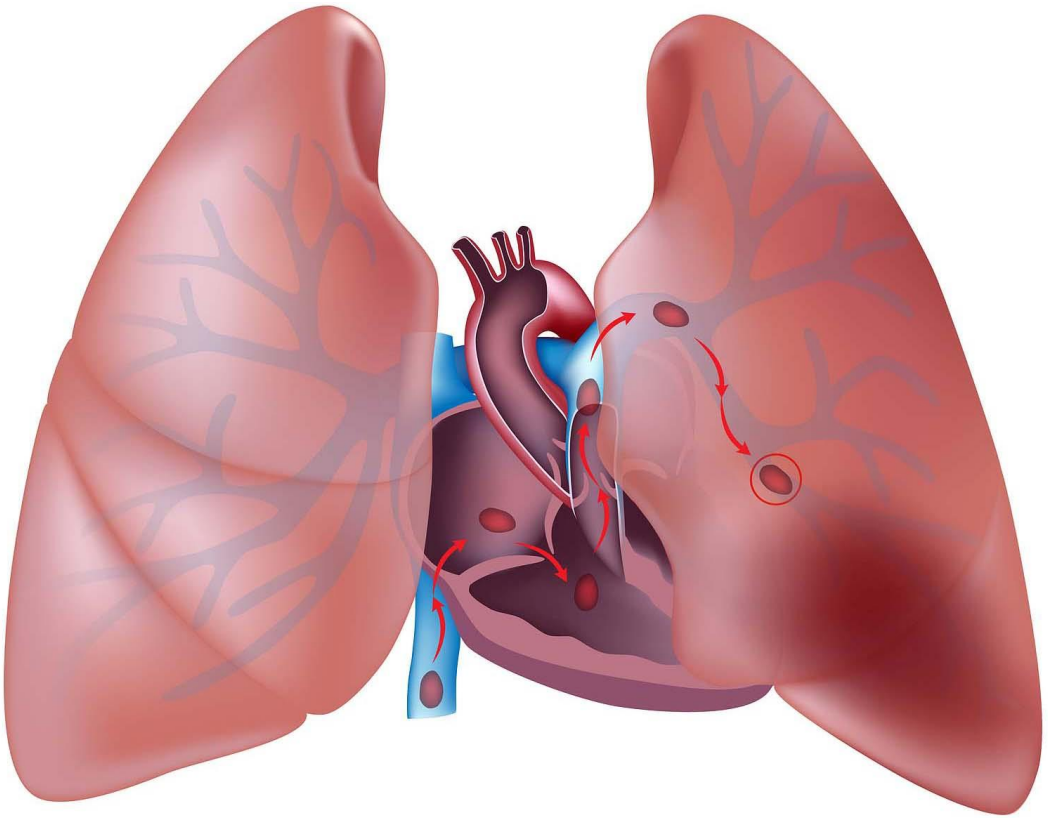
- Left ventricular failure
- Mitral stenosis
- Mitral incompetence

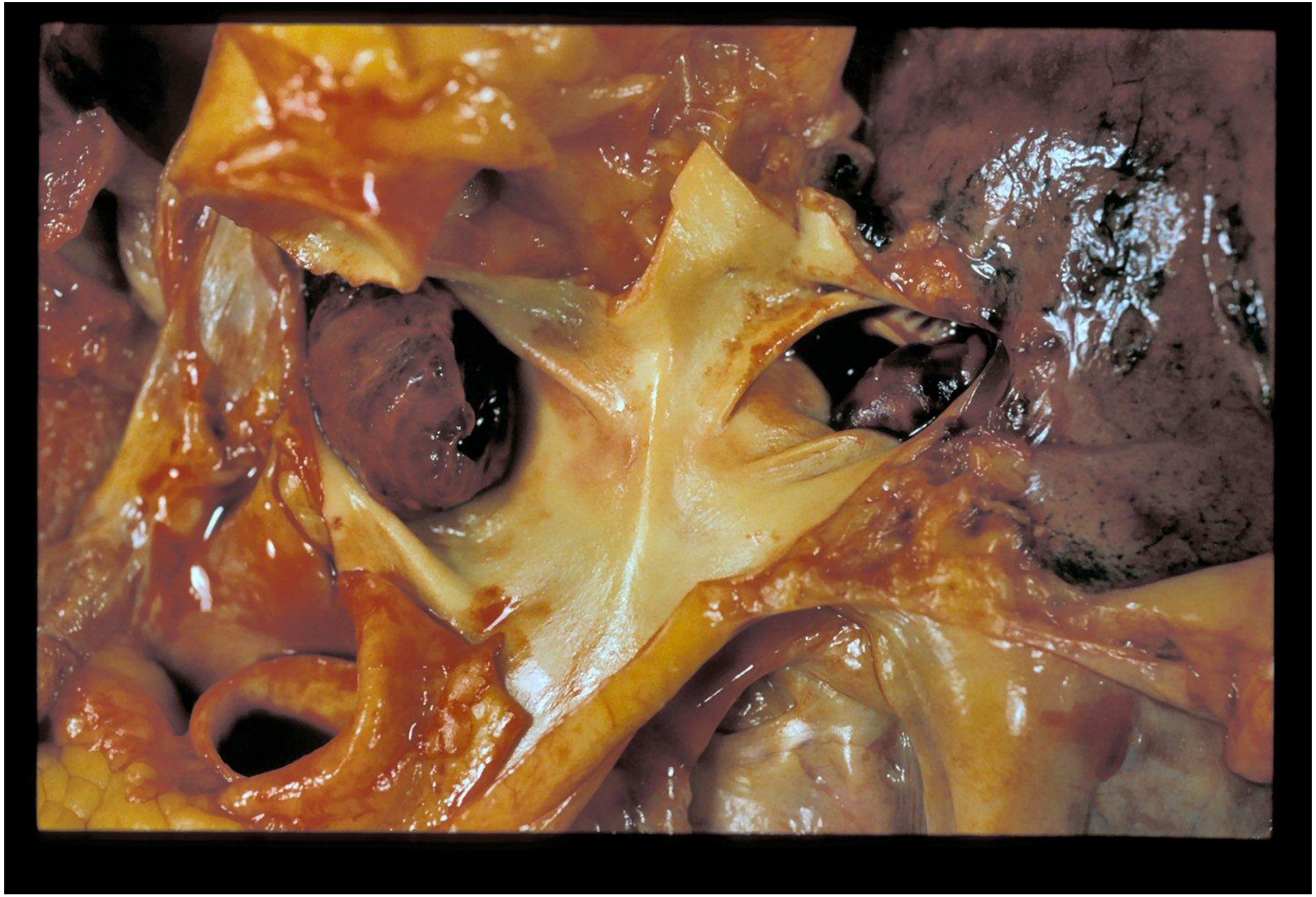
Increased P. venous pressure forces fluid into interstitial space. Initially compensated by lymphatic drainage

Development of pulmonary oedema

- Fluid builds up first in interstitial space “stiff lung”
- Eventually gets into alveolar space

Pulmonary embolism





Pulmonary Embolism

- More common than one would think
- Almost ¾ of all deaths from PE; not suspected of PE prior to death.
- Reported 10-15% mortality rate among hospitalized patients
- Often under-diagnosed

Pulmonary Embolism

- 70% of patients with confirmed PE have DVT
- 40% of patients with DVT have silent PE
- DVT limited to calf veins (distal DVT) seldom results in clinically obvious PE

Risk

- ~6.5% of patients have DVT on admission to ICU
- further 20-30% develop DVT during ICU stay
- risk highest amongst patients who have suffered major trauma (40-70%) and spinal cord injury (60-80%)

Patients with high risk for PE

- Elderly
- Multiple injuries
- Immobilization
- Prolonged bed-rest
- Intra vascular catheters

How/Why do Thrombi form?

- Blood stasis
- Hyper-coagulable states
- Vessel wall abnormalities

Mechanism of risk

- Changes in blood flow
  - venous stasis
    - immobilization
    - raised CVP
    - valvular damage due to previous thromboembolic disease

Mechanism of risk

- Changes in properties of blood
  - increased coagulation and/or platelet activity eg lupus anticoagulant
  - decrease in physiological anticoagulants and/or fibrinolytic activity common in critically ill patients
    - antithrombin III, protein S and protein C deficiencies
    - acquired activated protein C resistance
    - high levels plasminogen activator inhibitor

Mechanism of risk

- Changes in vessel wall
  - endothelial damage triggers coagulation
    - trauma
    - central venous catheters

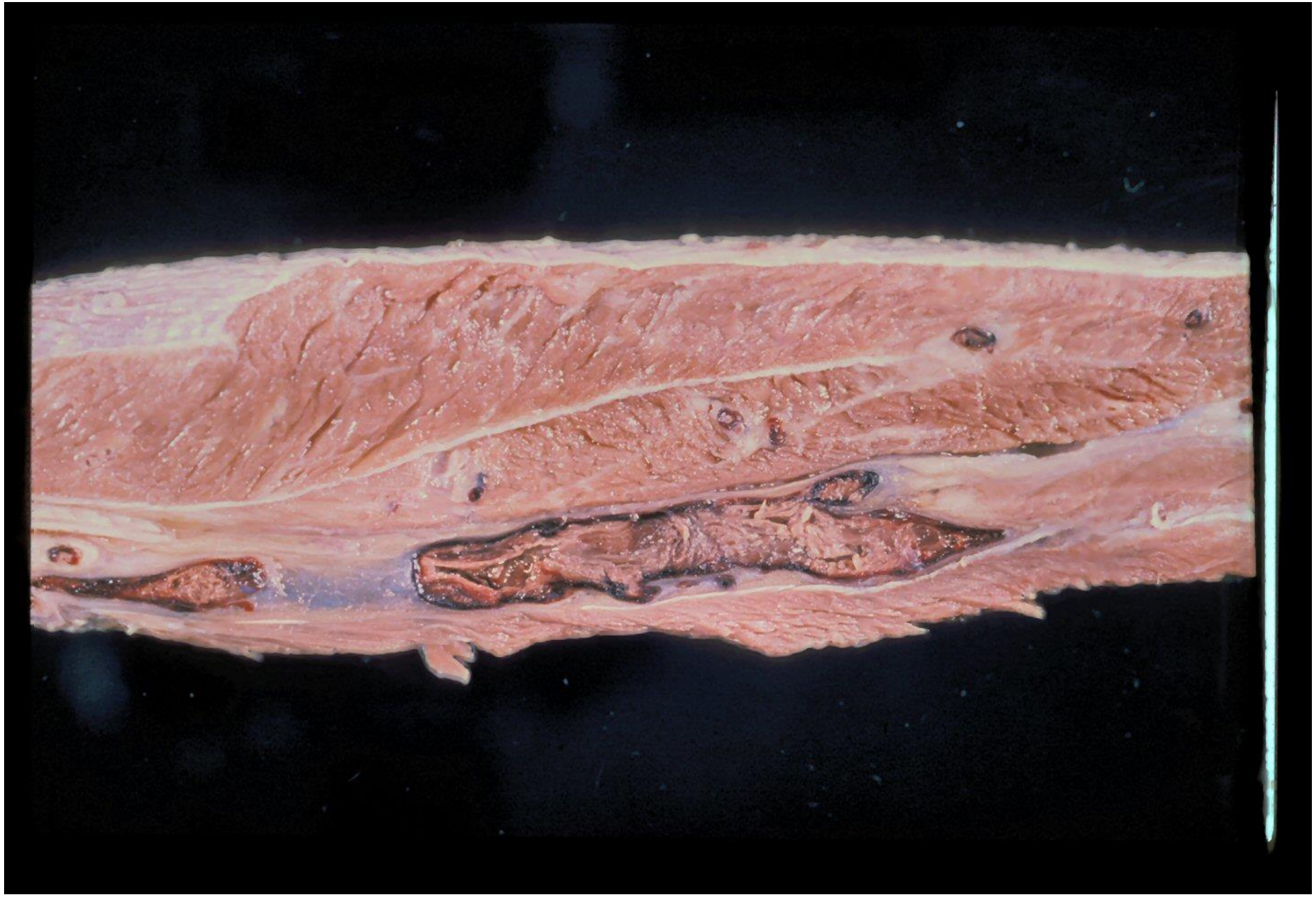
Predisposing factors

- LONG HAUL AIR TRAVEL
- OBESITY
- SMOKING
- OCP
- PREGNANCY
- HRT
- SURGERY

- TRAUMA
- MEDICAL CONDITIONS
  - ANTIPHOSPHOLIPID ANTIBODY SYNDROME
  - CANCER
  - SAH
  - COPD
- THROMBOPHILIA
  - FACTOR V LEIDEN
  - PT GENE MUTATION

Where do Emboli originate?

- Detached portions of venous thrombi that form in:
  - Deep veins of the lower extremities or pelvis
  - Right heart chamber
  - Superior vena cava



Where do emboli end up?

- R > L
- Lower lobes
- Pulmonary hemorrhage and infarction to ischemic area rare < 10% and occurs in the bases.
  - Lung has two blood supplies
    - Pulmonary arterial circulation
    - Bronchial circulation

Effects of PE

- Sudden death
- Severe chest pain/dyspnoea/haemoptysis
- Pulmonary infarction
- Pulmonary hypertension

Effects of PE depend on…

- Size of embolus
- Cardiac function
- Respiratory function

Effect of embolus size…

- Large emboli
  - Death
  - Infarction
  - Severe symptoms
- Small emboli
  - Clinically silent
  - Recurrent pulmonary hypertension

What happens when an emboli occurs?

- Systemic hypotension is indicative of increased severity and probably pulmonary hypertension
- Death from massive P.E. is from cardiovascular collapse rather than respiratory failure
- Resolution occurs rapidly with only a small percentage suffering permanent perfusion defects

What happens when an emboli occurs?

- Reduced or total cessation of pulmonary blood flow to the affected distal zone
  - Pulmonary arterial pressure increases
  - Bronchoconstriction
  - Surfactant production decreases- resulting in atelectasis
  - Arterial hypoxemia
    - High and low V/Q mismatch, intrapulmonary shunting, cardiogenic shock.

What happens when an emboli occurs?

- Increased PVR (50% occlusion necessary)
  - Dependant on amount of surface area involved, underlying cardiopulmonary reserve, and neurohormonal response
  - When mean PAP reaches >40 mmHg the RV will fail and collapse occurs

What do we look for clinically?

- No specific symptoms indicate presence of DVT
  - Pain and/or swelling of the extremity is most common.
- Dyspnea – esp. sudden onset
- Pleuritic chest pain
- Cough

What do we look for clinically?

- Apprehension
- Hemoptysis
- Physical findings include tachycardia, tachypnea, rales, and an accentuated pulmonary component of the second heart sound (loudP_2)

WELLS diagnostic scoring system for suspected PE

	points
• clinical s/sx of dvt(minimum of leg swelling and pain on palpation of deep veins	3.0
• alternative dx less likely	3.0
• heart rate > 100/min	1.5
• immobilization or surgery in the previous 4 weeks	1.5
• previous dvt/pe	1.5
• hemoptysis	1.0
• Malignancy (on tx, tx in the past 6 mo., or palliative)	1.0

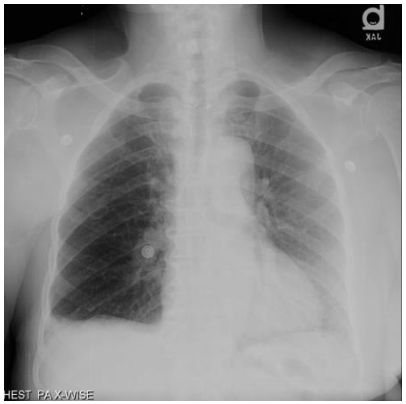
WELLS DIAGNOSTIC SCORING SYSTEM FOR SUSPECTED PE

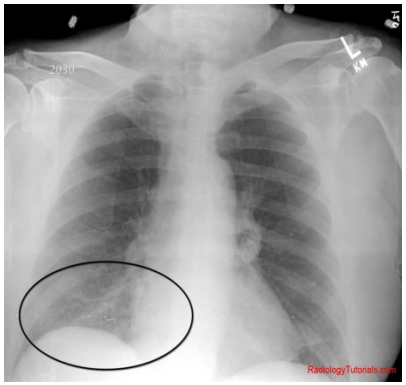
- MAXIMUM OF 12 POINTS
- </= 4 POINTS → 8%

How do we diagnose P.E.

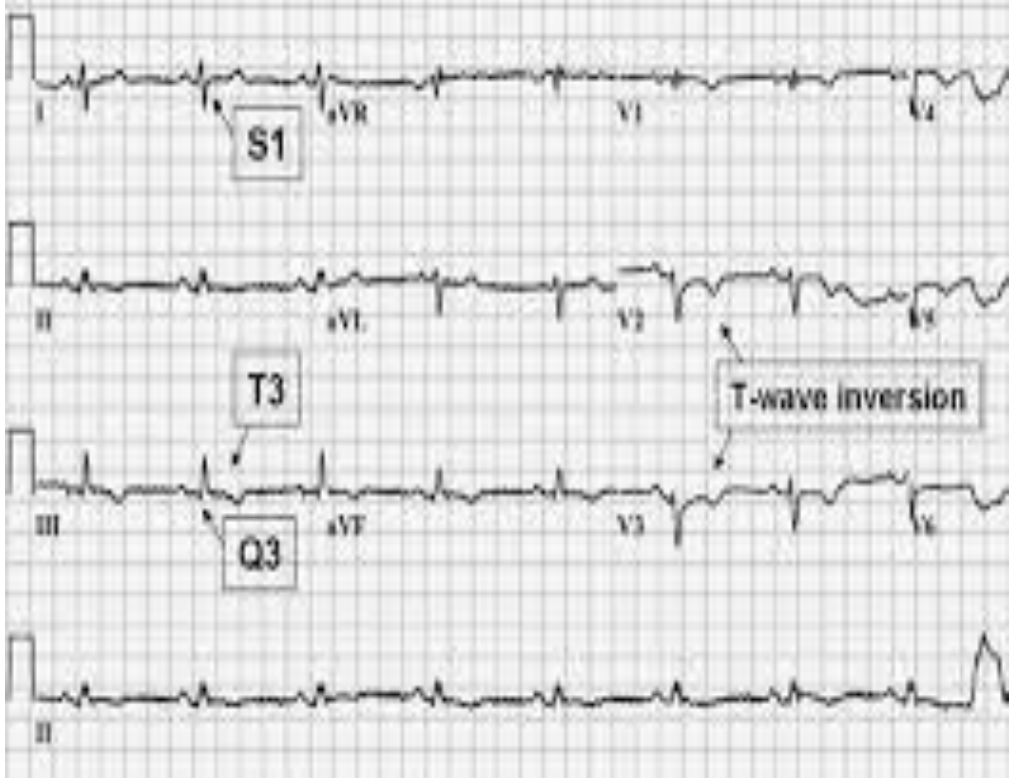
Diagnosis- Chest X ray

- Normal CXR + dyspnea may = P.E.
- CXR abnormal >80%
  - Dilation of the PA
  - RV cardiomegaly
  - Small pleural effusions
  - Increased density – infarcted area
  - Hyperlucency distal to emboli (Westermark sign)
  - Elevation of the diaphragm





ECG changes



- ECG abnormal almost 90% of the time
- Help rule out MI
- Sinus tachycardia
- Atrial arrhythmia
- S1 Q3 T3
- Depressed ST segment

Will an ABG tell us anything?

- Hypoxemia and hypocapnea may be present.
- 15-25% have $PaO_2 > 80$ mmHg and a normal $(A\text{-}a)O_2$.

How do we diagnose DVT?

- Blood test
  - D-dimer ELISA - >500ng/ml in 90%
  - Reflect plasmin's breakdown of fibrin and endogenous thrombolysis
  - Not specific
  - High negative predictive value
  - Elevated in MI, sepsis or any systemic illness

Diagnosis

Diagnostic studies for PE must be interpreted in conjunction with clinical suspicion .

– V/Q scan
– CT Angiography
– Pulmonary Angiography

Diagnosis of PE:

- PE is a very common and potentially life threatening problem.
- The presenting symptoms and signs are nonspecific.
- The clinician needs a high index of suspicion.

Diagnostic Tests: Pulmonary Angiography

- Advantages:
  - The “gold standard”; directly images pulmonary artery very effectively.
  - Allows measurement of pulmonary artery pressures.

- Disadvantages:
  - Invasive
  - Administration of intravenous radiocontrast.
  - Expensive.
  - Operator time/availability/skill.

Because of Disadvantages: Used as Last Resort in Difficult Cases

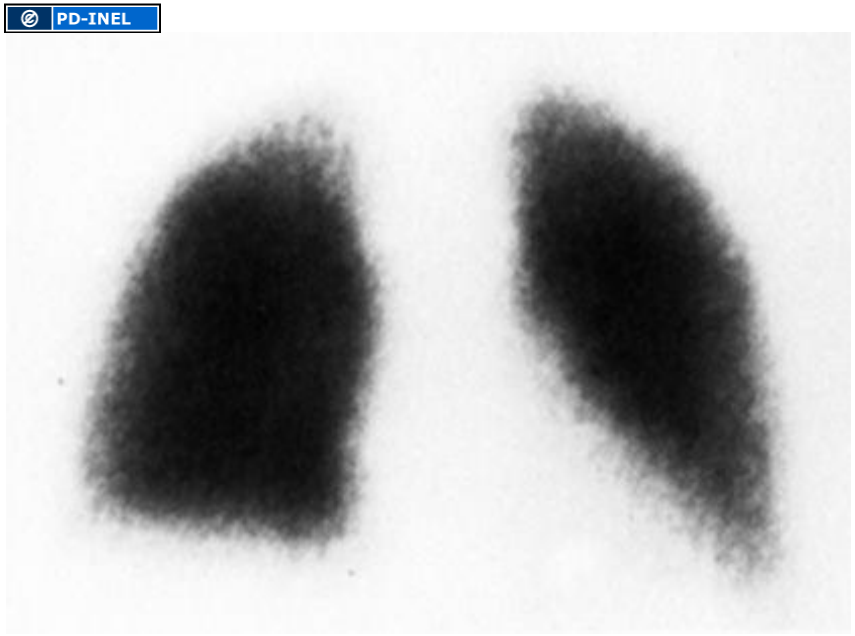
Radionucleotide V/Q Scan

- Perfusion Scanning: Venous injection with radiolabeled-macroaggregated albumin (technetium 99)

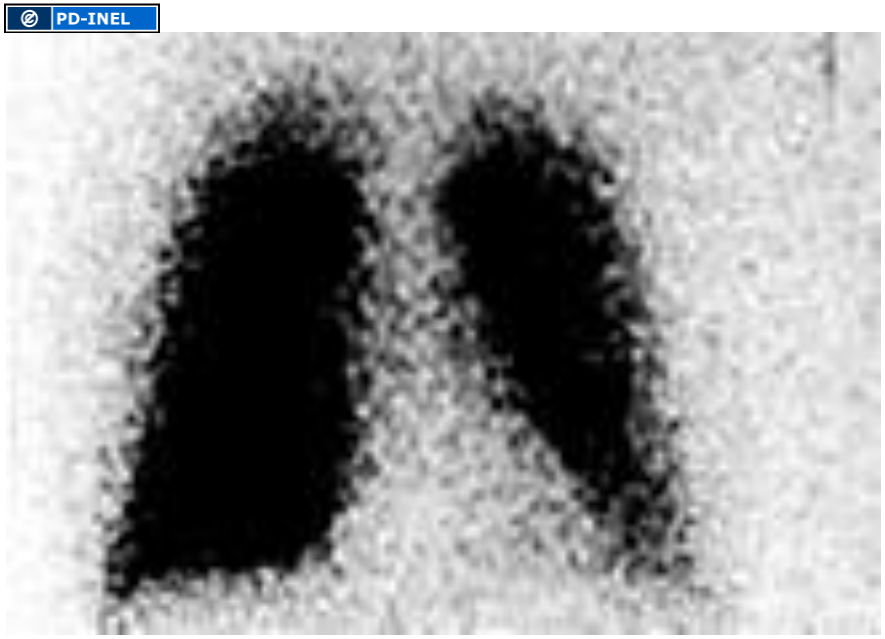
Diagnostic Tests: Radionucleotide V/Q Scan

- Ventilation Scanning: Inhalation of a gas mixture containing a different radiotracer (xenon 133)
  - In PE- areas of vascular obstruction should have loss of perfusion but preservation of ventilation
  - Processes such as pneumonia, COPD, obstructed large airway present as matched ventilation and perfusion defects

Diagnostic Tests: Radionucleotide V/Q Scan

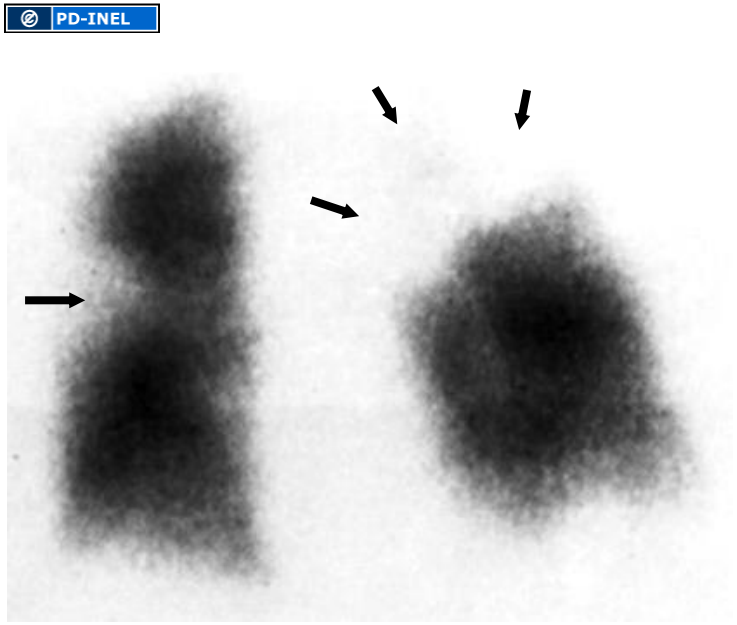


Normal Anterior Perfusion

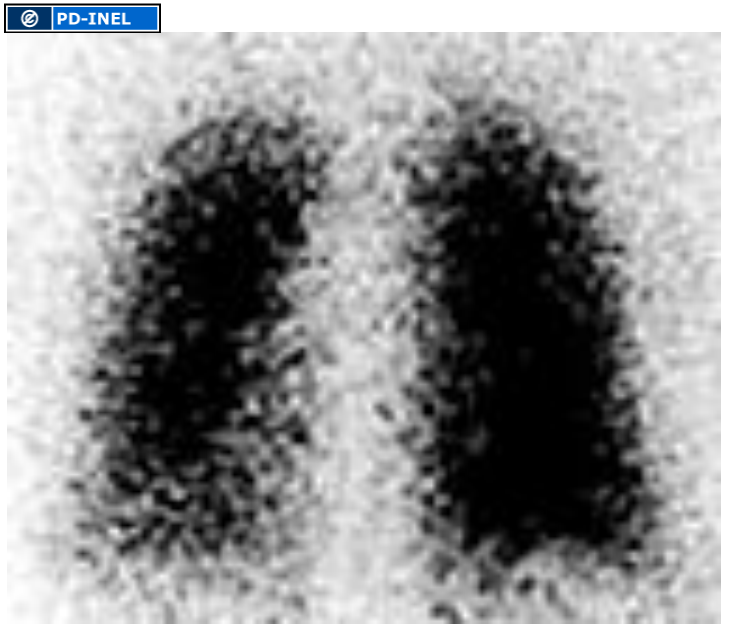


Normal Anterior Ventilation

Diagnostic Tests: Radionucleotide V/Q Scan



Abnormal Posterior Perfusion

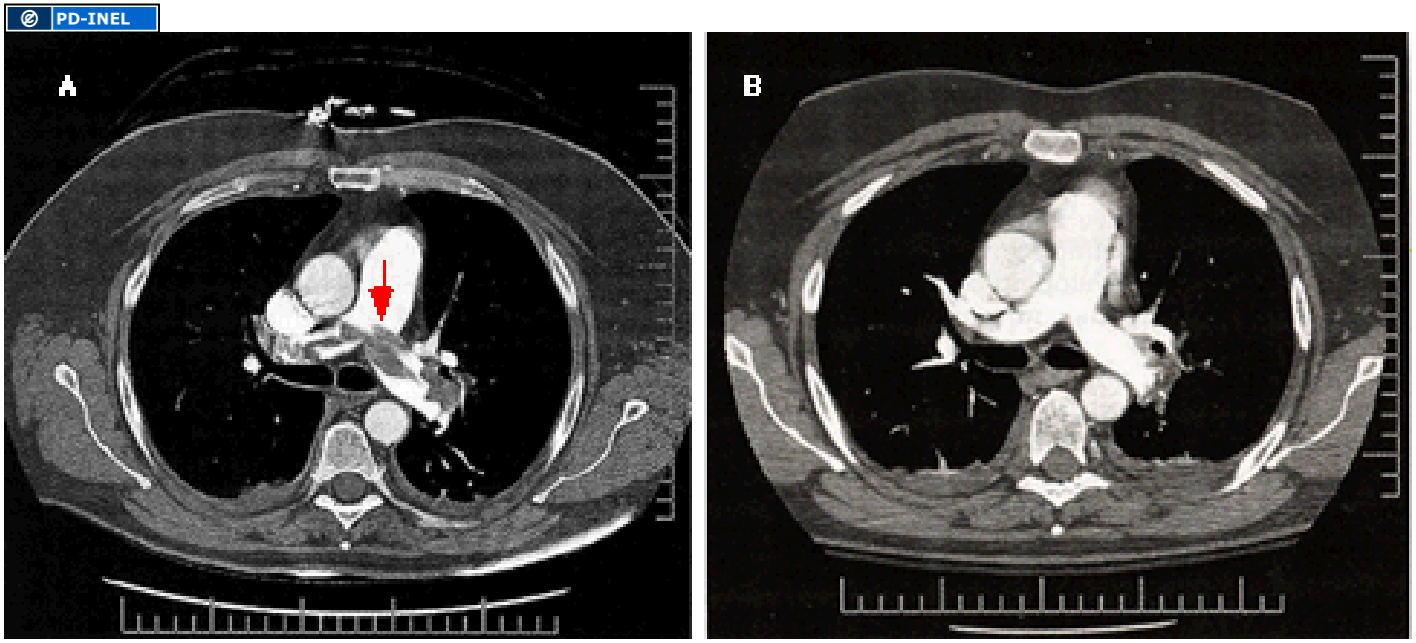


Normal Posterior Ventilation

Diagnostic Tests: CT Angiography

- Bolus radiocontrast injection given intravenously.
- High speed, multi-slice CT scanner takes thin section images.
- Excellent definition of main, lobar, and even segmental pulmonary arteries.
- May provide bonus information about the lungs and mediastinal structures.

Diagnostic Tests: CT Angiography

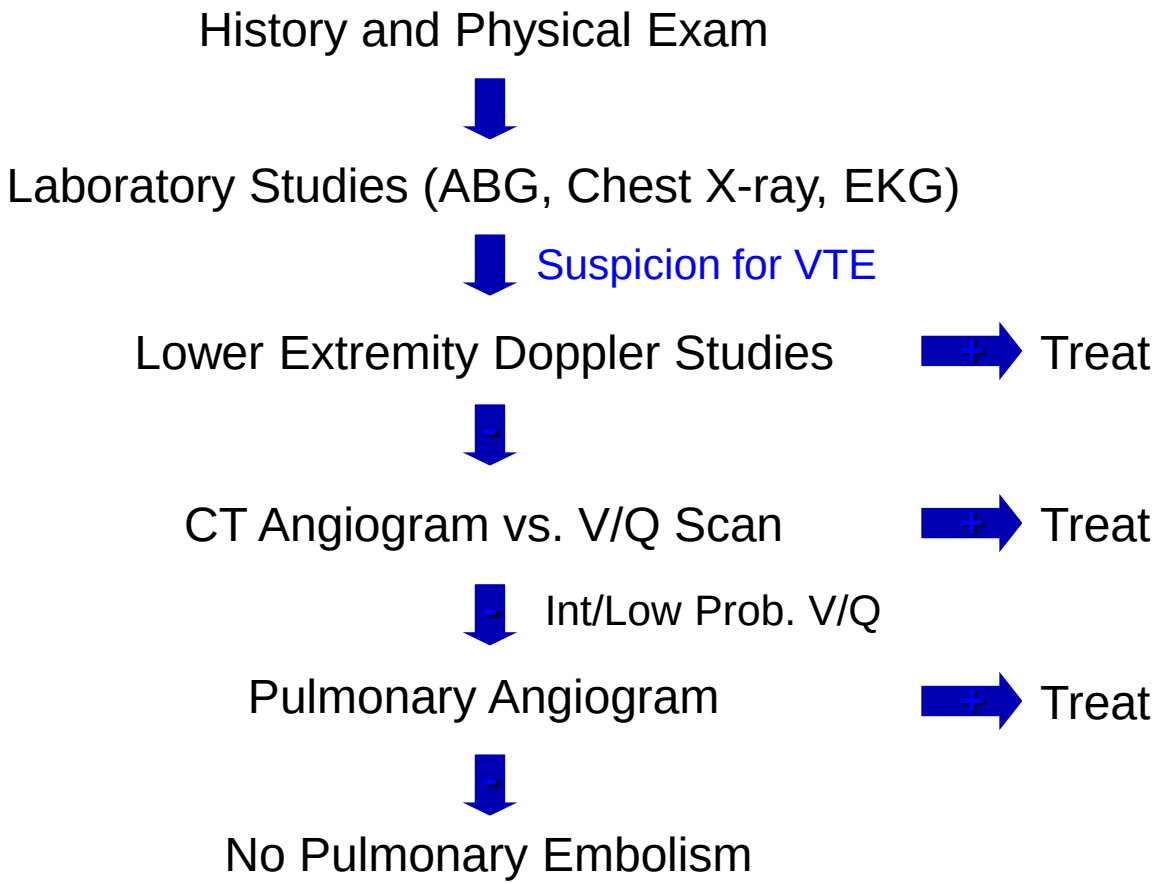


Saddle Embolus

Thrombolysis

Resolution

Diagnostic Algorithm for PE



Prevent PE?

- Most immobile hospitalized patients need prophylaxis for DVT
  - heparin, warfarin, low MW heparin, hepariods, dextran
  - Compression stockings, pneumatic calf compression, electrical calf stimulation.

Heparin & Warfarin

- Heparin – inhibits coagulation, does not lyse existing clots
  - Dose should be titrated to maximize effect without increasing risk from bleeding. (aPTT > 1.5 X control 45 – 70 seconds)
  - Effect needs to be achieved within 48 hours and treatment should last 5-7 days
- Oral warafin should be started within a couple days.

Heparin:

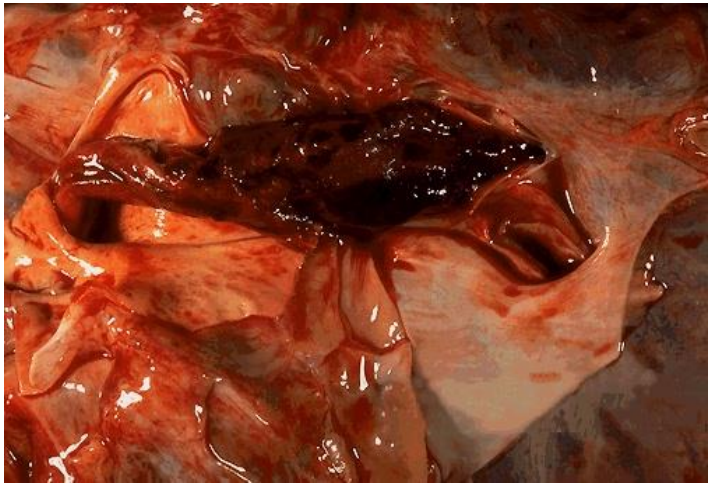
- Unfractionated heparin
  - short half-life: continuous infusion required.
  - variability requiring frequent laboratory studies.

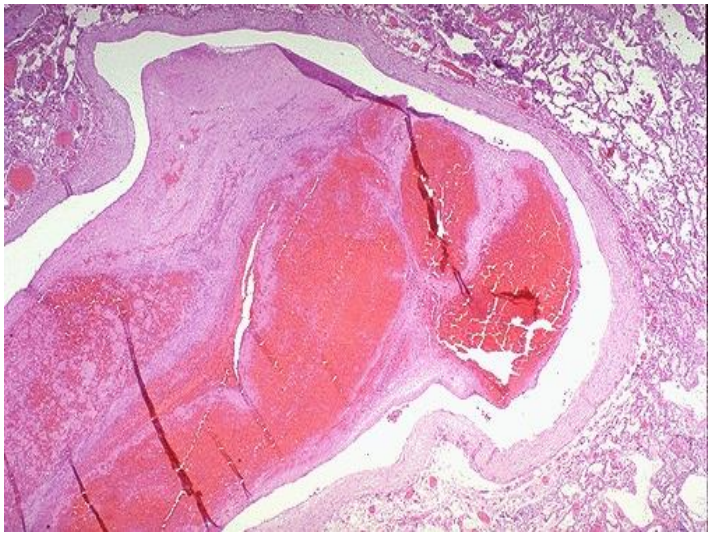
- Low molecular weight heparin-(enoxaparin, dalteparin)
  - longer half-life: twice daily subcutaneous injections.
  - standard dosing; no requirement for frequent lab monitoring.
  - stable patients without great physiologic compromise may be managed at home.

PE Management

- Depends on extent and status of pulmonary system
- Besides pharmacologic therapy, supportive therapy is used as needed.
  - O2 therapy – to treat hypoxemia
  - Fluids and vasopressors for hypotension and shock. (dopamine may reduce PVR and increase CO)
  - Thrombolytic therapy – streptokinase, urokinase, tissue plasminogen activator (TPA), retiplase
  - Embolectomy


cm 1 2 3 4 5





Primary pulmonary hypertension

Primary pulmonary hypertension

- persistent elevation of pulmonary artery pressure w/o any demonstrable cause
- characterized by a mean pap>25 mmHg at rest & > 30 mmHg during exercise
- diagnosis of exclusion

Classification of PHN (WHO)

- PULMONARY ARTERIAL HYPERTENSION
  - IDIOPATHIC PAH
  - FAMILIAL PAH
  - PAH RELATED TO:
    - CONNECTIVE TISSUE DISEASE
    - HIV INFECTION
    - PORTAL HPN
    - DRUGS/TOXIN
    - CONGENITAL HEART DISEASE
  - PERSISTENT PAH OF THE NEWBORN
  - PAH WITH VENULAR/CAPILLLARY INVOLVEMENT

Classification of PHN (who)

- pulmonary hypertension with left heart disease
  - atrial or ventricular
  - valvular
- pulmonary HPN with lung disease/hypoxemia
  - COPD
  - ILD
  - sleep disordered breathing
  - developmental abnormalities

Classification of pulmonary HPN

- pulmonary HPN due to chronic thrombotic or embolic disease
  - thromboembolic obstruction of proximal pulmonary arteries
  - thromboembolic obstruction of distal pulmonary arteries
  - nonthrombotic pulmonary emboli
- miscellaneous

Aetiology

- Passive, active, and reactive (active superimposed on passive)
- Passive" pulmonary hypertension is due to post-pulmonary capillary elevation and is therefore associated with a high PCWP
- Active" is due to the constriction or obstruction of capillary and precapillary vessels resulting in increased resistance to flow

Aetiology

- Passive
  - LVF
  - mitral valve disease
  - congenital cardiac disease (eg cor triatriatum)
  - congenital pulmonary vein stenosis
  - acquired obstruction of major pulmonary veins
  - left atrial myxoma or thrombus

Aetiology

- Active
  - pulmonary embolus
  - Schistosomiasis
  - primary pulmonary hypertension
  - Eisenmenger syndrome
  - disorders of ventilation

Aetiology

- Active

  collagen-vascular disease

  sickle haemaglobinopathies

  portal hypertension

  drugs and herbal remedies

  diffuse pulmonary amyloidosis

  pulmonary vasculitis

Epidemiology

- is more common in females
- familial disease present in 7% of cases
- rare & can occur @ any age
- often misdiagnosed

Pathogenesis of PPH

- develops as a result of abnormal proliferation of vascular smooth muscle cells affecting all 3 layers of vessel wall

- leads to hyperplasia, medial hypertrophy and adventitial proliferation

Pathogenesis OF PPH

- WHAT INITIATES → UNKNOWN
- CLUES
  - GENETIC PREDISPOSITION –
    - *BMPR2* MUTATION
    - $K_V1.5$ CHANNEL DEFECT

Pathogenesis of PPH

- damage to endothelium alters the balance between vasoconstrictive mediators & vasodilators
- resulting in vasoconstriction
- evidence shows this vasoconstriction resolves early & development of irreversible vascular damage progresses

MOST common symptoms

- dyspnea
- angina
- syncope
- cough
- hemoptysis
- hoarseness
- Raynaud’s phenomenon

Most common symptoms

- dyspnea
  - cardinal symptom - >95% of pts
  - breathlessness as presenting symptom in 60% esp. on exertion
  - cause: inadequacy of cardiac output relative to metabolic requirements
  - severity does not correlate w/ elevation of pulmonary artery pressure

Physical findings

- severe PPH
  - cold hands and feet
  - diminished peripheral pulse
  - low bp
  - reduced pulse pressure

Physical findings

- signs of systemic HPN
  - promonent jugular venous α wave, exagerqated by abdominal compression
  - prominent c-v wave – tricuspid regurgitation

Physical findings

- loud 2nd heart sound
- palpable R ventricular heave & impulse of PA
- both pulmonary ejection & tricuspid regurgitation murmurs

Physical findings

- signs of right ventricular failure are common
- cyanosis
- no digital clubbing occurs in PPH

Diagnosis

- blood studies impt part
  - FBC – polycythemia, anemia, thrombocytopenia,
- CXR
  - suggests presence
  - clues of underlyng conditions
  - protrusion of main pulmonary artery, peripheral oligemia, increased c-t ratio

Diagnosis

- Respiratory function tests
  - ABGs – low PaCo2 and normal pH
  - PFT – n exp. flow rates w/ n or mildly reduced lung volumes
  - exercise testing – bring out physiologic abn; heart rate and anaerobic threshold at low levels of exercise

Diagnosis

- electrocardiography
  - ECG shows right axis deviation & rv hypertrophy & strain
  - ECG criteria for RVH
    - QRS axis in frontal plane >/= 110
    - R wave in lead v1 > 5mm
    - RS ratio in v1 > 1
    - RS ratio in v6 < 1
  - right atrial enlargement

Diagnosis

- ECHO cardiogram
  - documenting and rule out mitral valve disease, lv systolic or diastolic dysfunction

Diagnosis

- scintigraphy
  - perfusion lung scan
    - pph vs. chronic pte
    - 3 patterns
      - large multiple segmental defects
      - multiple ill-defined defects
      - no defects

Diagnosis

- cardiac catheterization
  - mandatory to
    - document presence and severity
    - rule out cardiac causes
    - det. acute vasoreactivity using pharmacologic agents
  - may reveal elevated r atrial pressure, increased pulm. arterial pressure, and depressed cardiac output

Diagnosis

- most common & most important noninvasive test is v/q scan
- PFT's
- pulmonary angiography & open lung biopsy
- R heart catheterization is useful in determining degree of impairment & prognosis

Treatment

- often fatal
- comprehensive medical approach
- avoid circumstances that may increase pulm. art. pressure and decrease cardiac output
- prevention of conception w/o ocp

Treatment

- calcium channel antagonists
- iv epoprostenol (pg i_2)
- prostacyclin analogues
- endothelin receptor analogues

Treatment

- calcium channel antagonists
  - 6% will benefit
  - acute reduction in pulm. art. pressure and pulm. vasc. resistance
  - nifedipine, diltiazem and amlodopine

Treatment

- iv epoprostenol (pg i_2)
  - used either as primary mode of Rx or as a bridge to transplantation
  - produce sustained improvement in hemodynamics and exercise tolerance and prolonged survival

Treatment

- prostacyclin analogues
  - treprostinil avail. sq injection
  - improve exercise tolerance and pulmonary hemodynamics
  - drawback: pain in infusion site

Treatment

- endothelin receptor analogues
  - bosentan – only oral agent
  - improve 6 minute walk distance and functional class
  - 125mg bid
  - adverse effect: elevated hepatic enzymes

Treatment

- lung transplantation
  - tx for failing medical treatment
  - complication: immunosuppression, obliteration brochiolitis

Pulmonary hypertension in COPD

- frequent complication of COPD
- multifactorial
  - loss of vascular surface caused by destruction of lung parenchyema
  - compression of the vascular bed
  - alveolar hypoxemia
  - increased pap & vascular resistance

Physical examination

- presence of PHN in pts. w/COPD correlates well w/ severity of the disease
- pts. w/ severe hypoxemia (<55 mmHg) almost always have severe PHN

Treatment

- treat underlying disease – COPD
- bronchodilators
- oxygen
- oral vasodilators don’t help