دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کرمان

Pulmonary vascular disease

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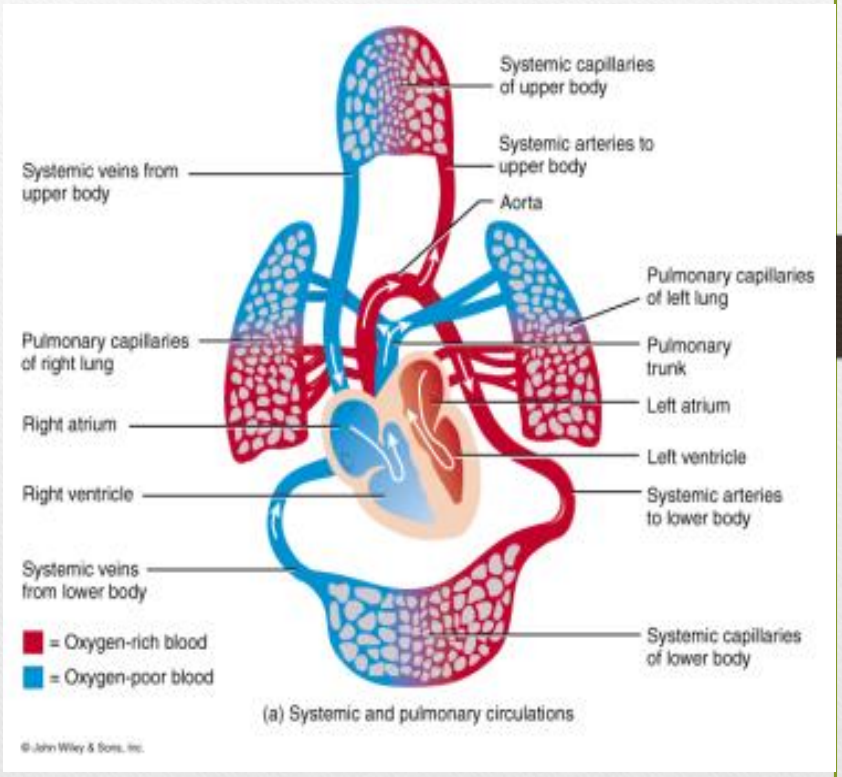
Pulmonary embolus

- Pulmonary embolism is a life-threatening condition that occurs when a clot of blood or other material blocks an artery in your lungs.
- This is an extremely common and highly lethal condition that is a leading cause of death in all age groups.
- One of the most prevalent disease processes responsible for in-patient mortality (30%)
- Overlooked diagnosis.

Pulmonary Blood Flow

- Pulmonary embolism is a life-threatening condition that occurs when a clot of blood or other material blocks an artery the lungs.



PATHOPHYSIOLOGY

Inflammation takes center stage as a trigger of acute PE and DVT. Inflammation-related risk factors and medical illnesses are now linked as precipitants of VTE

TABLE 279-1 Inflammation-Linked Conditions That Can Trigger PE or DVT
Ulcerative colitis
Crohn's disease
Rheumatoid arthritis
Psoriasis
Diabetes mellitus, type 2
Obesity/metabolic syndrome
Hypercholesterolemia, especially elevated LDL cholesterol
Lipoprotein(a)
Pneumonia
Acute coronary syndrome
Acute stroke
Cigarette smoking
Sepsis/septic shock
Erythropoiesis-stimulating agents
Blood transfusion
Cancer

Abbreviations: DVT, deep-venous thrombosis; LDL, low-density lipoprotein; PE, pulmonary embolism.

Prothrombotic States

The two most common autosomal dominant genetic mutations are
(1) factor V Leiden, which causes resistance to the endogenous anticoagulant activated protein C (which inactivates clotting factors V and VIII),
(2) the prothrombin gene mutation, which increases the plasma prothrombin concentration (Chaps. 65 and 117). Antithrombin, protein C, and protein S are naturally occurring coagulation inhibitors. Deficiencies of these inhibitors are associated with VTE but are rare. Antiphospholipid antibody syndrome is an acquired (not genetic) thrombophilic disorder that predisposes to both venous and arterial thrombosis.

Counterintuitively, the presence of genetic mutations such as heterozygous factor V Leiden and prothrombin gene mutation does not appear to increase the risk of recurrent VTE. However, patients with antiphospholipid antibody syndrome may warrant indefinite-duration anticoagulation, even if the initial VTE was provoked by trauma or surgery

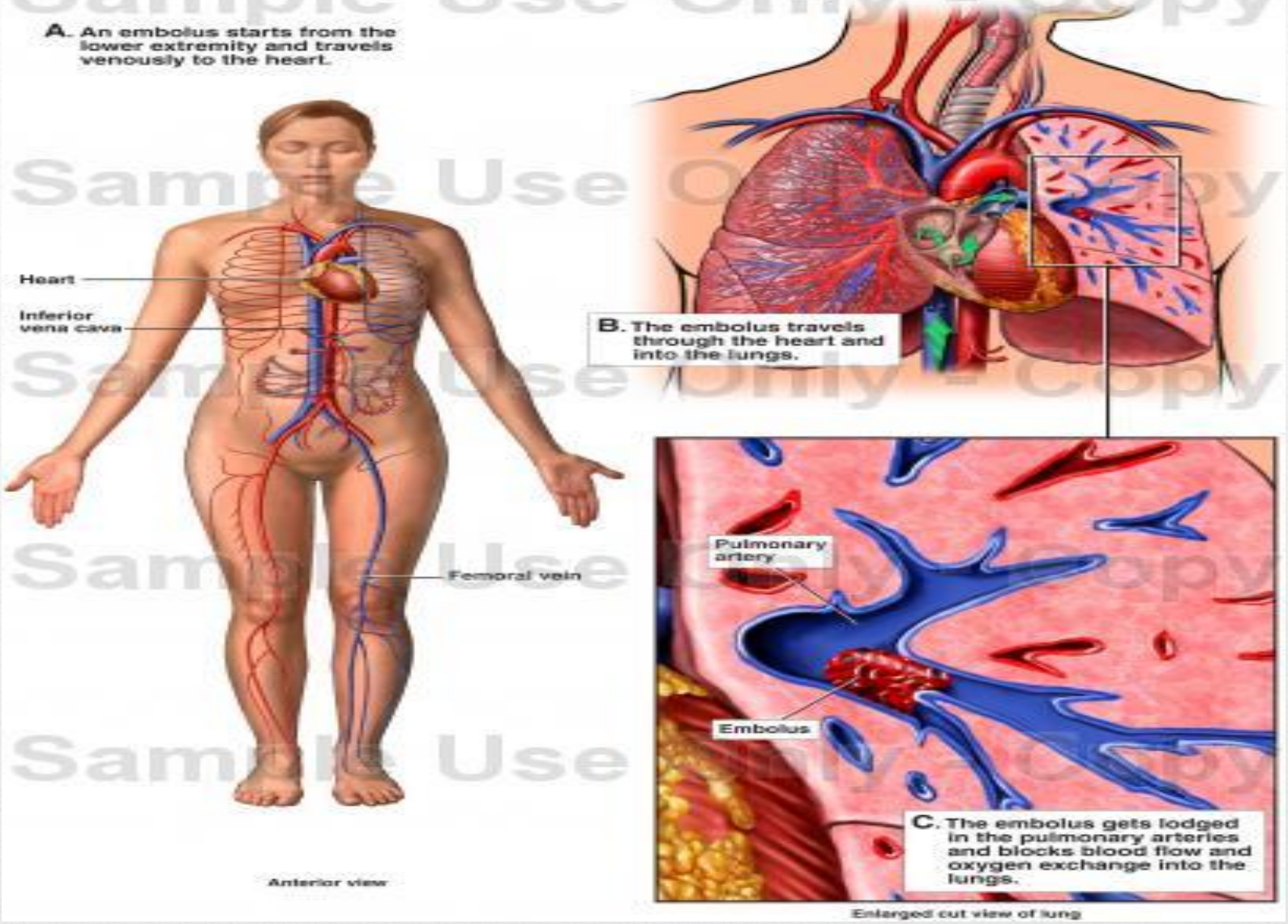
Clinical Risk Factors

- cancer,
- obesity,
- cigarette smoking,
- systemic arterial hypertension,
- chronic obstructive pulmonary disease,
- chronic kidney disease,
- long-haul air travel,
- air pollution,
- estrogen-containing contraceptives,
- pregnancy,
- postmenopausal hormone replacement,
- surgery,
- and
- trauma. Sedentary lifestyle is increasingly prevalent. A Japanese study found that each 2 h per day increment of television watching is associated with a 40% increased likelihood of fatal PE.

Activated Platelets

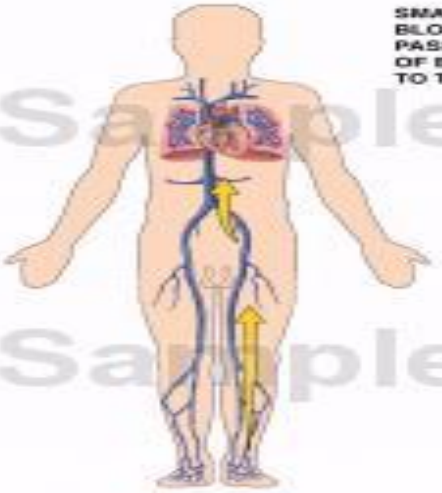
Virchow's triad of venous stasis, hypercoagulability, and endothelial injury leads to recruitment of activated platelets, which release microparticles. These microparticles contain proinflammatory mediators that bind neutrophils, stimulating them to release their nuclear material and form web-like extracellular networks called neutrophil extracellular traps. These prothrombotic networks contain histones that stimulate platelet aggregation and promote platelet-dependent thrombin generation. Venous thrombi form and flourish in an environment of stasis, low oxygen tension, and upregulation of proinflammatory genes.

Mechanism of Pulmonary Embolism



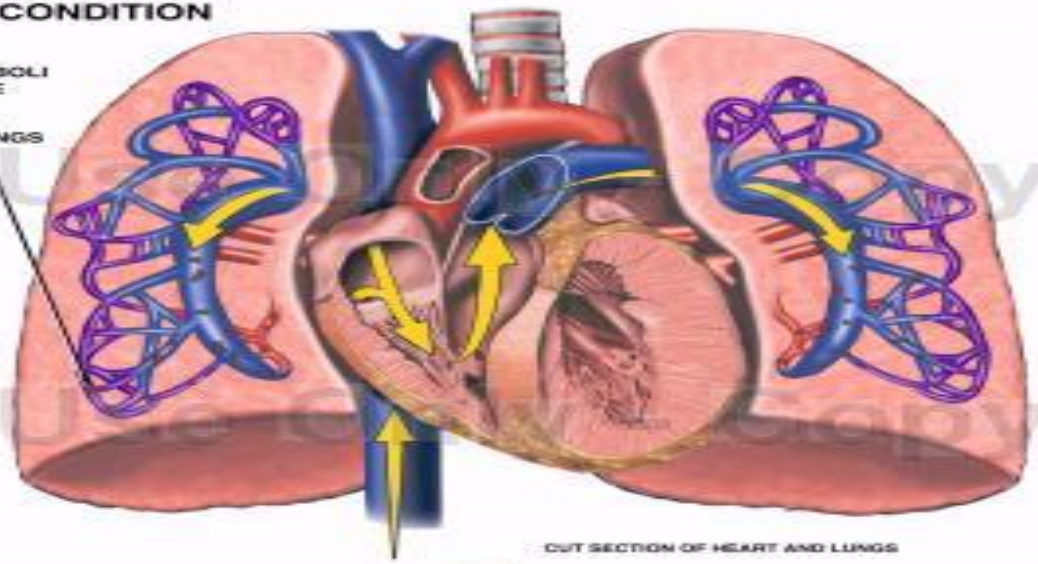
Pulmonary Embolism

INITIAL CONDITION



ARROWS INDICATE THE PATHWAY OF THE EMBOLI FROM THE LOWER LEFT LEG UP TO THE THORAX.

SMALL EMBOLI BLOCK THE PASSAGE OF BLOOD TO THE LUNGS



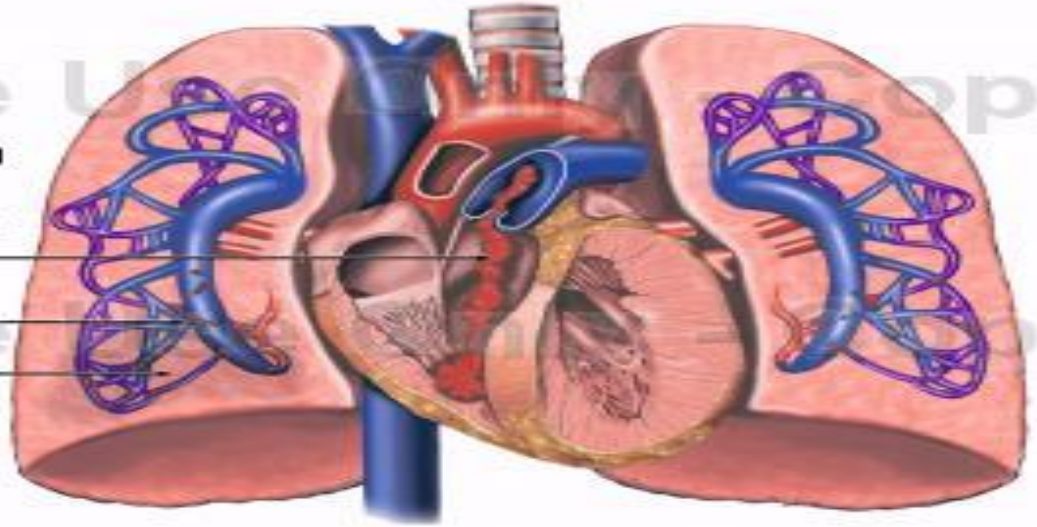
CUT SECTION OF HEART AND LUNGS

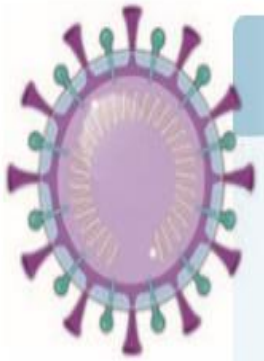
ULTIMATE CONDITION

EMBOLUS MEASURING 39 x 1.8 cm BLOCKS THE RIGHT VENTRICLE AND THE PULMONARY TRUNK

SMALL EMBOLI (AT LEAST 48 HOURS OLD)

INFARCTION OF THE LOWER LOBE OF THE RIGHT LUNG





Sars-COV-2

A

Risk factors

- Acute illness
- Bed-ridden, stasis
- Genetics
- Fever
- Diarrhea
- Sepsis
- Liver injury
- CKD
- COPD
- HF
- Malignancy

Inflammatory response → Endothelial dysfunction Superinfected

Tissue factor
↓TFPI

Lymphopenia

Inflammatory cytokines
↑IL-6, CRP

B

Hemostatic abnormalities

- Pulmonary microthrombi
- Intravascular coagulopathy
- Myocardial injury
- ↑Cardiac biomarkers

- ↑D-dimer, FDPs, PT
- ↓Platelets

C

Clinical outomes

Venous thromboembolism

Myocardial infarction

Disseminated intravascular coagulation

TFPI, tissue factor pathway inhibitor

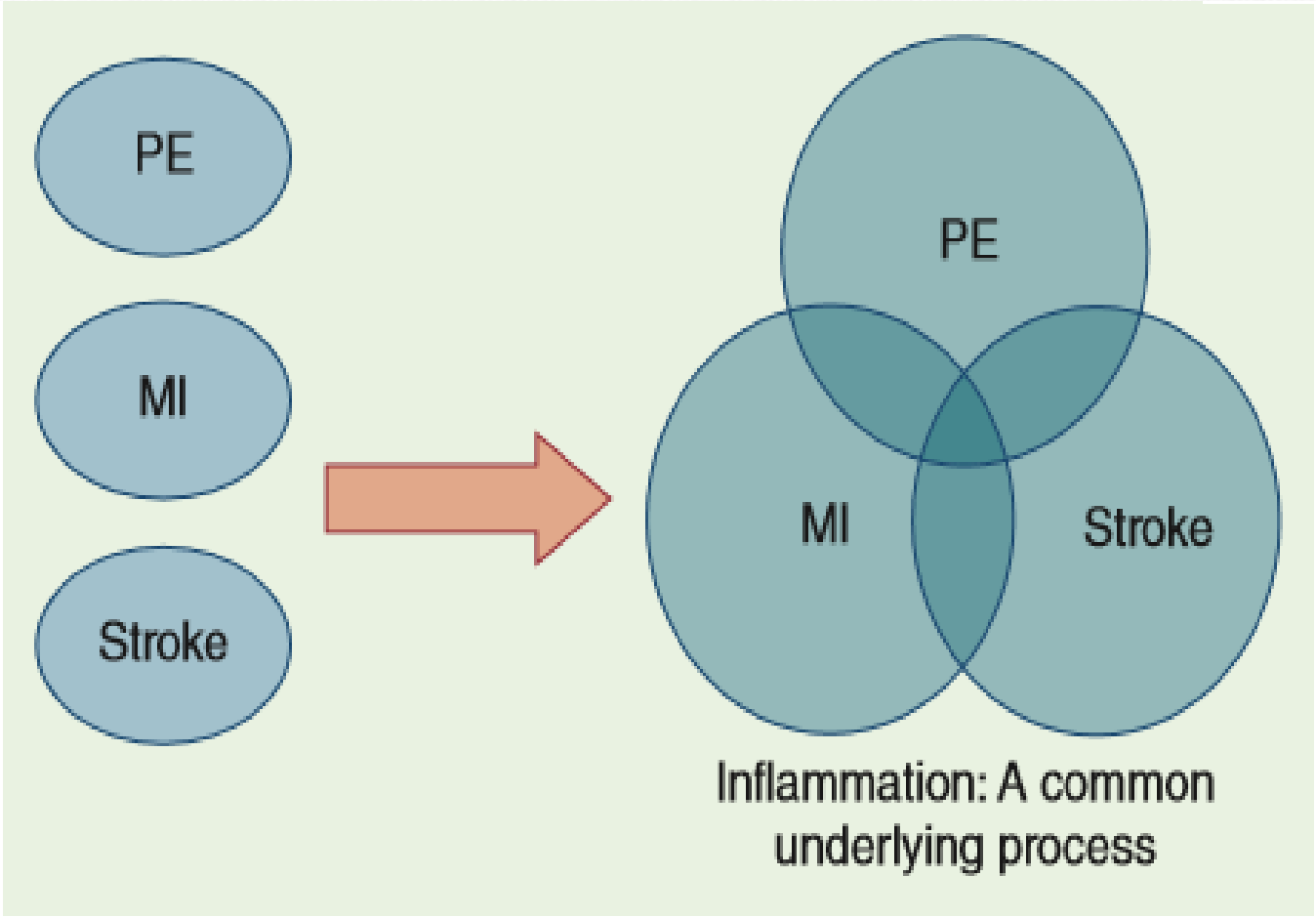


FIGURE 279-4 Broad interaction between venous thromboembolism and atherothrombosis. MI, myocardial infarction; PE, pulmonary embolism.

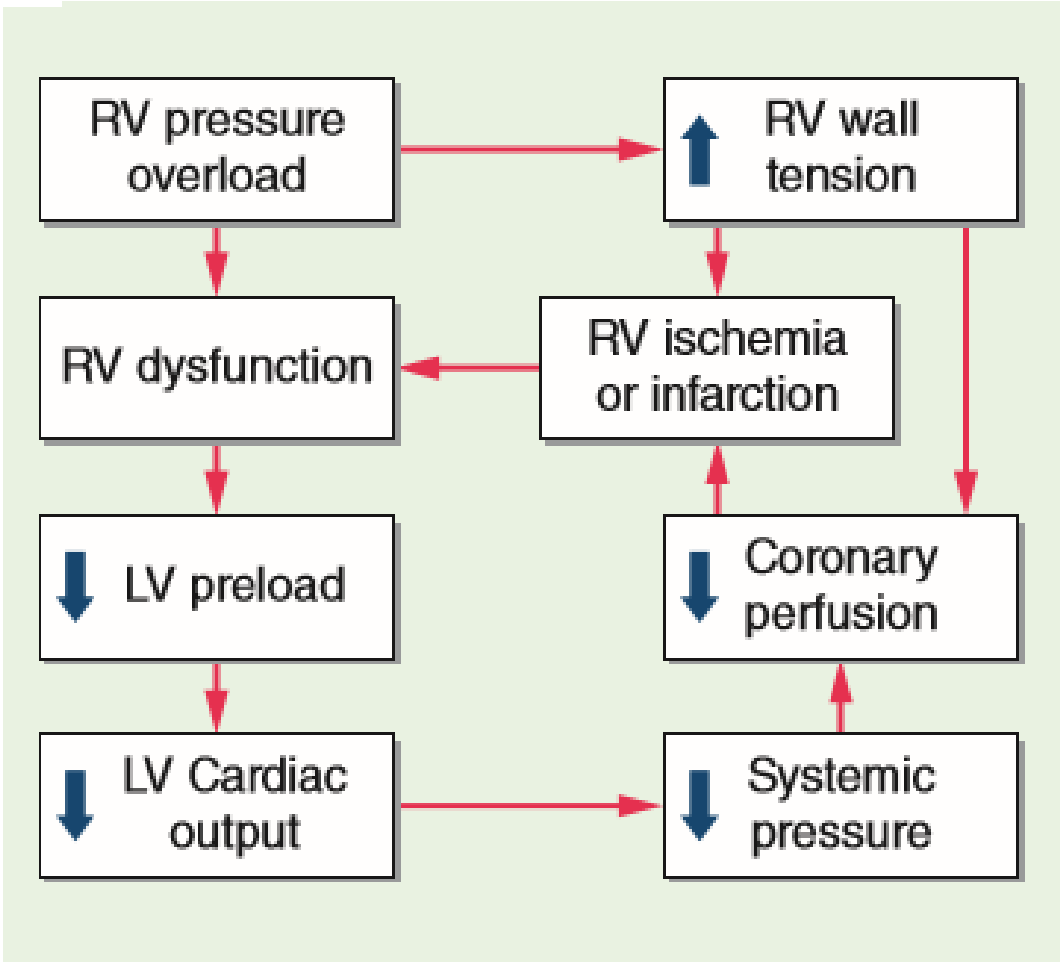


FIGURE 279-6 Pathophysiology of pulmonary embolism (PE). LV, left ventricular; RV, right ventricular.

Physiology The most common gas exchange abnormalities are arterial hypoxemia and an increased alveolar-arterial O2 tension gradient, which represents the inefficiency of O2 transfer across the lungs. Anatomic dead space increases because breathed gas does not enter gas exchange units of the lung

Other pathophysiologic abnormalities include the following:

1. Increased pulmonary vascular resistance due to vascular obstruction or platelet secretion of vasoconstricting neurohumoral agents such as serotonin. Release of vasoactive mediators can produce ventilation-perfusion mismatching at sites remote from the embolus, thereby accounting for discordance between a small PE and a large alveolar-arterial O2 gradient.
2. Impaired gas exchange due to increased alveolar dead space from vascular obstruction, hypoxemia from alveolar hypoventilation relative to perfusion in the nonobstructed lung, right-to-left shunting, or impaired carbon monoxide transfer due to loss of gas exchange surface.

. 3. Alveolar hyperventilation due to reflex stimulation of irritant receptors.
4. Increased airway resistance due to constriction of airways distal to the bronchi.
5. Decreased pulmonary compliance due to lung edema, lung hemorrhage, or loss of surfactant

Why is this PE so important?

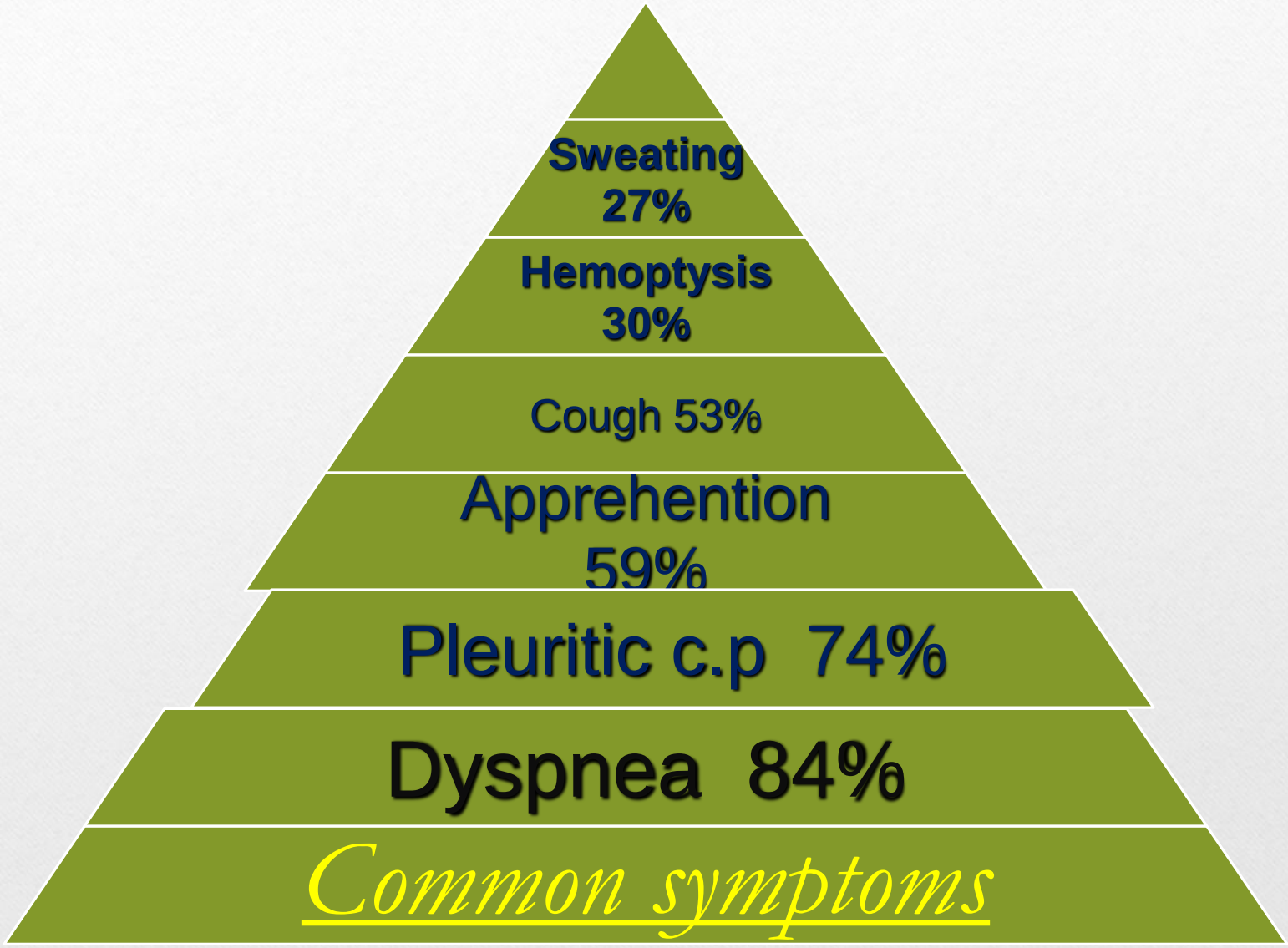
- Prompt diagnosis and treatment can dramatically reduce the mortality and morbidity rate.
- Majority of the cases are unrecognised clinically.
- One third of the patients who survive an initial PE die of a future embolic episode.
- Many patients who die of PE have not had any diagnostic workup nor have they received any prophylaxis for the disease.
- In most cases the CLINICIANS have not even considered the diagnosis of PE.

Pathophysiology

- PE is not a disease in and of itself.
- It is often a fatal complication of underlying venous thrombosis.
- Normally microthrombi (RBC,Platelets and Fibrin) are formed and lysed with in the venous circulatory system.
- Under pathological condition these microthrombi may escape and propagate and will block the pulmonary blood vessels causing PE

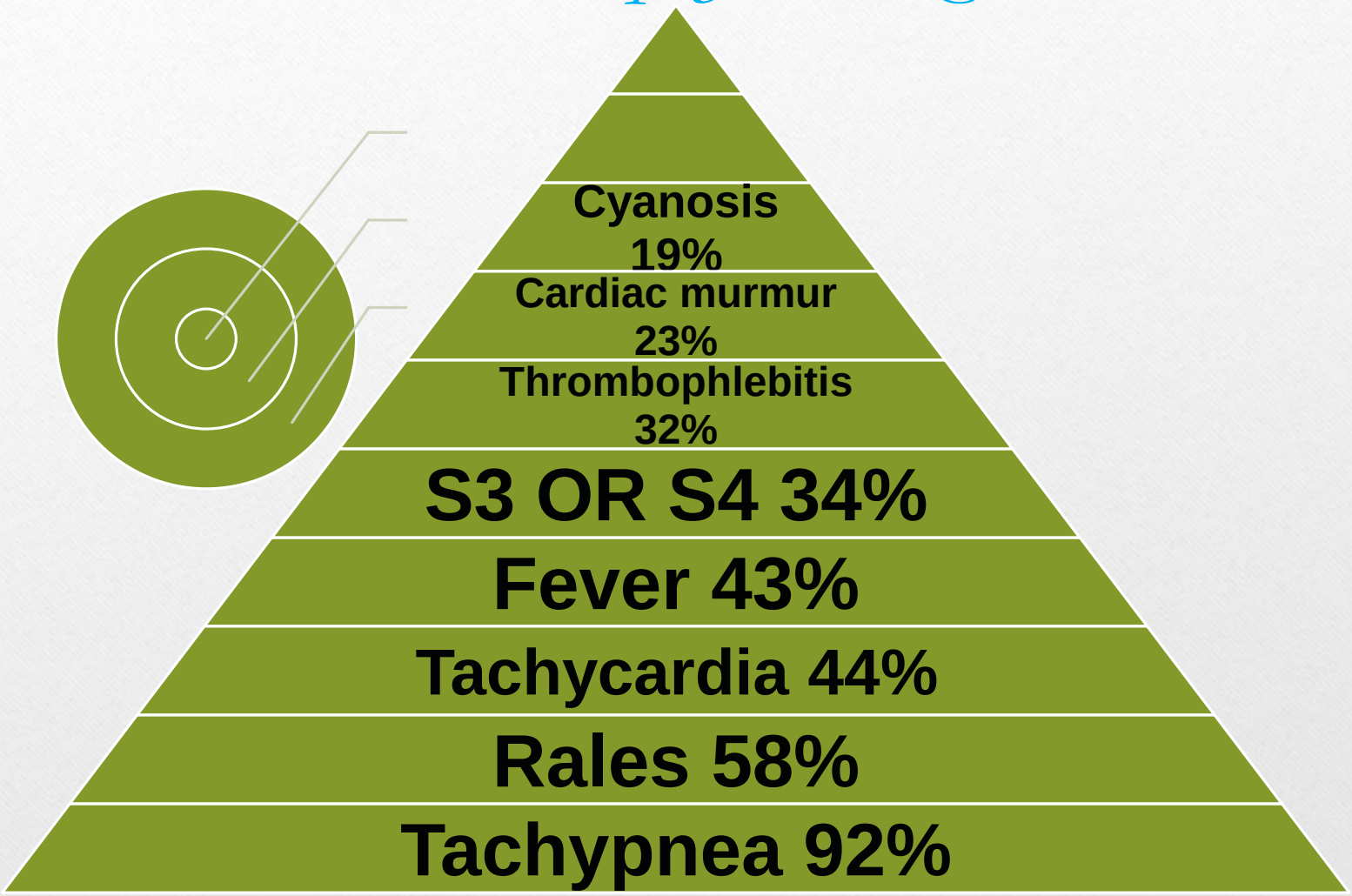
Facts about PE.

- 3rd most common cause of death.3000000million death
- 2nd most common cause of unexpected death in most age groups.
- 60% of patients dying in the hospital have had a PE.
- Diagnosis has been missed in about 70% of the cases



Common symptoms

Common physical signs



Incidence of Signs and Symptoms of Pulmonary Embolism

	Massive PE (%)*	Submassive PE (%)*	PE Without Preexisting Cardiopulmonary Disease
Dyspnea	85	82	73
Pleuritic chest pain	64	85	66
Cough	53	52	37
Hemoptysis	23	40	13
Tachypnea	95 (>16/min)	87 (>16/min)	70 (>20/min)
Tachycardia (>100/min)	48	38	30
Increased P2	58	45	23
Rales	57	60	51
Phlebitis	36	26	11

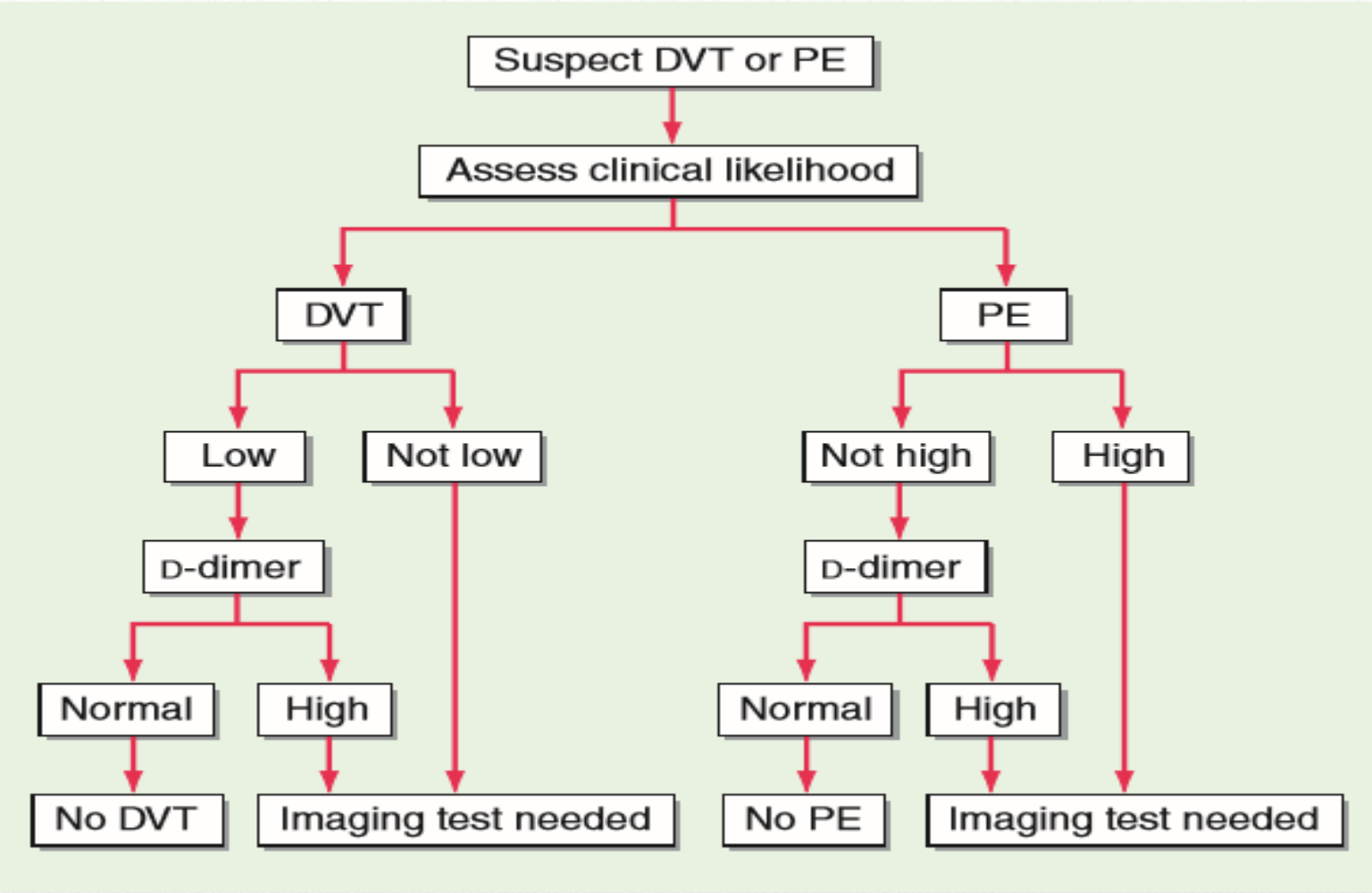
TABLE 279-3 Differential Diagnosis of DVT and PE
DVT
Ruptured Baker's cyst
Muscle strain/injury
Cellulitis
Acute postthrombotic syndrome/venous insufficiency
PE
Pneumonia, asthma, chronic obstructive pulmonary disease
Congestive heart failure
Pericarditis
Pleurisy: "viral syndrome," costochondritis, musculoskeletal discomfort
Rib fracture, pneumothorax
Acute coronary syndrome
Anxiety
Vasovagal syncope

Recommendations for clinical assessment

- Clinical assessment should be made before imaging.
- Clinical assessment should be made by an objective method.

CLASSIFICATION OF PULMONARY EMBOLISM AND DEEP-VENOUS Pulmonary Embolism Massive (high-risk) PE accounts for 5–10% of cases and is usually characterized by systemic arterial hypotension and extensive thrombosis affecting at least half of the pulmonary vasculature. Dyspnea, syncope, hypotension, and cyanosis are hallmarks of massive PE. Patients with massive PE may present in cardiogenic shock and can die from multisystem organ failure. Submassive (intermediate-risk) PE accounts for 20–25% of patients and is characterized by RV dysfunction despite normal systemic arterial pressure. The combination of right heart failure and release of cardiac biomarkers such as troponin indicates a high risk of clinical deterioration. Low-risk PE constitutes about 65–75% of cases. These patients have an excellent prognosis.

Low Clinical Likelihood of DVT if Point Score Is Zero or Less; Moderate Likelihood if Score Is 1 to 2; High Likelihood if Score Is 3 or Greater	
CLINICAL VARIABLE	**DVT SCORE**
Active cancer	1
Paralysis, paresis, or recent cast	1
Bedridden for >3 days; major surgery <12 weeks	1
Tenderness along distribution of deep veins	1
Entire leg swelling	1
Unilateral calf swelling >3 cm	1
Pitting edema	1
Collateral superficial nonvaricose veins	1
Alternative diagnosis at least as likely as DVT	–2
High Clinical Likelihood of PE if Point Score Exceeds 4	
CLINICAL VARIABLE	**PE SCORE**
Signs and symptoms of DVT	3.0
Alternative diagnosis less likely than PE	3.0
Heart rate >100/min	1.5
Immobilization >3 days; surgery within 4 weeks	1.5
Prior PE or DVT	1.5
Hemoptysis	1.0
Cancer	1.0



How to decide whether diagnostic imaging is needed

DIAGNOSTIC TESTING

- ABG
- CHEST RADIOGRAPHY
- D- dimer
- ECG
- ECHO CARDIOGRAPHY
- CT ANGIOGRAM
- LEG ULTRASOUND
- VENTILATION / PERFUSION SCAN
- ANGIOGERAPHY

D-Dimer Assays.

- Gainfully employed to select patients for further radiological imaging.
- It is a cross linked fibrin degradation product and a plasma marker of fibrin lysis.
- Serum level less than 500ng/L excludes PE with 90-95% accuracy.
- Unfortunately a positive test is non specific (specificity only 25 – 67% and occurs in about 40 – 69% of the patients).

Levels increase in patients with

myocardial infarction,
pneumonia,
sepsis,
cancer,
the postoperative state,
in the second or third trimester of pregnancy

D-Dimer Rapid ELISA Pathway

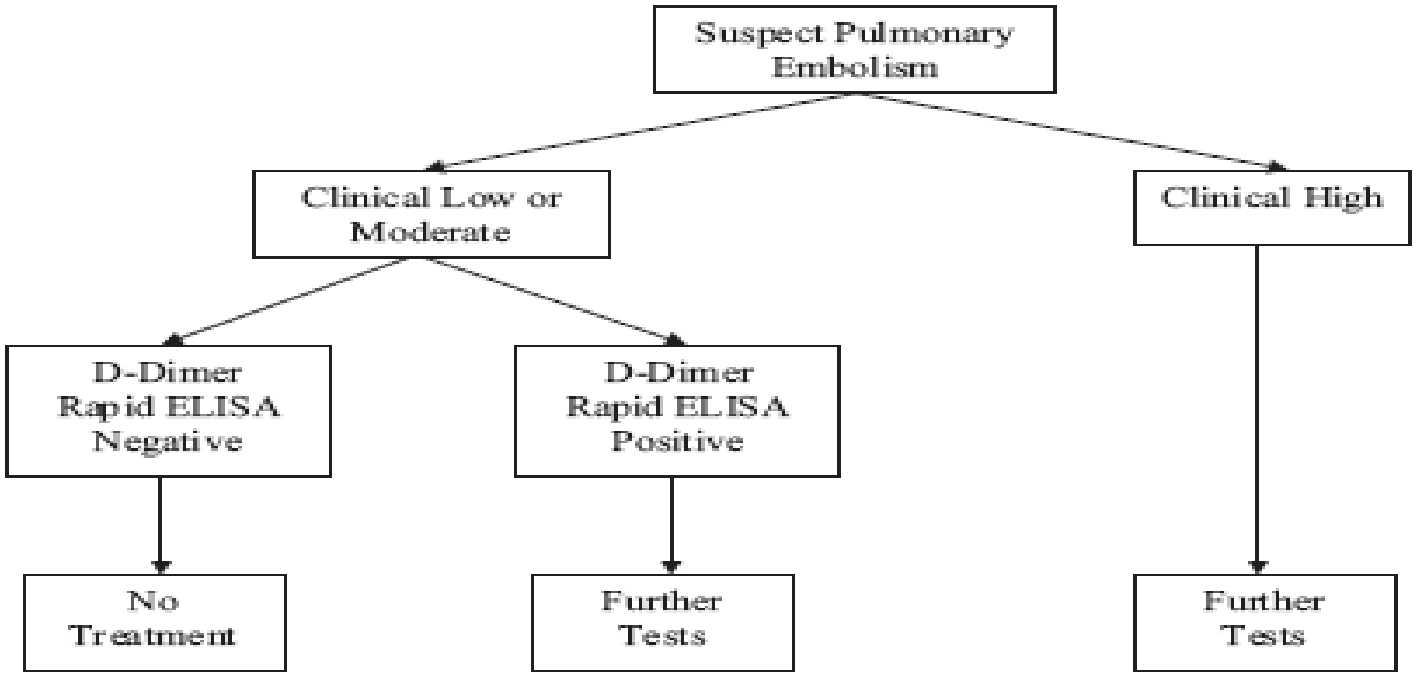


Figure 1 Pathway for D-dimer by quantitative rapid ELISA in combination with clinical assessment. If clinical assessment is low or moderate probability, and D-dimer rapid ELISA is negative, pulmonary embolism would be excluded. If clinical assessment is high probability, further testing is necessary irrespective of the results of D-dimer testing. ELISA = enzyme-linked immunosorbent assay.

PATIENTS WITH LOW PROBABILITY CLINICAL ASSESSMENT

The post-test probability of pulmonary

embolism ranges from 0.7% to 2% with a normal D-dimer rapid ELISA.

No further testing is required if D-dimer

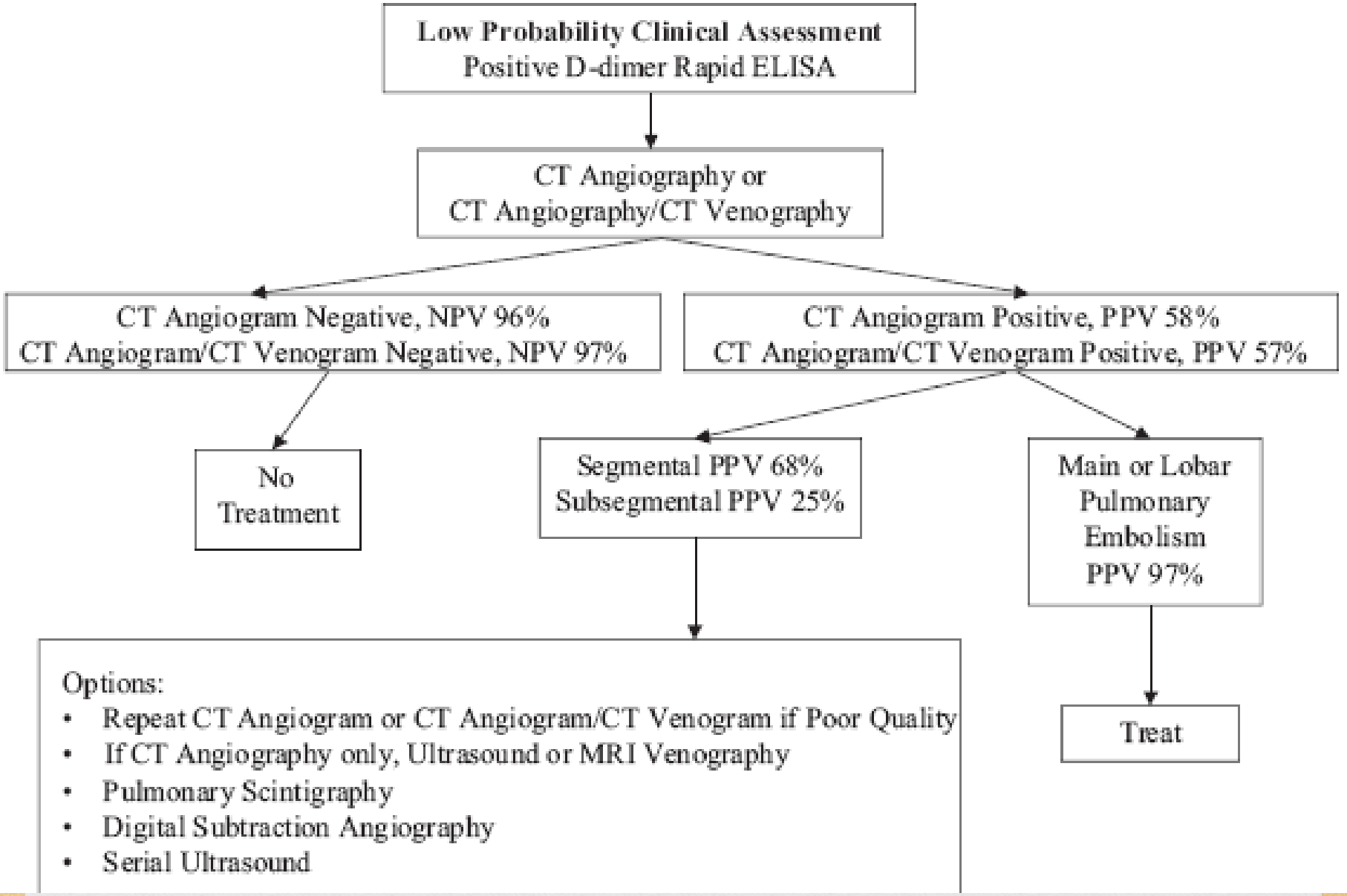
is normal in a patient with a low probability clinical assessment.

Additional testing with venous ultrasound or gadolinium enhanced magnetic resonance venography is optional.

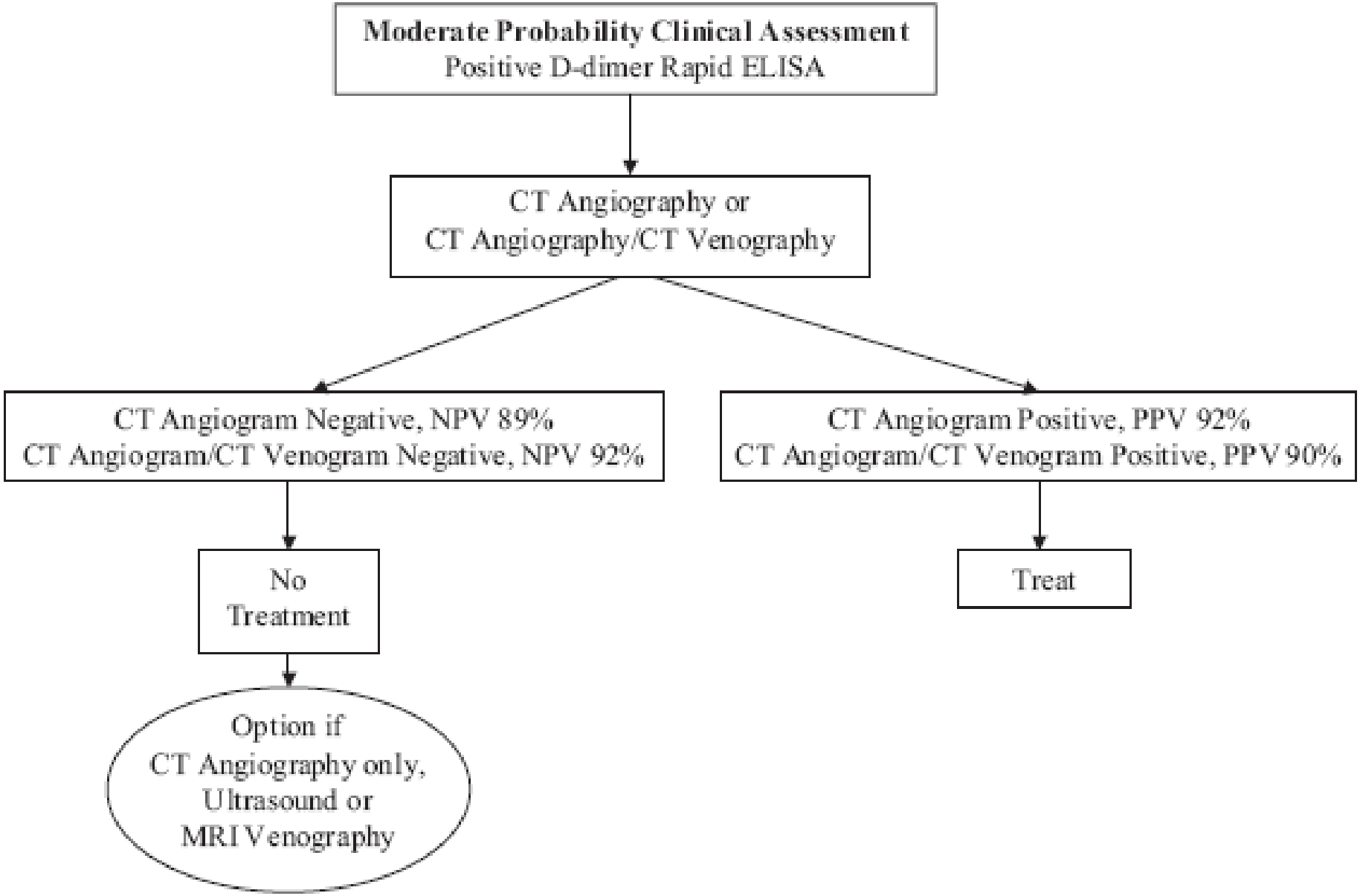
Recommendations for patients with low probability clinical assessment

- Perform a D-dimer rapid ELISA.
- No further testing is required if D-dimer is normal.
- If D-dimer is positive, CT angiography/CT venography is recommended by most PIOPED II investigators.

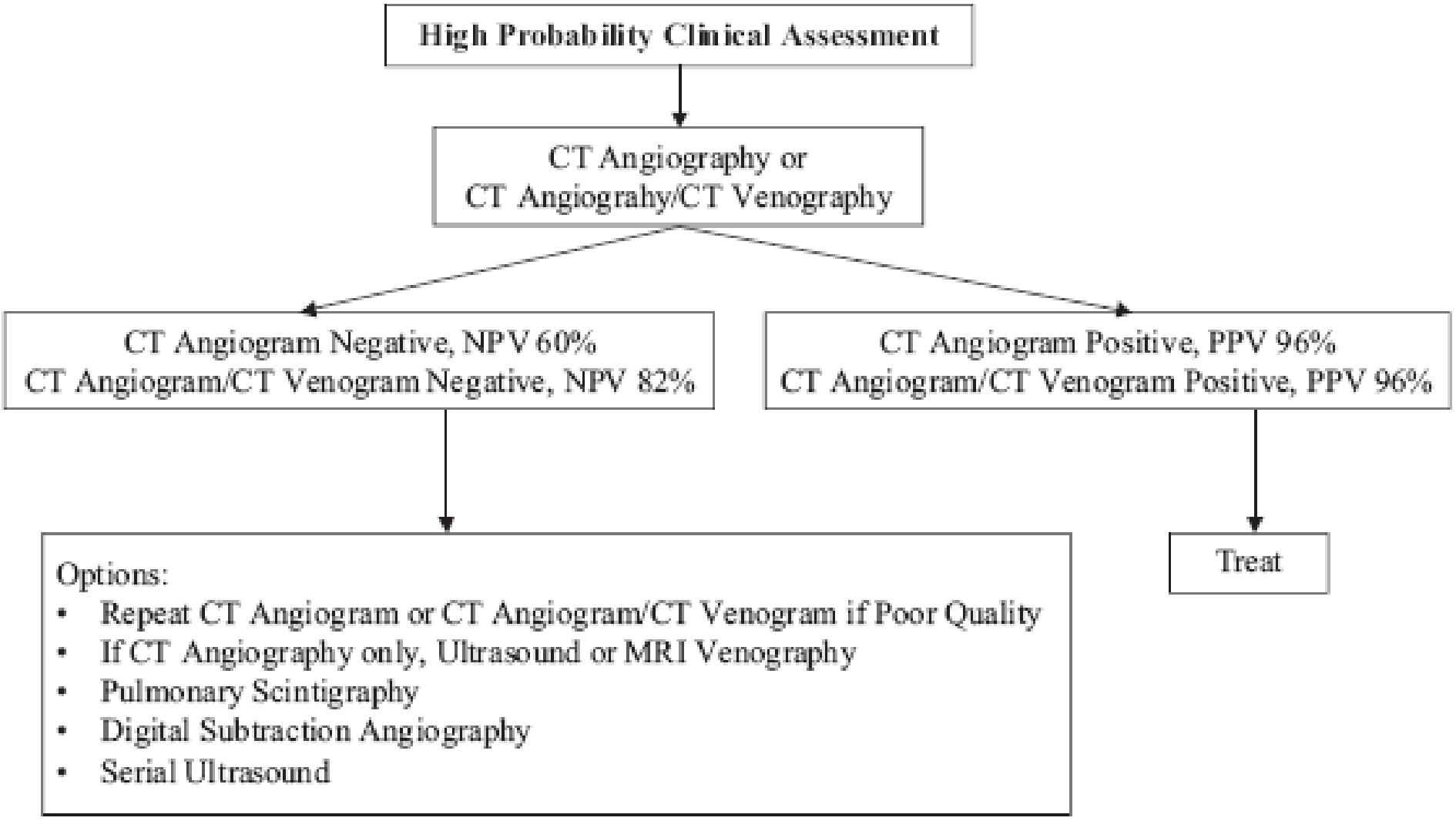
Patients with Low Probability Clinical Assessment



Patients with Moderate Probability Clinical Assessment

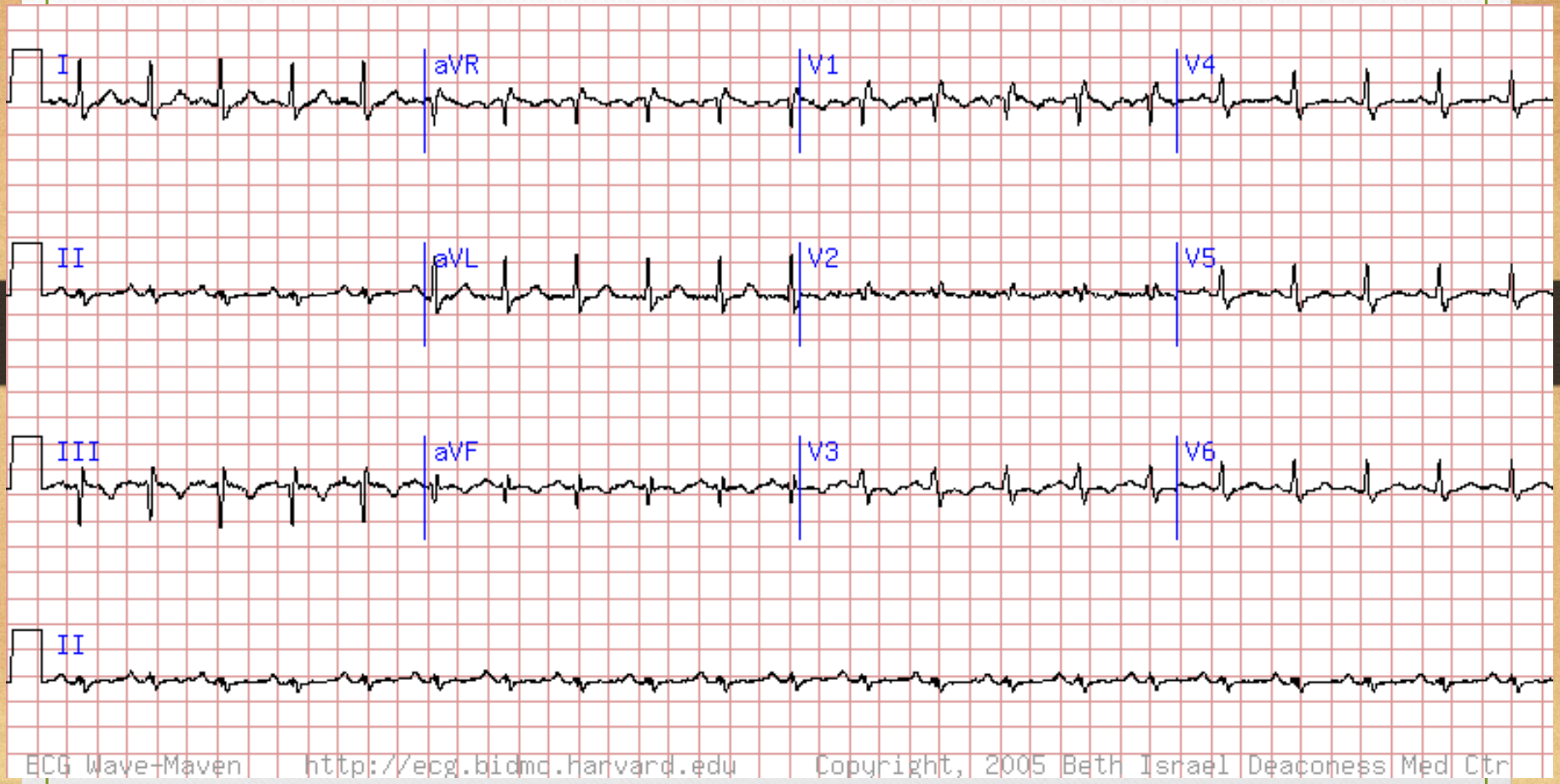


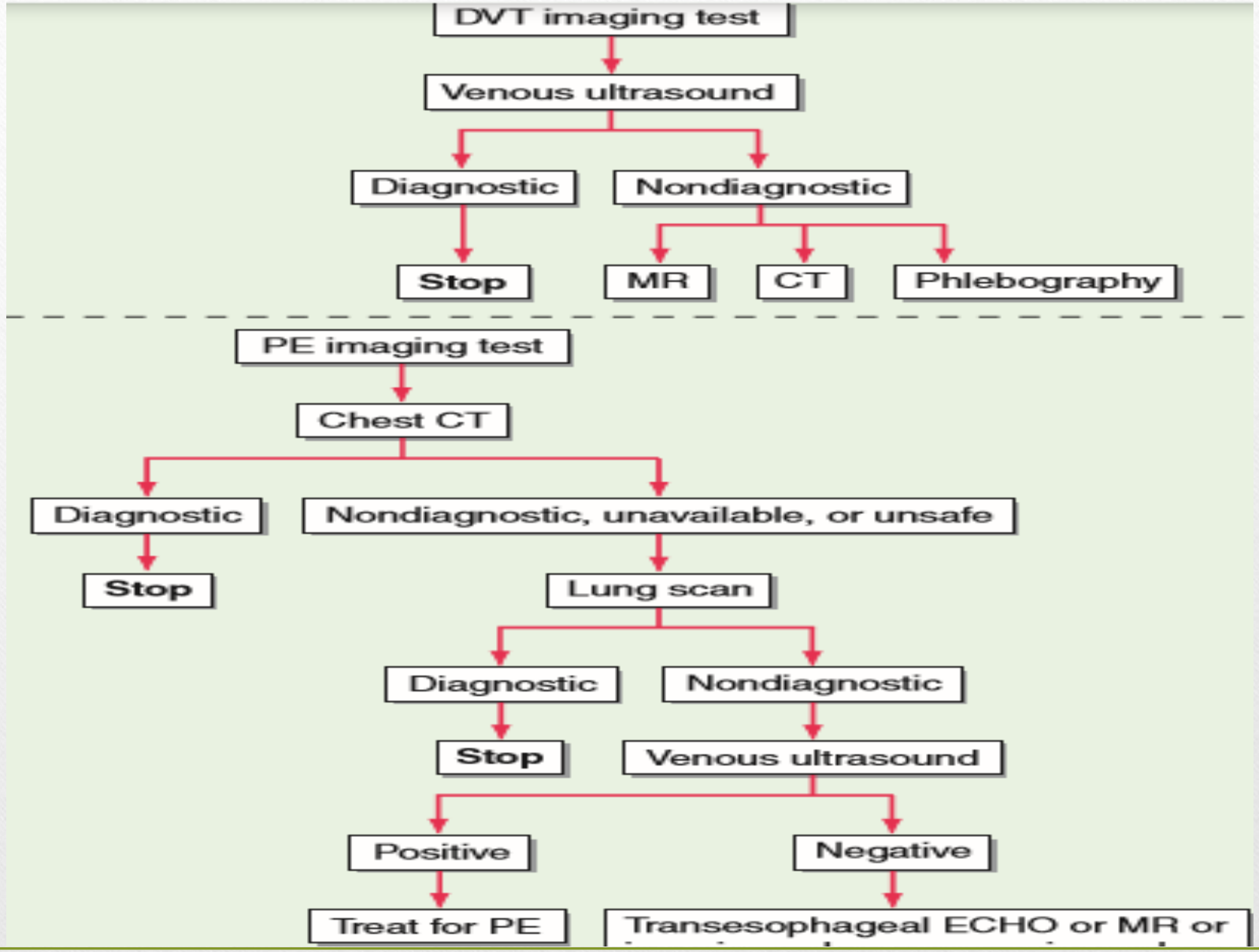
Patients with High Probability Clinical Assessment



Nonthrombotic PE etiologies include fat embolism after pelvic or long bone fracture, tumor embolism, bone marrow, and air embolism. Cement embolism and bony fragment embolism can occur after total hip or knee replacement. Intravenous drug users may inject themselves with a wide array of substances that can embolize, such as hair, talc, and cotton. Amniotic fluid embolism occurs when fetal membranes leak or tear at the placental margin

ELECTROCARDIOGRAM ABNORMALITY



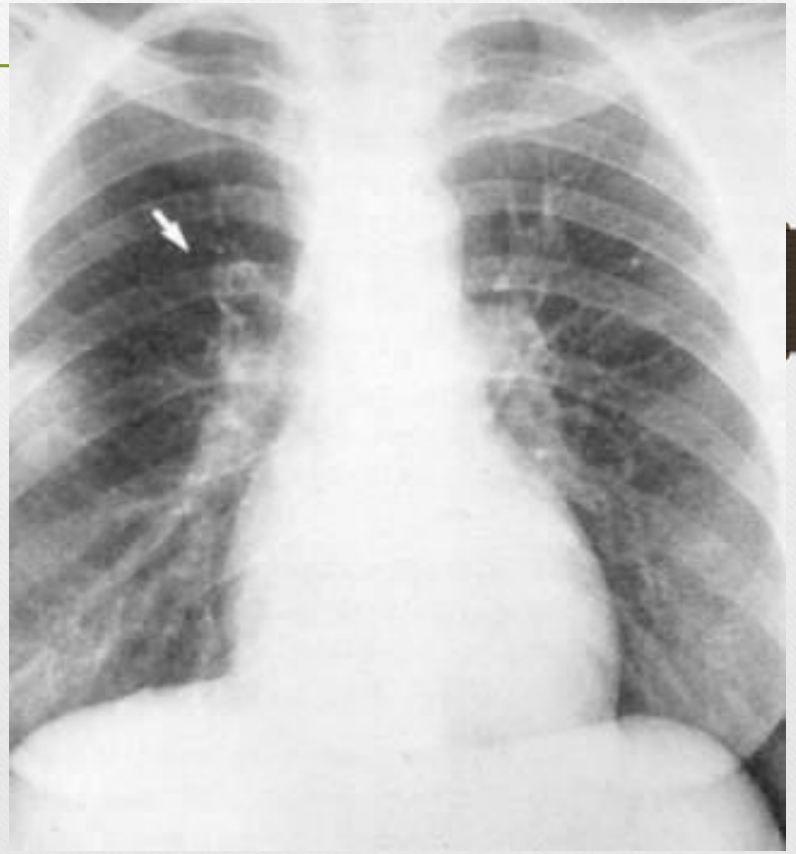

DVT imaging test
Venous ultrasound
Diagnostic
Nondiagnostic
Stop
MR
CT
Phlebography
PE imaging test
Chest CT
Diagnostic
Nondiagnostic, unavailable, or unsafe
Stop
Lung scan
Diagnostic
Nondiagnostic
Stop
Venous ultrasound
Positive
Negative
Treat for PE
Transesophageal ECHO or MR or

Plain film radiography **Chest X-ray**

- Initial CxR always **NORMAL**.
- May show – Collapse, consolidation, small pleural effusion, elevated diaphragm.
- Pleural based opacities with convex medial margins are also known as a Hampton's Hump

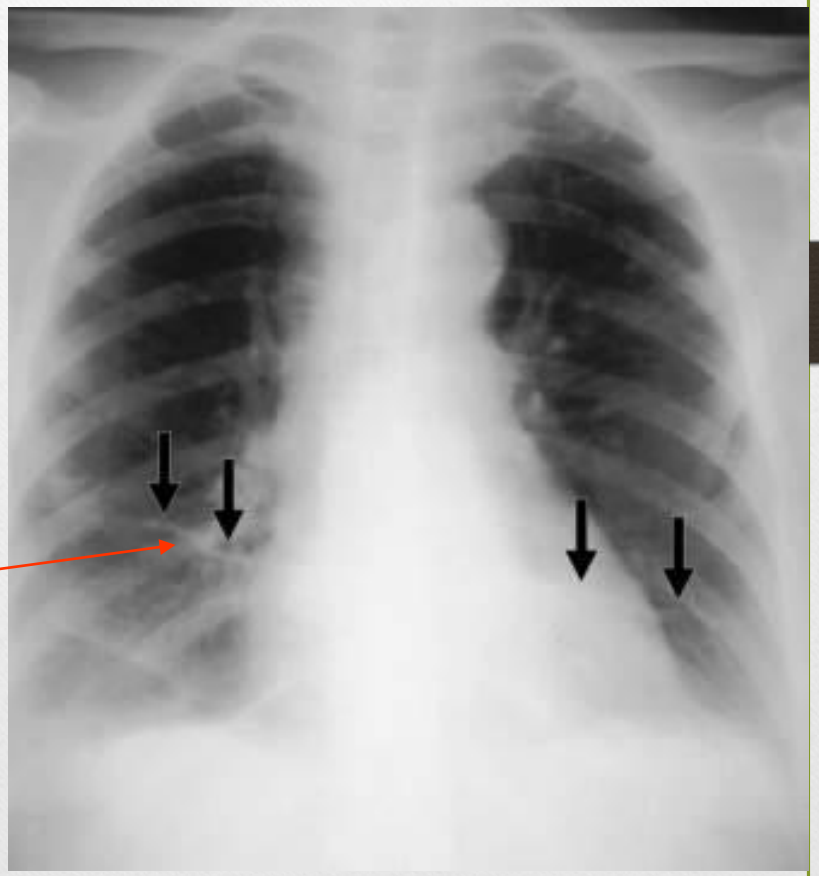
Plain film radiography **Chest X-ray**

- Initial CxR always **NORMAL**.
- May show – Collapse, consolidation, small pleural effusion, elevated diaphragm.
- **Westermark sign** – Dilatation of pulmonary vessels proximal to embolism along with collapse of distal vessels, often with a sharp cut off.



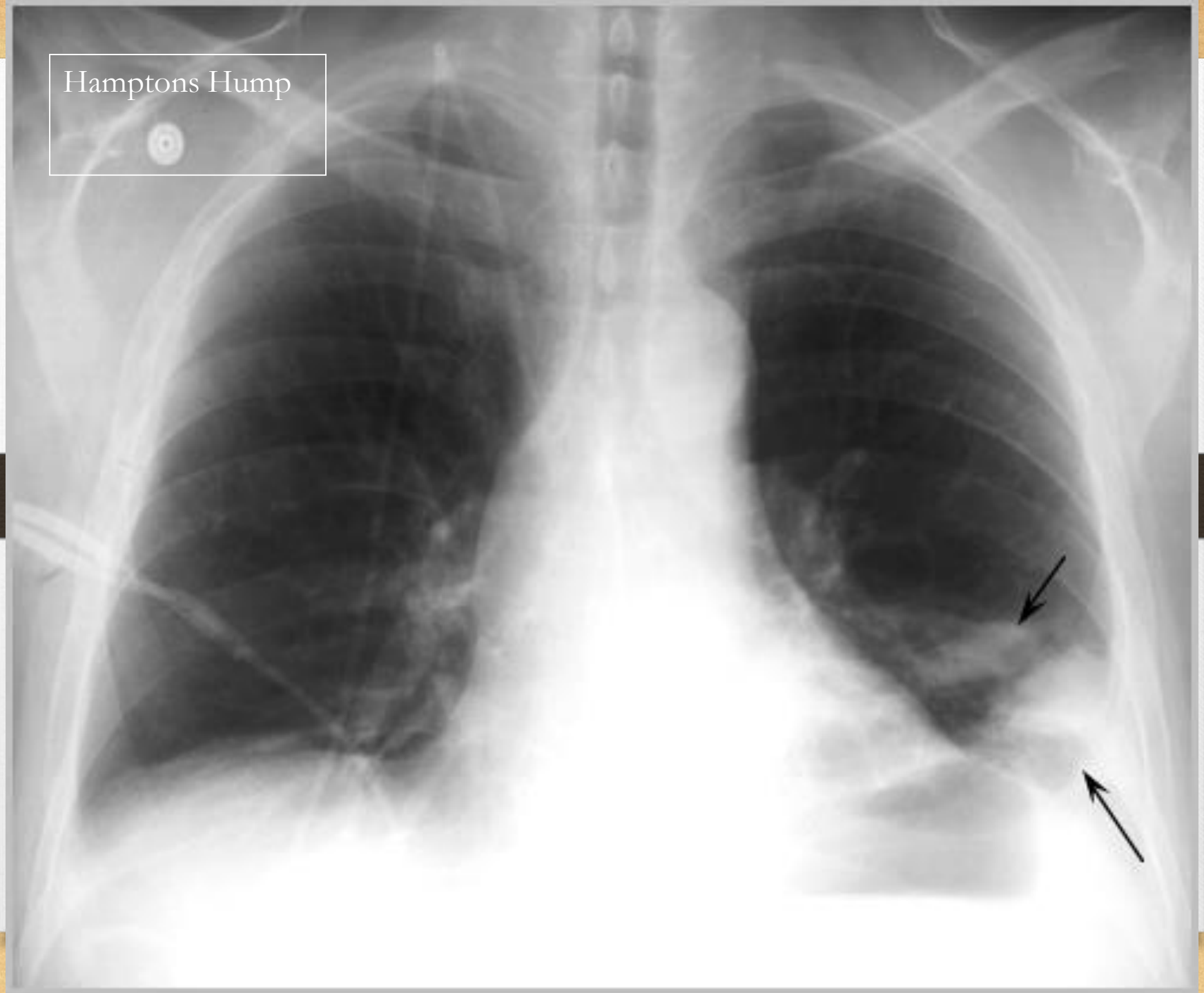
Embolism with Infarction

- Consolidation
- Cavitation
- Pleural effusion (bloody in 65%)
- SSA
- No air bronchograms
- "Melting" sign of healing
- Heals with linear scar

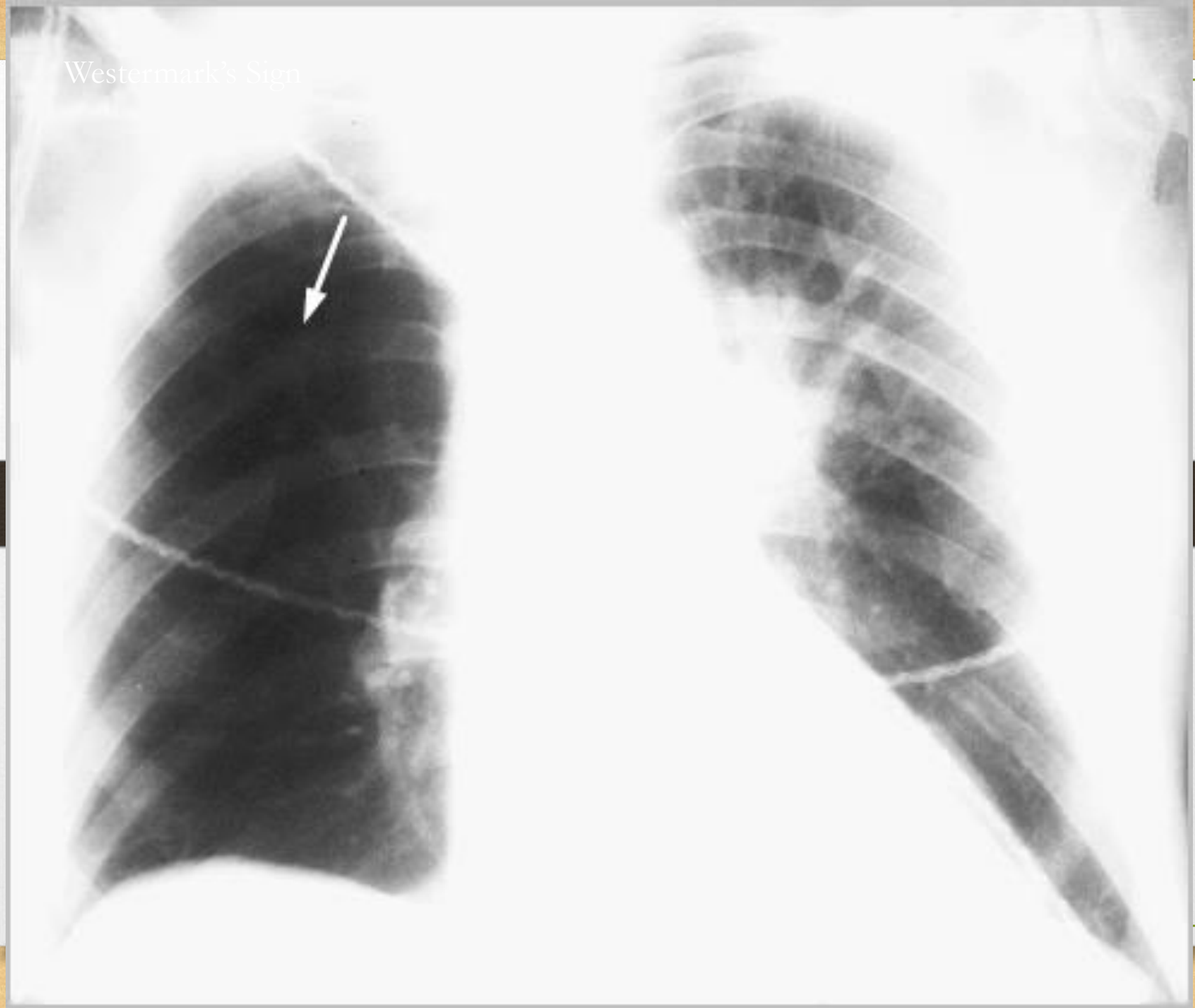


Hampton's Hump

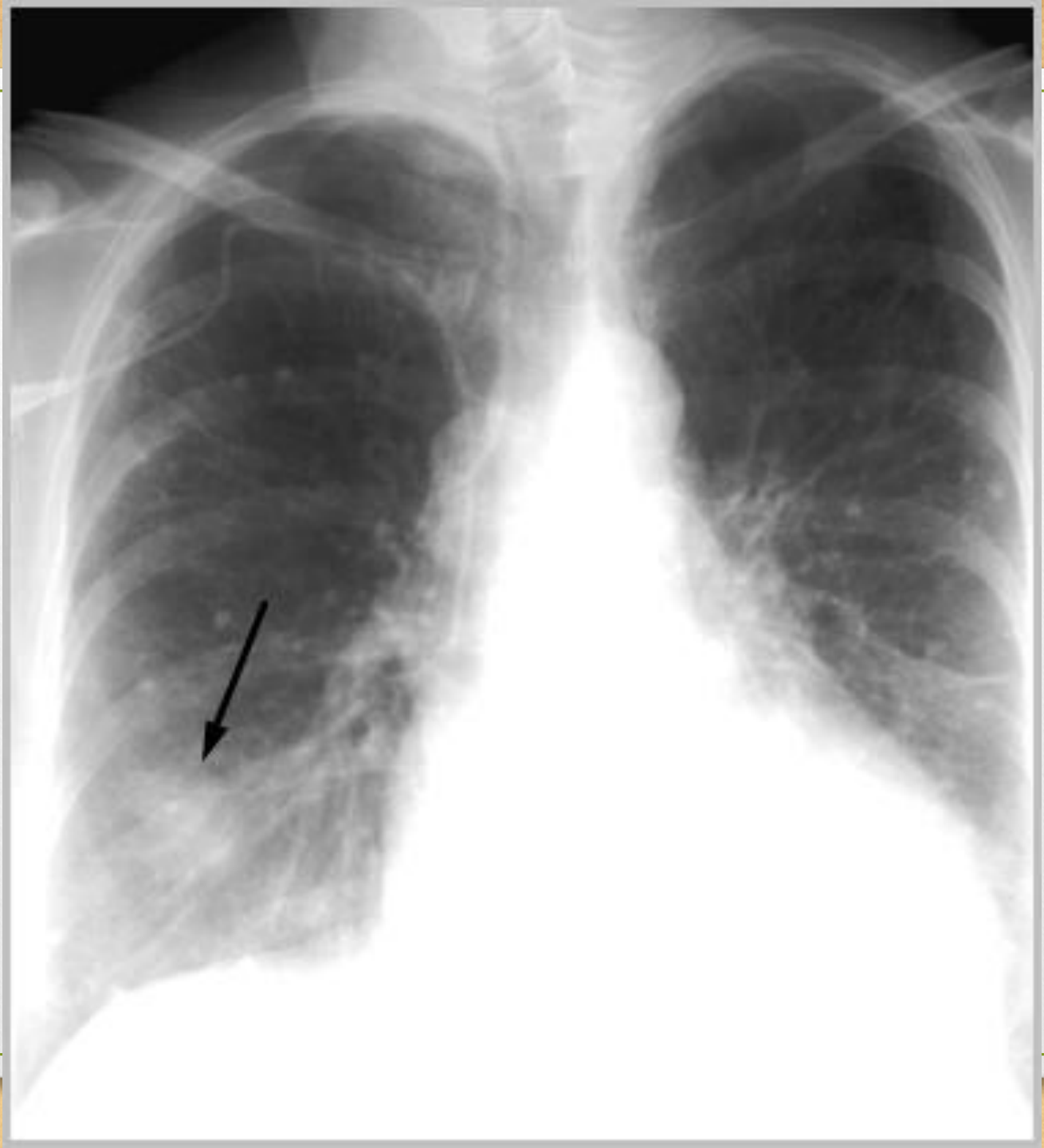
- Pleural based opacities with convex medial margins are also known as a Hampton's Hump. This may be an indication of lung infarction. However, that rate of resolution of these densities is the best way to judge if lung tissue has been infarcted. Areas of pulmonary hemorrhage and edema resolve in a few days to one week. The density caused by an area of infarcted lung will decrease slowly over a few weeks to months and may leave a linear scar

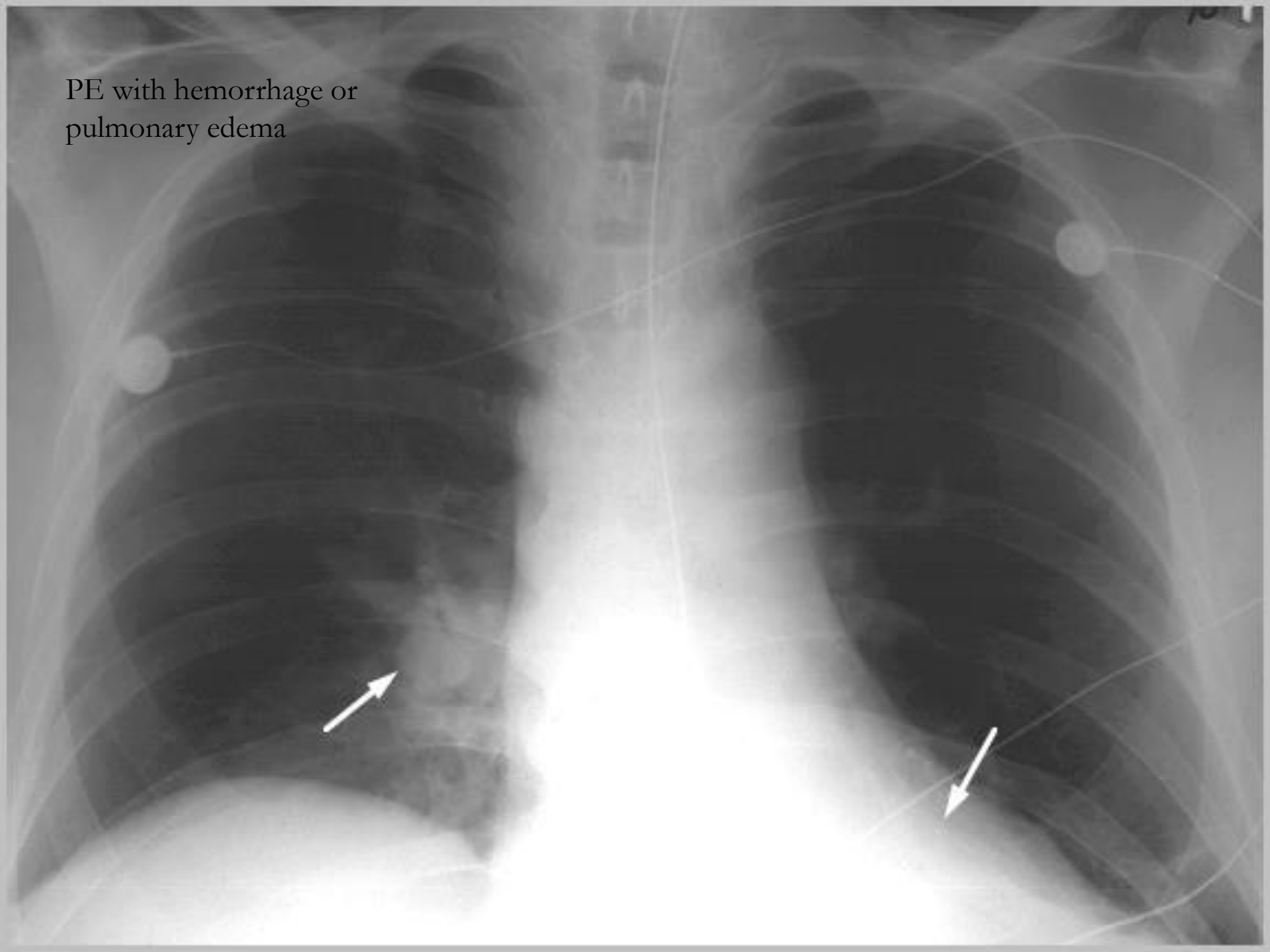

Hamptons Hump

Westermark's Sign



PE which appears like a mass.



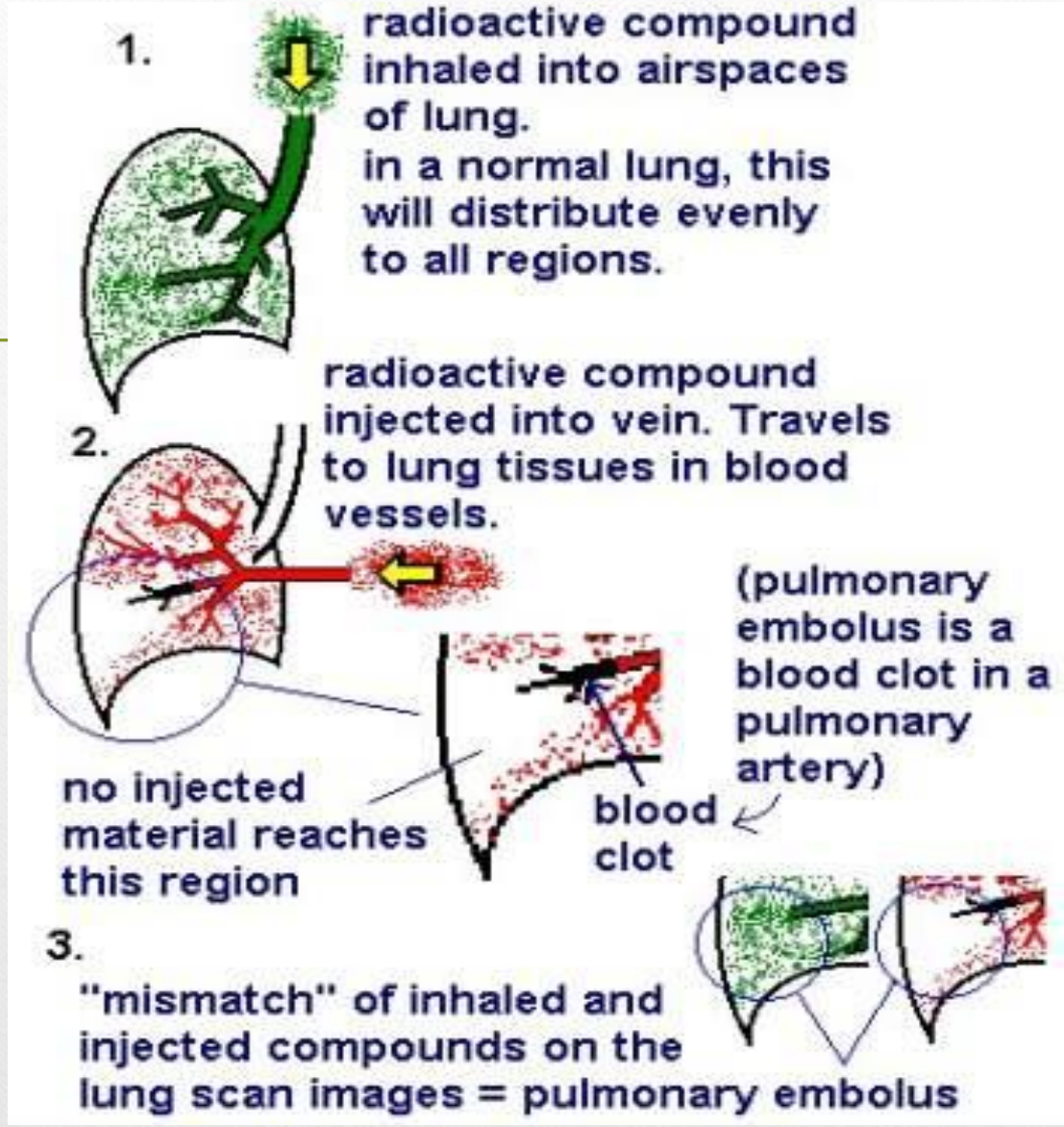

PE with hemorrhage or
pulmonary edema

PE with effusion and elevated diaphragm

V/Q Scanning.

- Single most important diagnostic modality for detecting PE.
- Always indicated when PE is suspected and there is no other diagnosis.
- Non diagnostic V/Q scan is not an acceptable end point in the workup of PE.
- 1 in every 25 pts sent home after a normal V/Q scan actually has a PE that has been **MISSED.**

V/Q Scanning


1.
radioactive compound inhaled into airspaces of lung.
in a normal lung, this will distribute evenly to all regions.
2.
radioactive compound injected into vein. Travels to lung tissues in blood vessels.
(pulmonary embolus is a blood clot in a pulmonary artery)
no injected material reaches this region
blood clot
3.
"mismatch" of inhaled and injected compounds on the lung scan images = pulmonary embolus

V/Q Scanning.

- Ventilation-perfusion scanning is a radiological procedure which is often used to confirm or exclude the diagnosis of pulmonary embolism. It may also be used to monitor treatment.
- The ventilation part of the scan is the inhalation of Krypton 81m, which has a short half life and is a pure gamma emitter. Ventilation is assessed under a gamma camera.

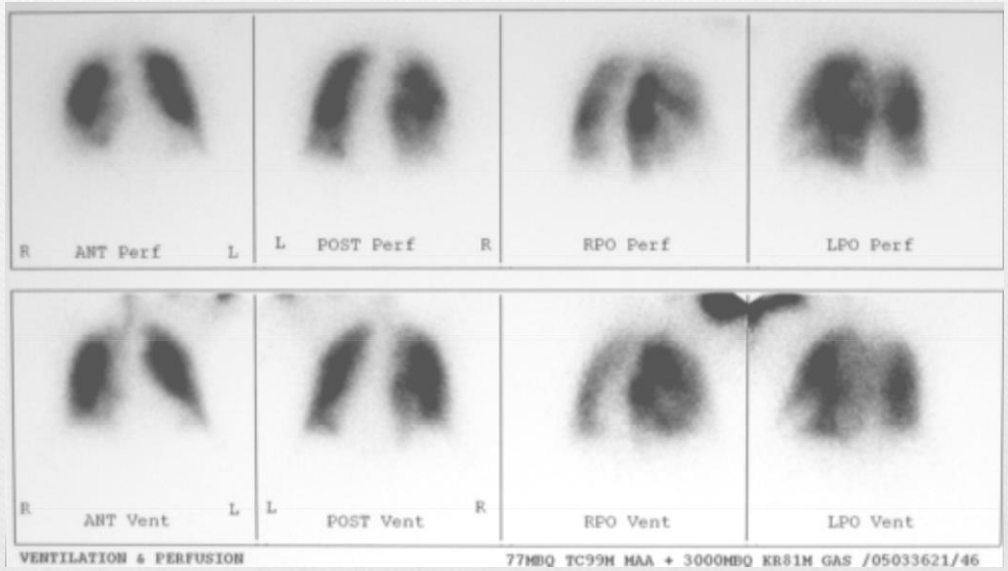
V/Q Scanning.

- The perfusion part of the scan is achieved by injecting the patient with technetium 99m, which is coupled with macro aggregated albumin (MAA). This molecule has a diameter of 30 to 50 micrometres, and thus sticks in the pulmonary capillaries. Sufficiently few molecules are injected for this not to have a physiological effect. An embolus shows up as a cold area when the patient is placed under a gamma camera. The MAA has a half life of about 10 hours

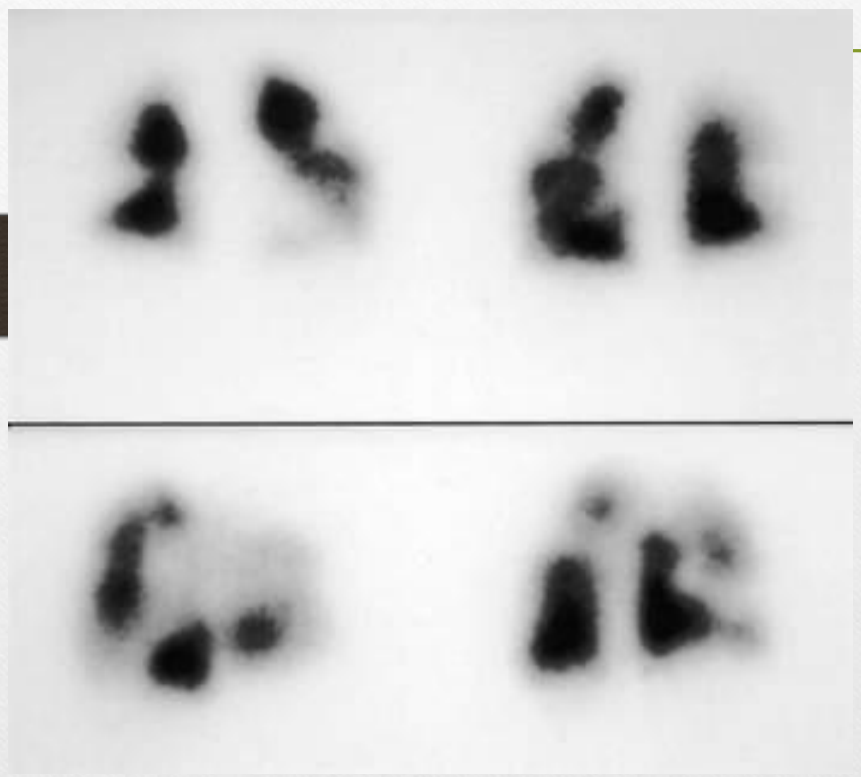
VQ Scan results

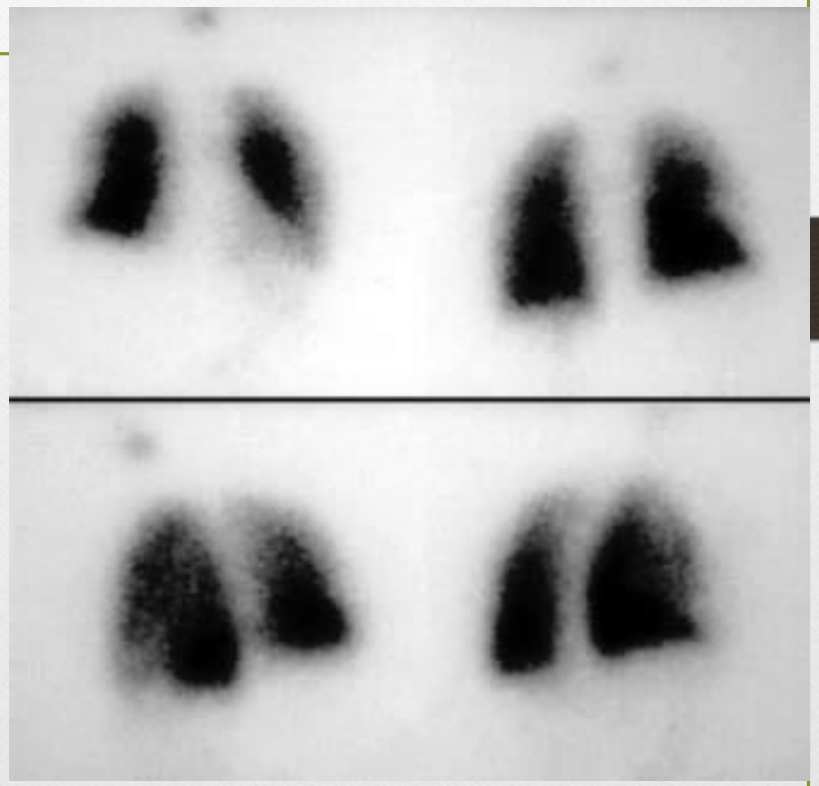
- Presence of several large focal perfusion defects not matched by ventilation defects indicates a high probability of PE !!!!!
- Normal scan basically excludes PE and indicates for other explanations for the pts condition.
- High probability – start Rx.
- Low probability – withhold Rx – can do CT / angiogram.
- Intermediate probability – can do CT / angio

VQ Scan results 1



VQ Scan results 2





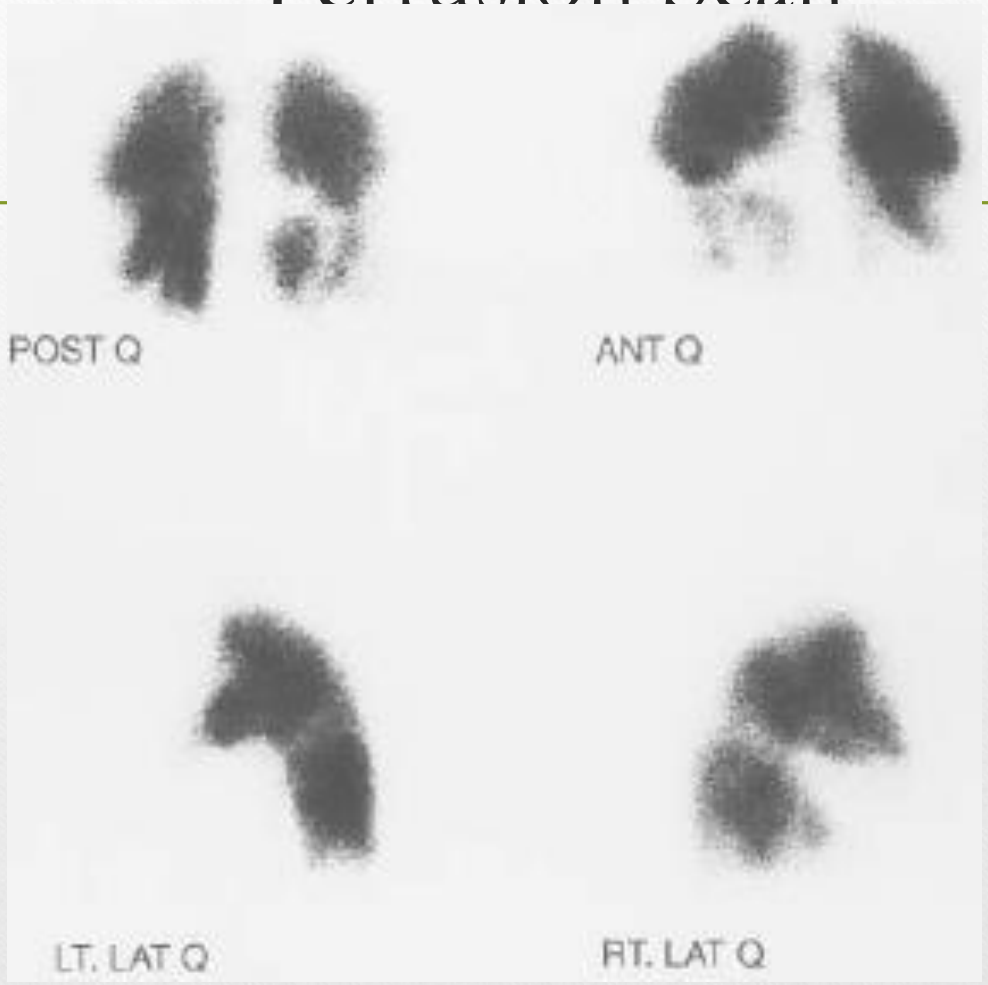
Perfusion

Mismatch

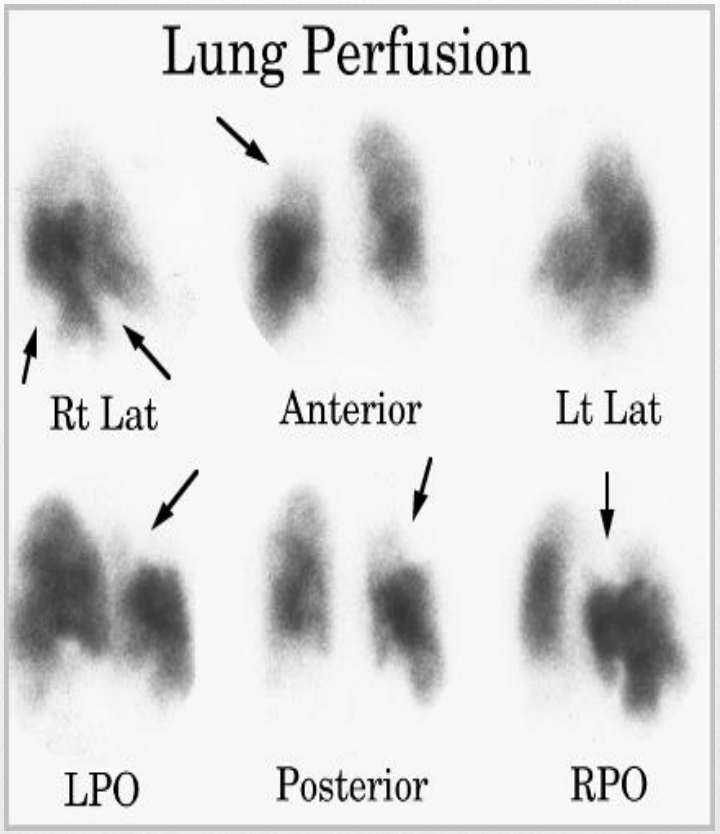
Ventilation

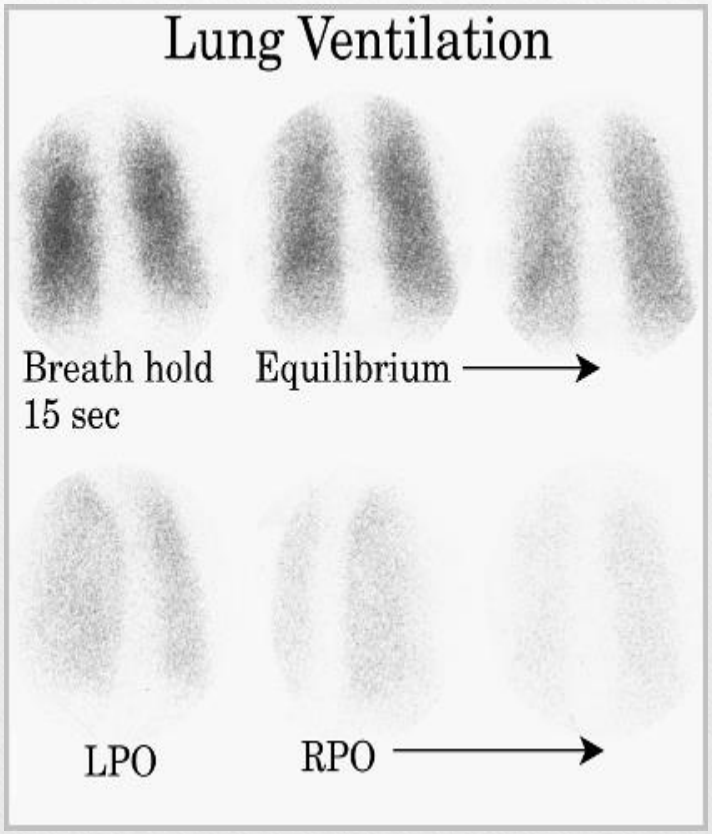
Normal V/Q Scan

Perfusion Scan



High Probability V/Q Scan





Spiral CT

- HRCT (spiral) CT with CT angiography is a promising technique.
- CT unlikely to miss any lesion.
- CT has better sensitivity, specificity and can be used directly to screen for PE.
- CT can be used to follow up “non diagnostic V/Q scans.

Spiral / Multislice CT

- Early problems in scan speed and detecting contrast in coronary arteries
- Bolus tracking system now start scan sequence on arrival of contrast in the pulmonary trunk
- Current protocol 100 mls contrast 20 gauge needle

  3ml / second

Cavitation is observed frequently in septic infarcts, but it is rarely seen in bland infarcts.

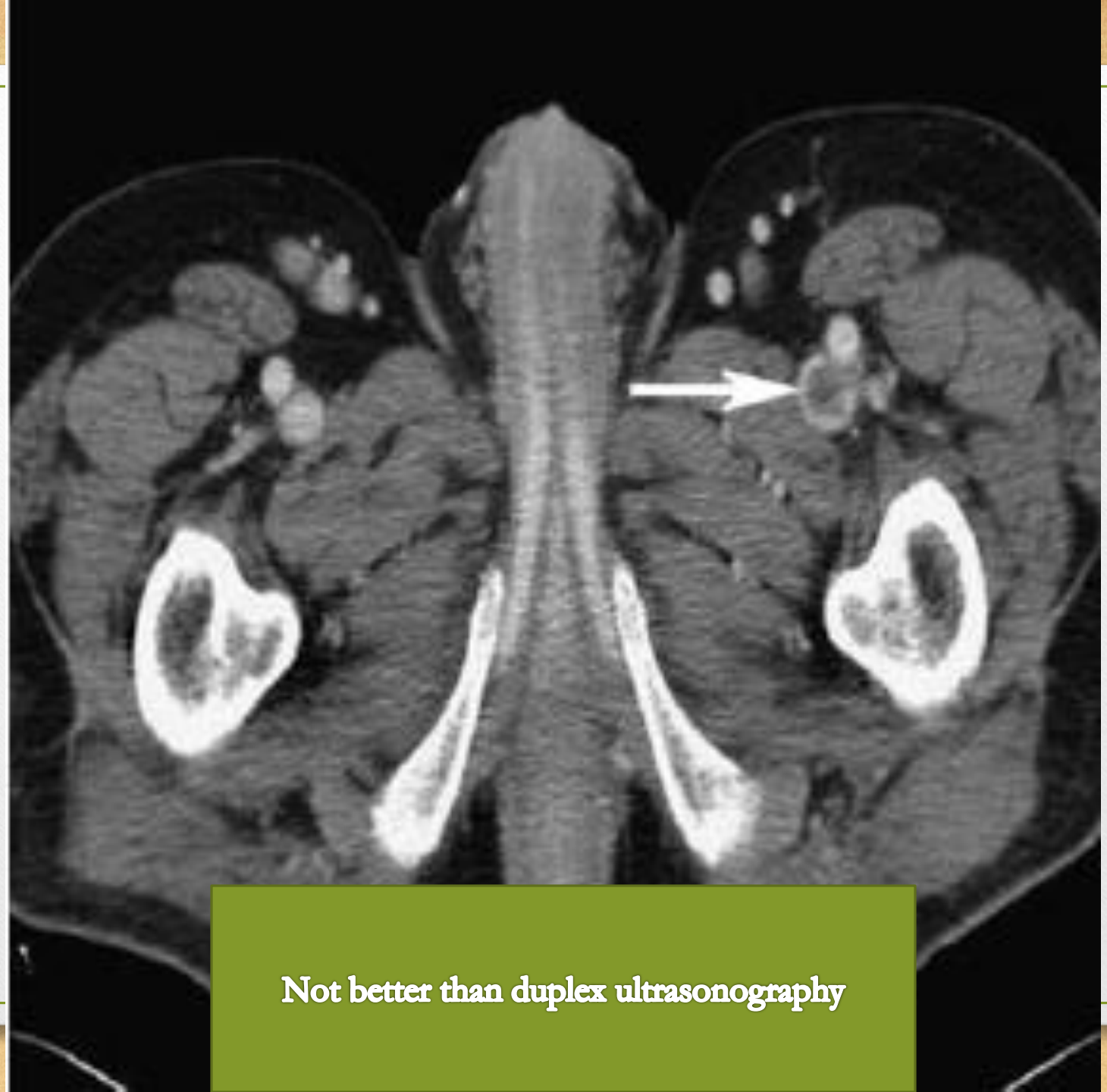
Lower Extremity Evaluation

A number of criteria are used to diagnose venous thrombosis, the most reliable of which is non-compressibility of a venous

segment.

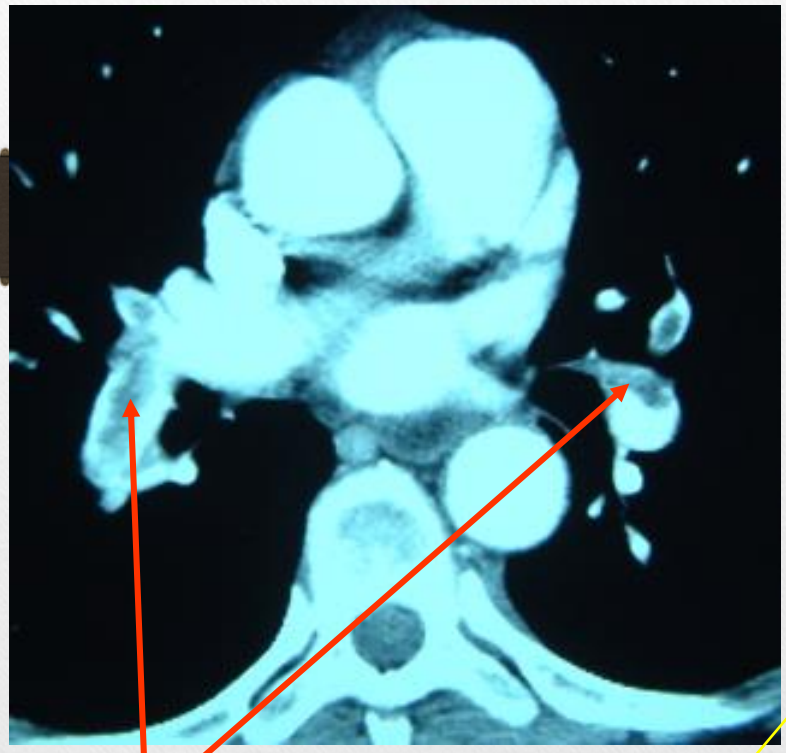
Secondary, less reliable criteria include the presence of echogenic material within the venous lumen, venous distention,

and loss of phasicity, response to Valsalva, and augmentation of spontaneous flow

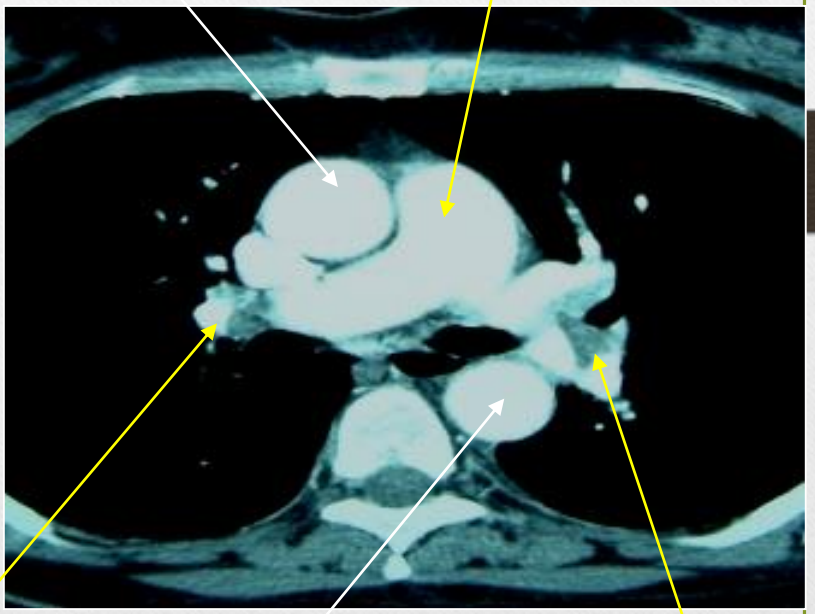


Not better than duplex ultrasonography

Spiral / Multislice CT Results



Thrombus



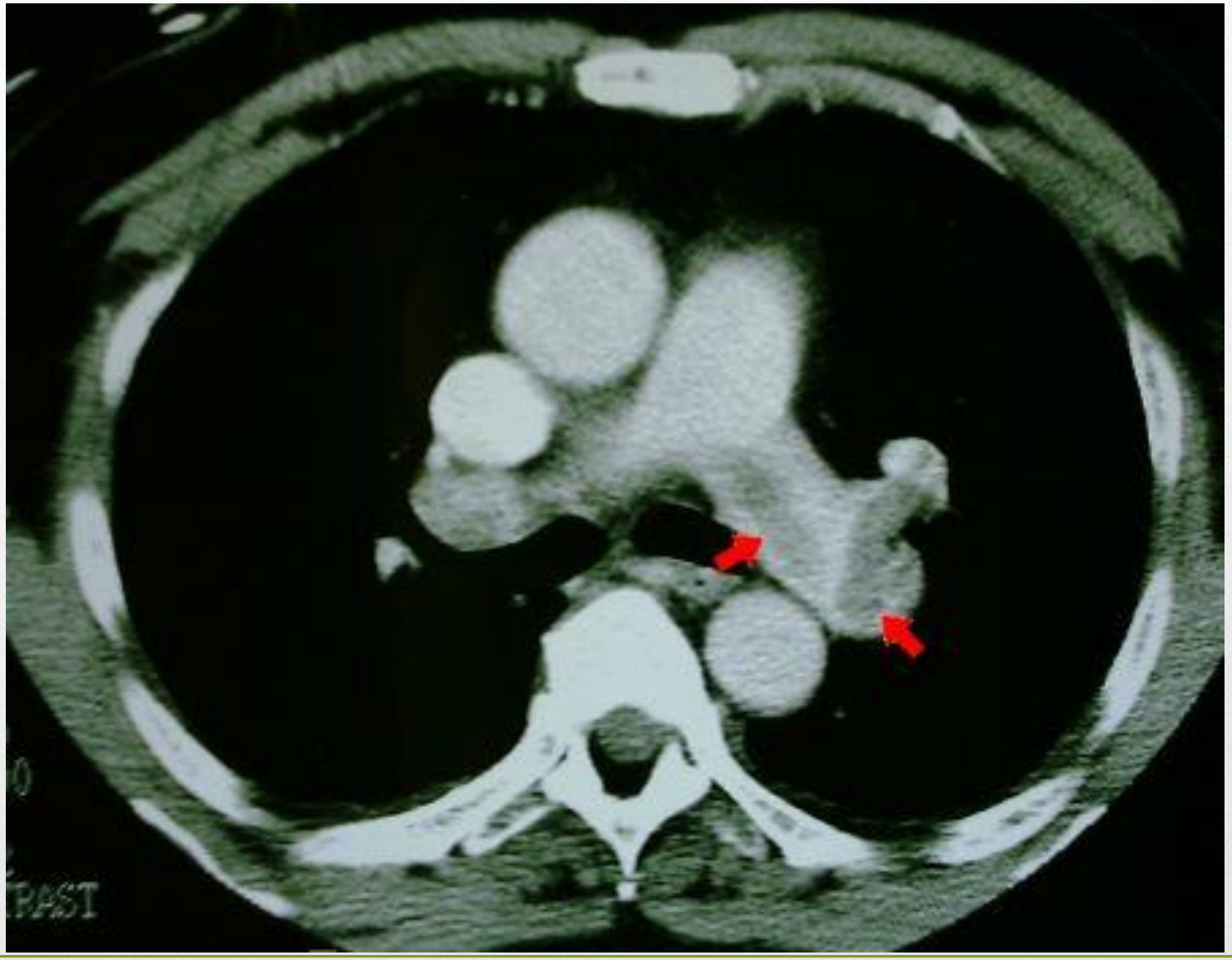
Ascending Aorta

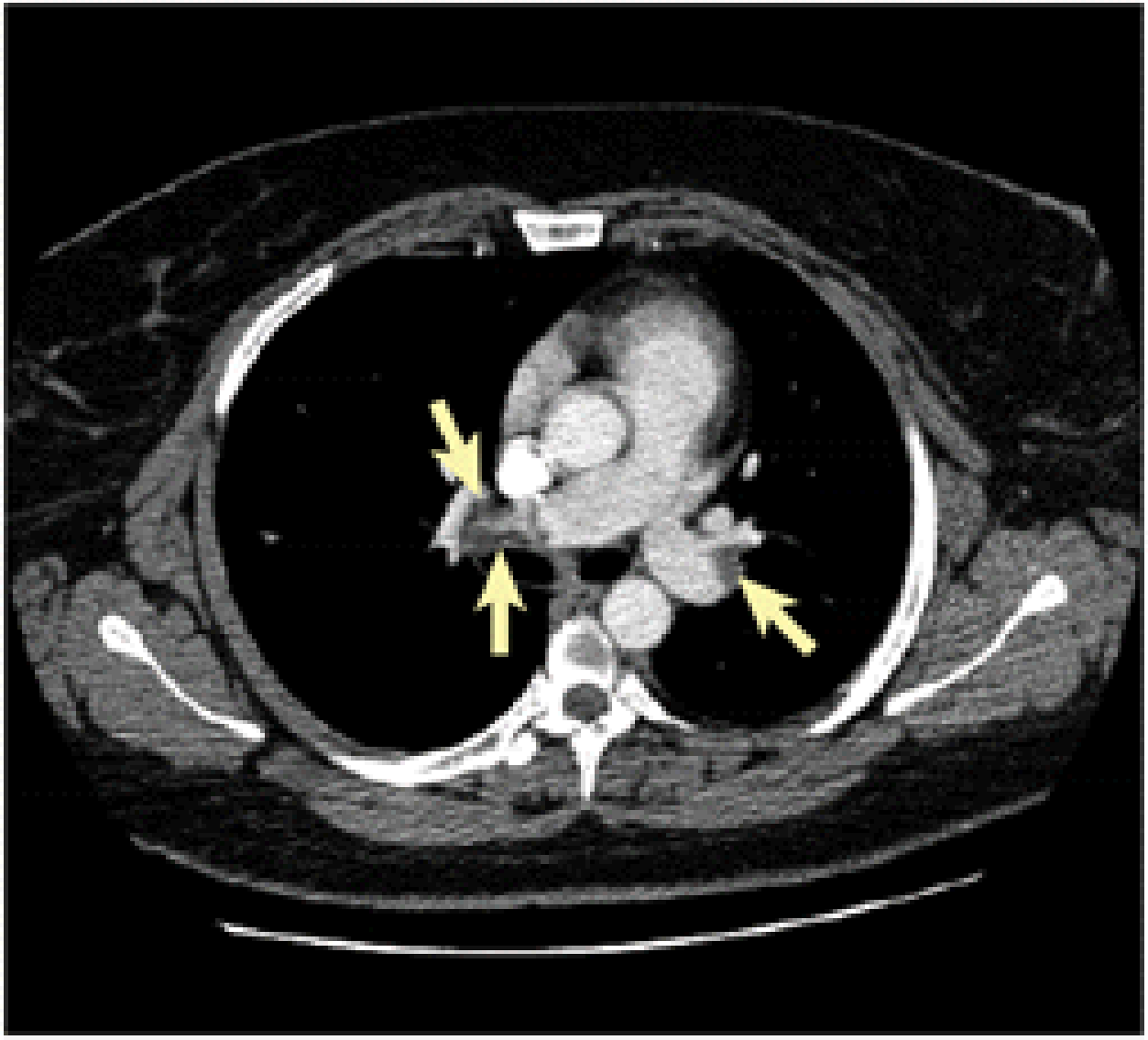
Main Pulmonary Artery

Descending Aorta

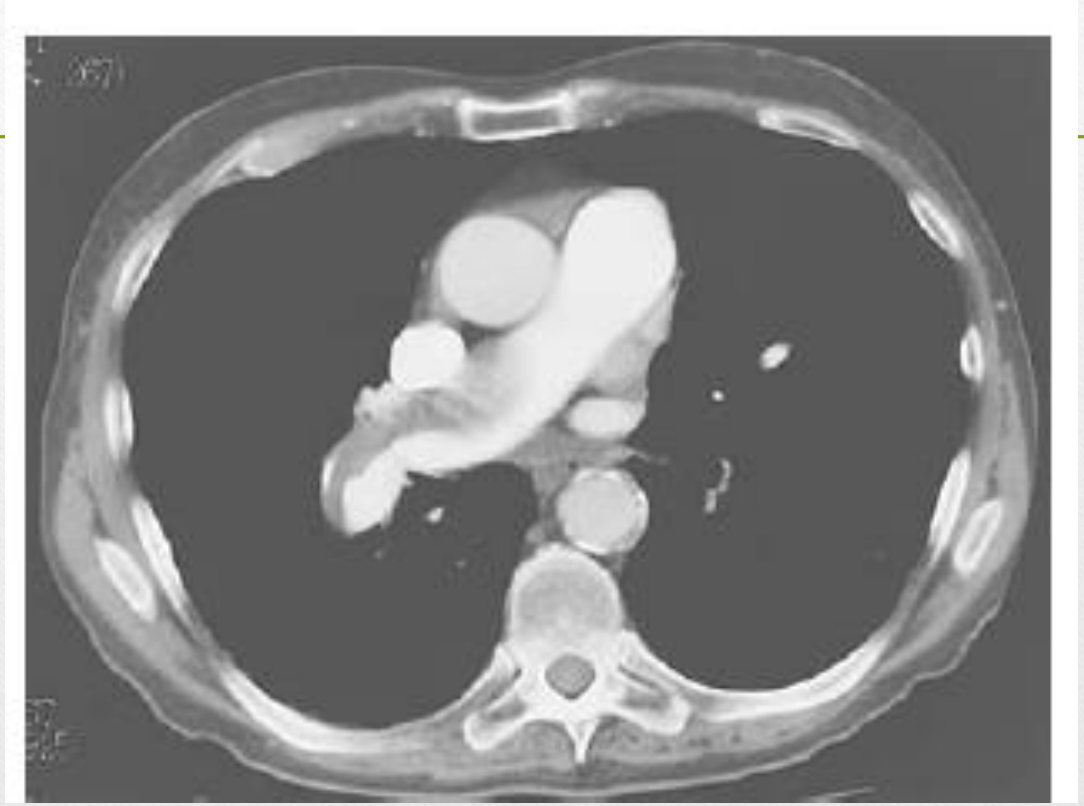
Rt Pulmonary Artery

Lt Pulmonary Artery

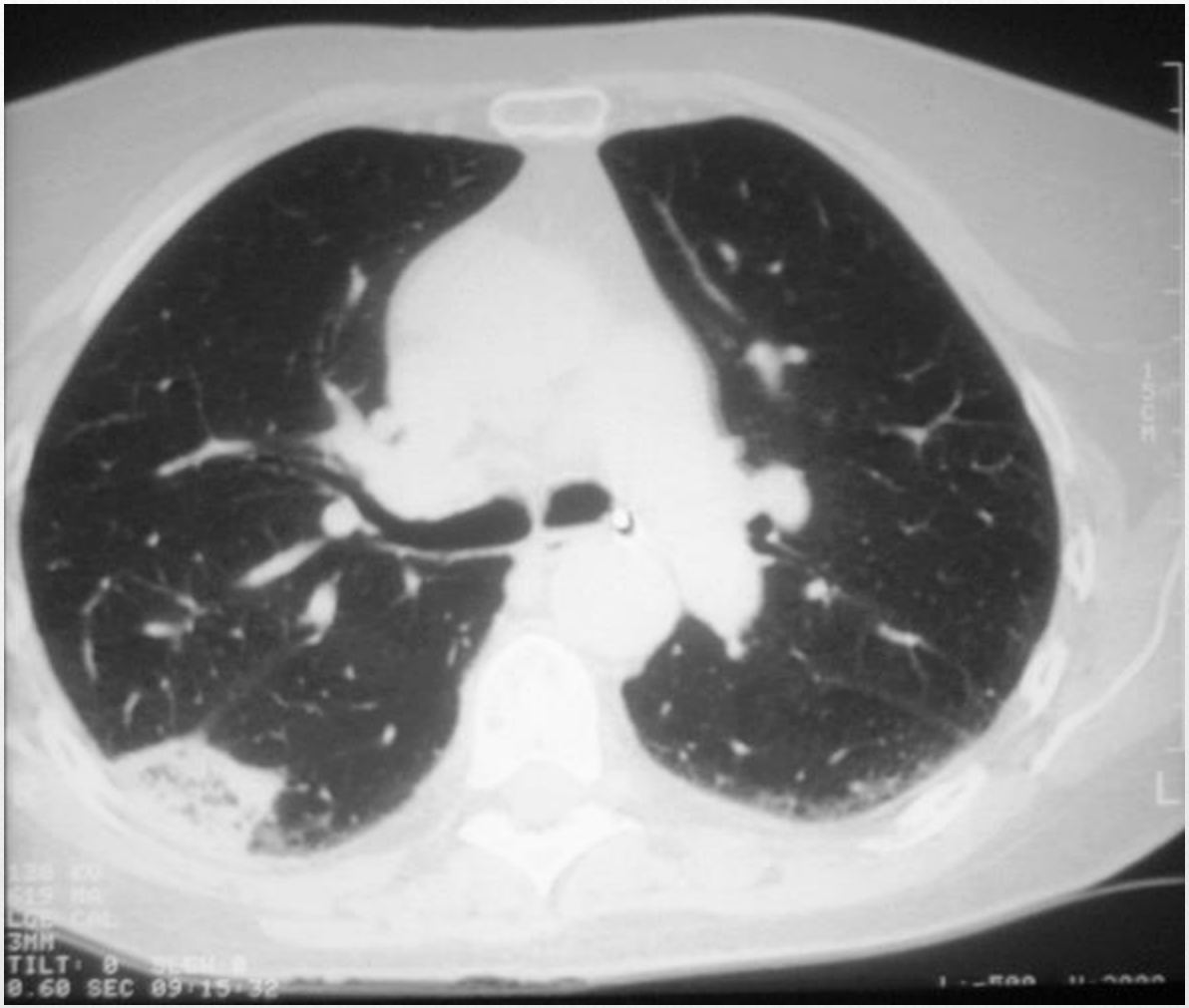




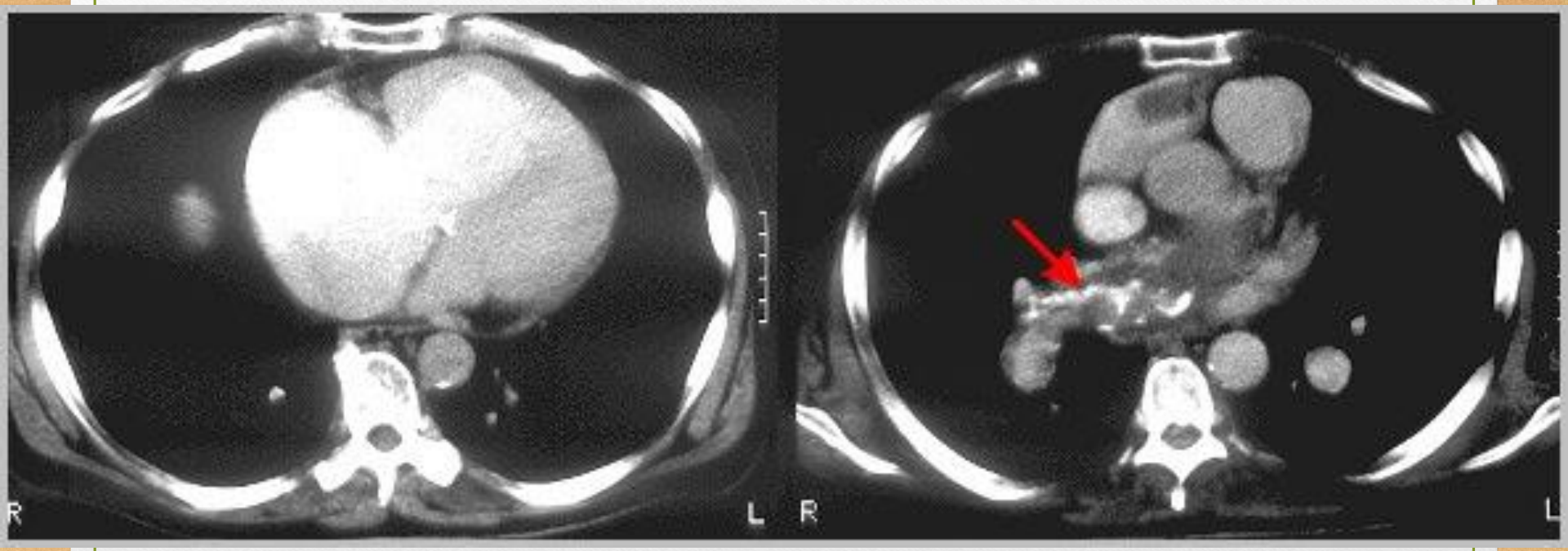
Spiral CT Scan

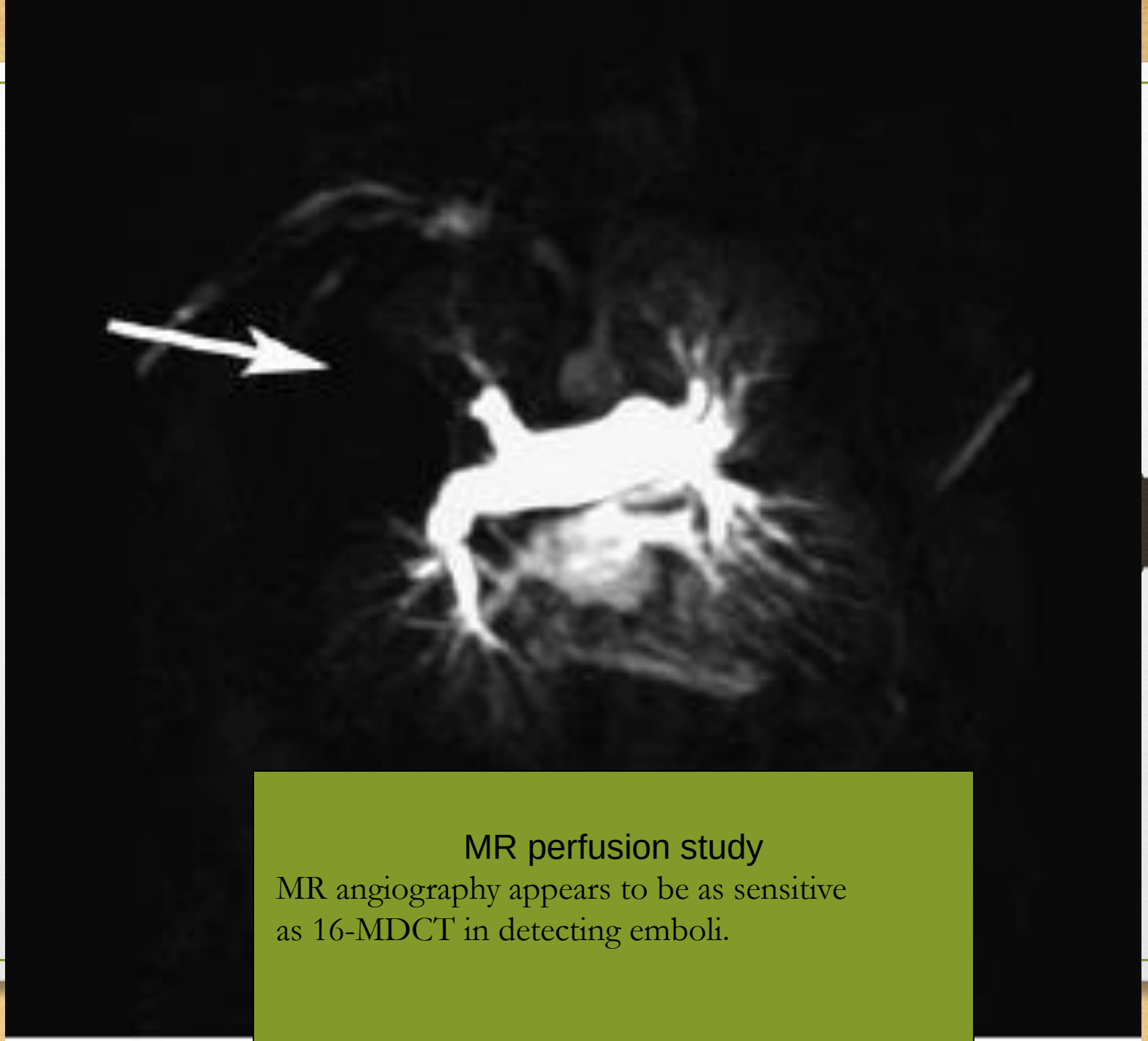


CT revealing pulmonary infarct



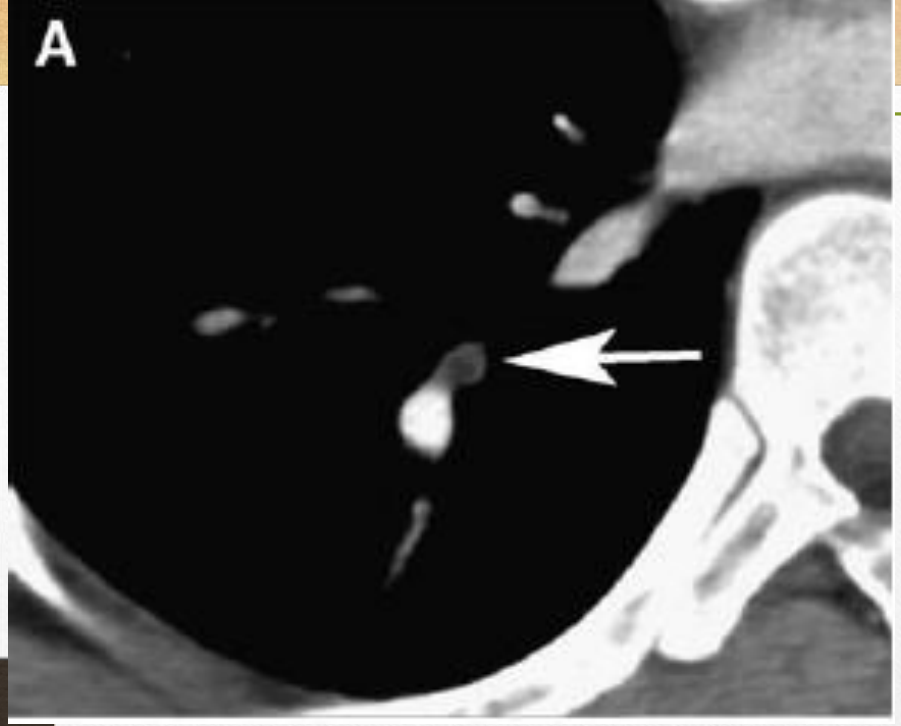
CT revealing emboli in pulmonary artery.

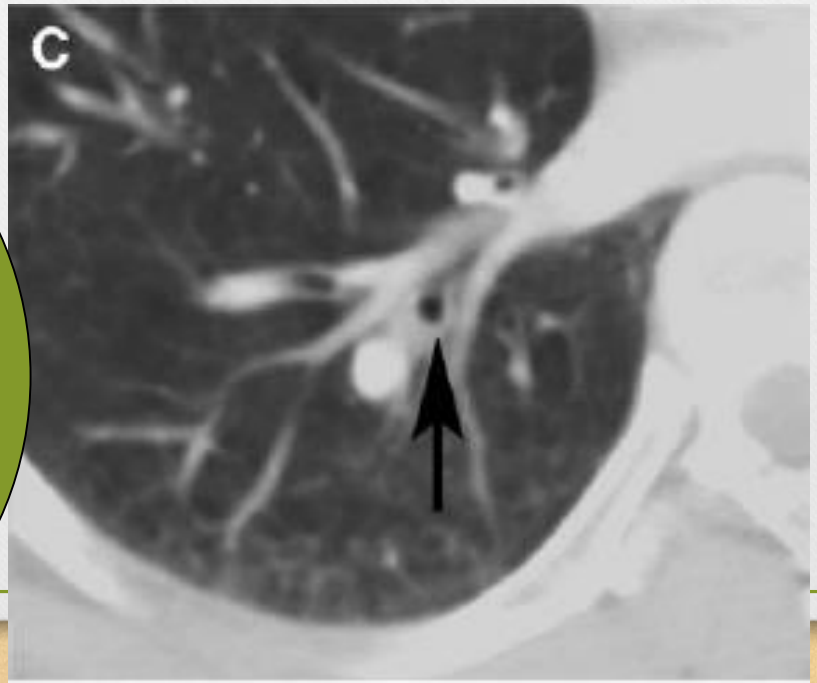




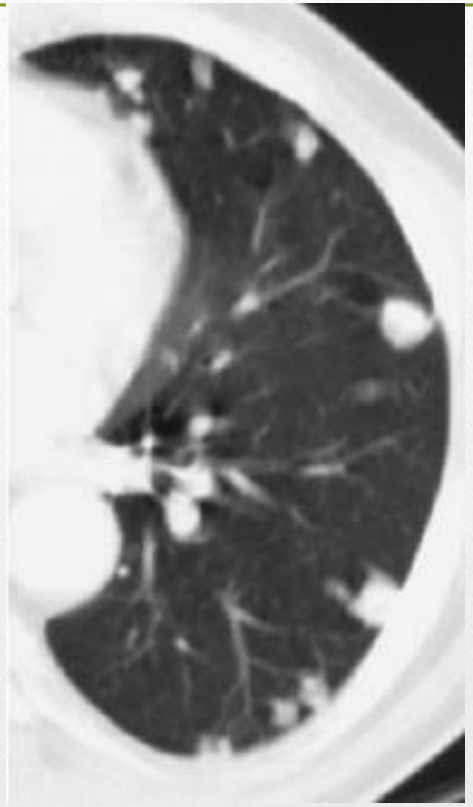
MR perfusion study

MR angiography appears to be as sensitive as 16-MDCT in detecting emboli.



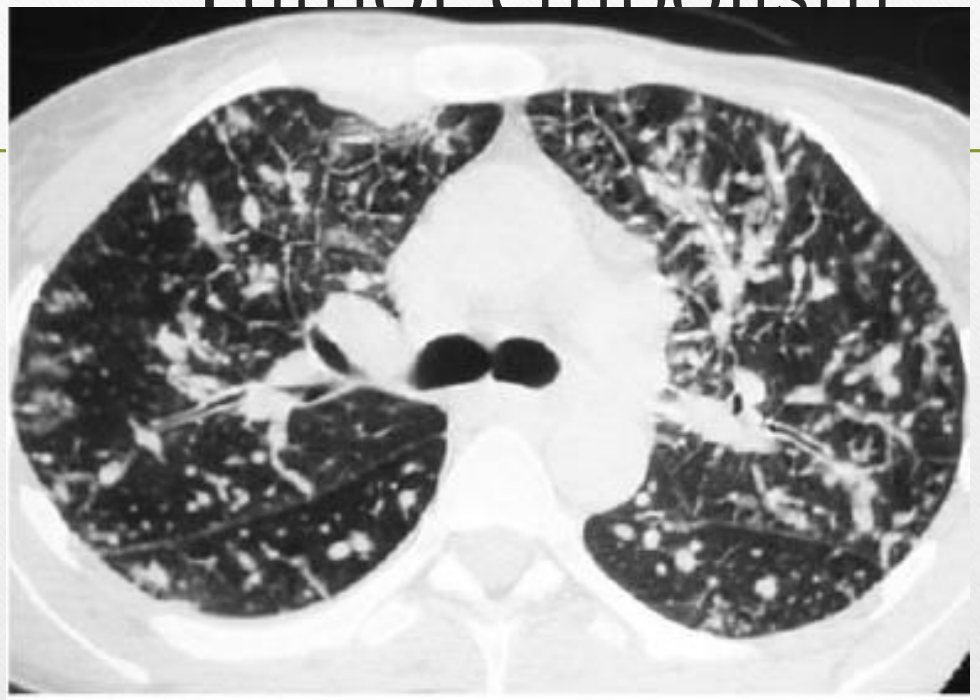


Mucos plug as filling defect



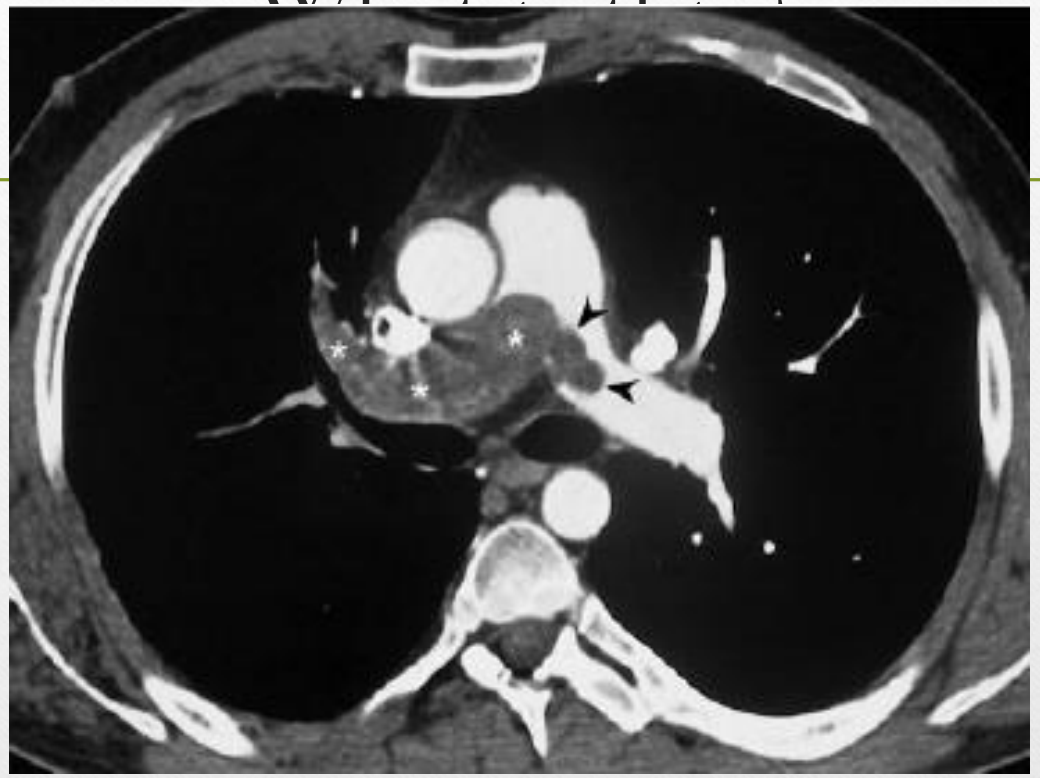
Parasitic emboli

Tumor embolism



RCC,HCC,Breast,Stomach ,Chorocarcioma,MM,Prostate

What is this?



Pulmonary Angiogram

- **GOLD STANDARD**.
- Positive angiogram provides 100% certainty that an obstruction exists in the pulmonary artery.
- Negative angiogram provides > 90% certainty in the exclusion of PE.

Pulmonary Angiogram

- Catherterisation of the subclavian vein
- Catheter
- Subclavian vein – Superior vena cava – right atrium – right ventricle – main pulmonary artery
- Contrast
- DSA

Pulmonary Angiogram

- Catherterisation of the subclavian vein
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- Subclavian vein – Superior vena cava – right atrium – right ventricle – main pulmonary artery
- Contrast
- DSA

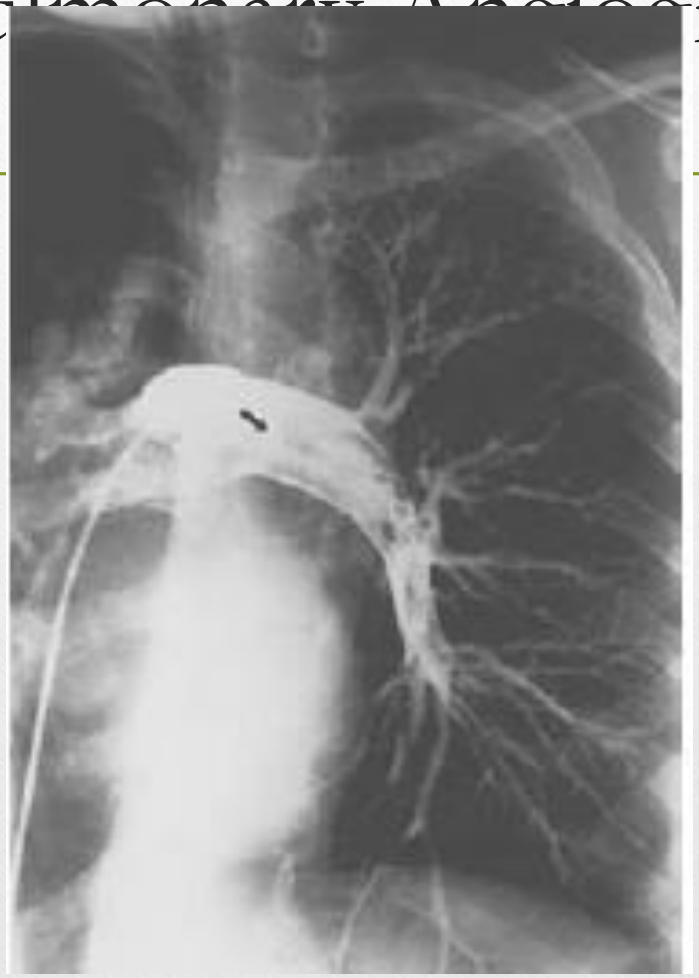
Pulmonary Angiogram

Pulmonary Angiogram

Pulmonary Angiogram

- **<u>Westermark sign</u>** – Dilatation of pulmonary vessels proximal to embolism along with collapse of distal vessels, often with a sharp cut off.

Pulmonary Angiography



TREATMENT

Deep-Venous Thrombosis

PRIMARY THERAPY

SECONDARY PREVENTION

Anticoagulation or placement of an inferior vena cava (IVC) filter constitutes secondary prevention of VTE.

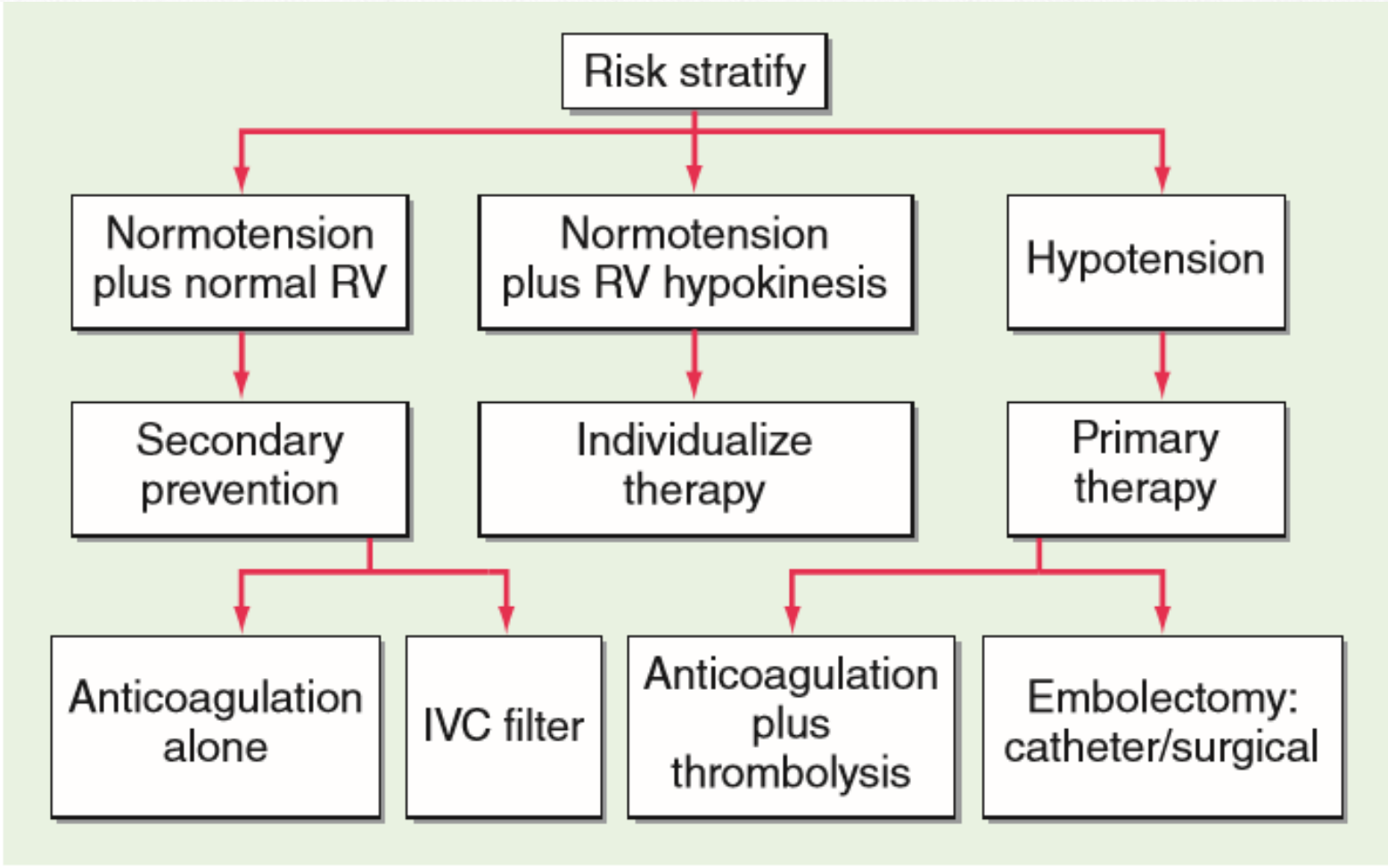


FIGURE 279-12 Acute management of pulmonary thromboembolism. IVC, inferior vena cava; PE, pulmonary embolism; RV, right ventricular.

Treatment

- Emergency treatment and hospitalization are necessary. In cases of severe, life-threatening pulmonary embolism, definitive treatment consists of dissolving the clot with thrombolytic therapy. Anticoagulant therapy prevents the formation of more clots and allows the body to re-absorb the existing clots faster.

Treatment

Thrombolytic therapy (clot-dissolving medication) includes streptokinase, urokinase, or t-PA. Anticoagulation therapy (clot-preventing medication) consists of heparin by intravenous infusion initially, then oral warfarin (Coumadin). Subcutaneous low-molecular weight heparin is often substituted for intravenous heparin in many circumstances.

Thrombolytic therapy

In patients with pulmonary embolism who present with hemodynamic compromise,

patients who develop hemodynamic compromise during conventional therapy with heparin,

patients with embolism associated with intracavitary right heart thrombi

Serologic predictors of recurrence

Residual lower extremity venous thrombosis by ultrasonography,

Elevated D-dimer levels

Elevated Factor VIII levels

An abnormally short aPTT

Treatment

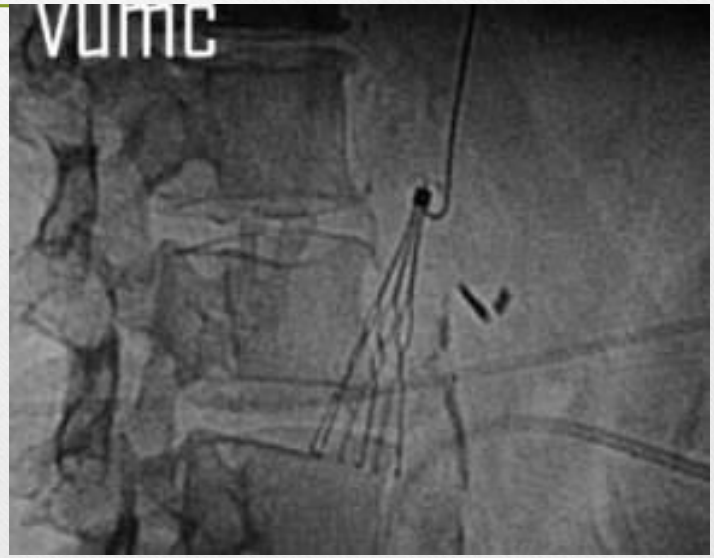
- In patients who cannot tolerate anticoagulation therapy, an inferior vena cava filter (IVC filter) may be placed. This device, placed in the main central vein in the abdomen, is designed to block large clots from traveling into the pulmonary vessels. Oxygen therapy may be required to maintain normal oxygen concentrations.

IVC filter

- A variety of filtering devices can be sited in the inferior vena cava in order to trap thrombus from pelvic and lower limb origins. They are surpassing surgical methods of preventing pulmonary embolus, e.g. femoral vein ligation, because they have a similar efficacy but are associated with a lesser morbidity. They are particularly indicated in patients who have a contraindication to anticoagulation or who have ongoing pulmonary embolism despite full anticoagulation.

IVC filter

- The filter is inserted percutaneously with only local anaesthesia via jugular or femoral routes. The filters are commonly sited below the renal vein.
- Even with a filter, there is a 5% risk of recurrent pulmonary embolus. Similarly, the complication of leg swelling can occur. Hence, anticoagulation is continued for several months.



Complications

- Palpitations
- heart failure or shock
- respiratory distress (severe breathing difficulty)
- sudden death
- hemorrhage (usually a complication of thrombolytic or anticoagulation therapy)
- pulmonary hypertension with recurrent pulmonary embolism

Expectations (prognosis)

- It is difficult to assess the prognosis of pulmonary embolism, because many cases are never diagnosed. Often, the prognosis is related to the disease that puts the person at risk for pulmonary embolism (cancer, major surgery, trauma, etc.). In cases of severe pulmonary embolism, where shock and heart failure occur, the death rate may be greater than 50%

Thanks for your attention!!