Venous Thromboembolism (VTE)

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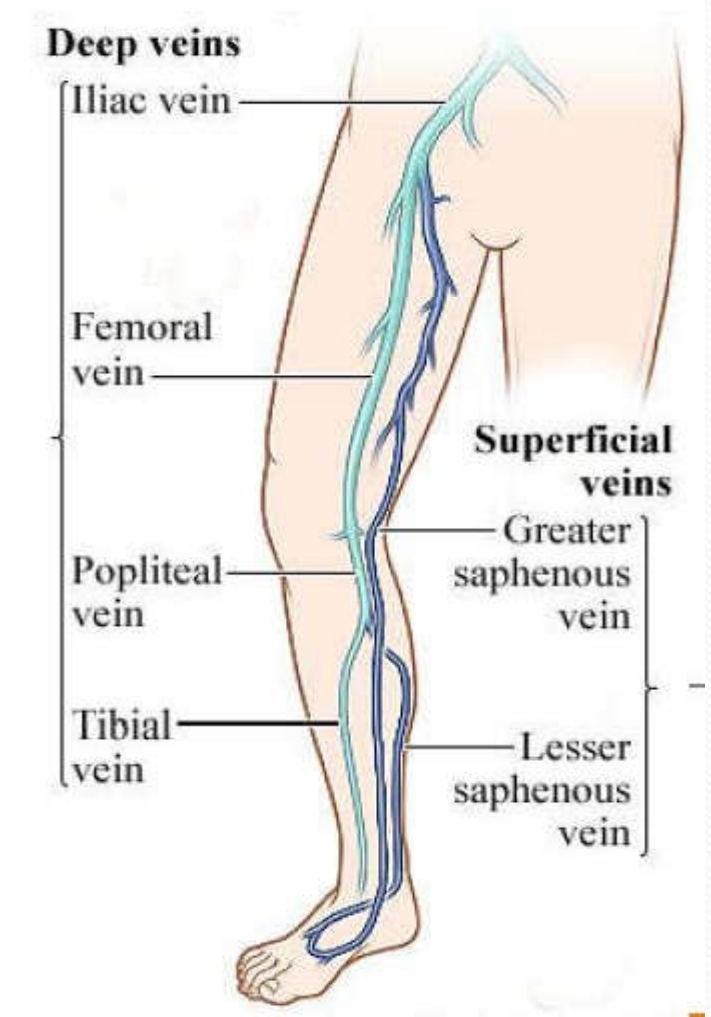
Venous thromboembolism

- A blood clot or thrombus *(thrombo-)* which is usually formed in the systemic veins *(venous)* that eventually dislodges, migrates and embolizes *(-embolism)* into another location in the vascular system.
- Pulmonary arterial system is by far the most common site where thrombus usually embolizes and results in a distal blood flow obstruction with the consequent serious effects. This process is entirely known as pulmonary embolism (PE).
- Deep venous thrombosis (DVT) , where the clot is formed in a deep vein, is by far the most common primary site for VTE.

- PE and DVT is considered as a continuum of one clinical entity (VTE) and diagnosing either PE or DVT is an indication for treatment.

- Thrombosis can occur in any vein of the leg or pelvis, but is particularly found in veins of the calf (commonly iliac/femoral/popliteal veins).

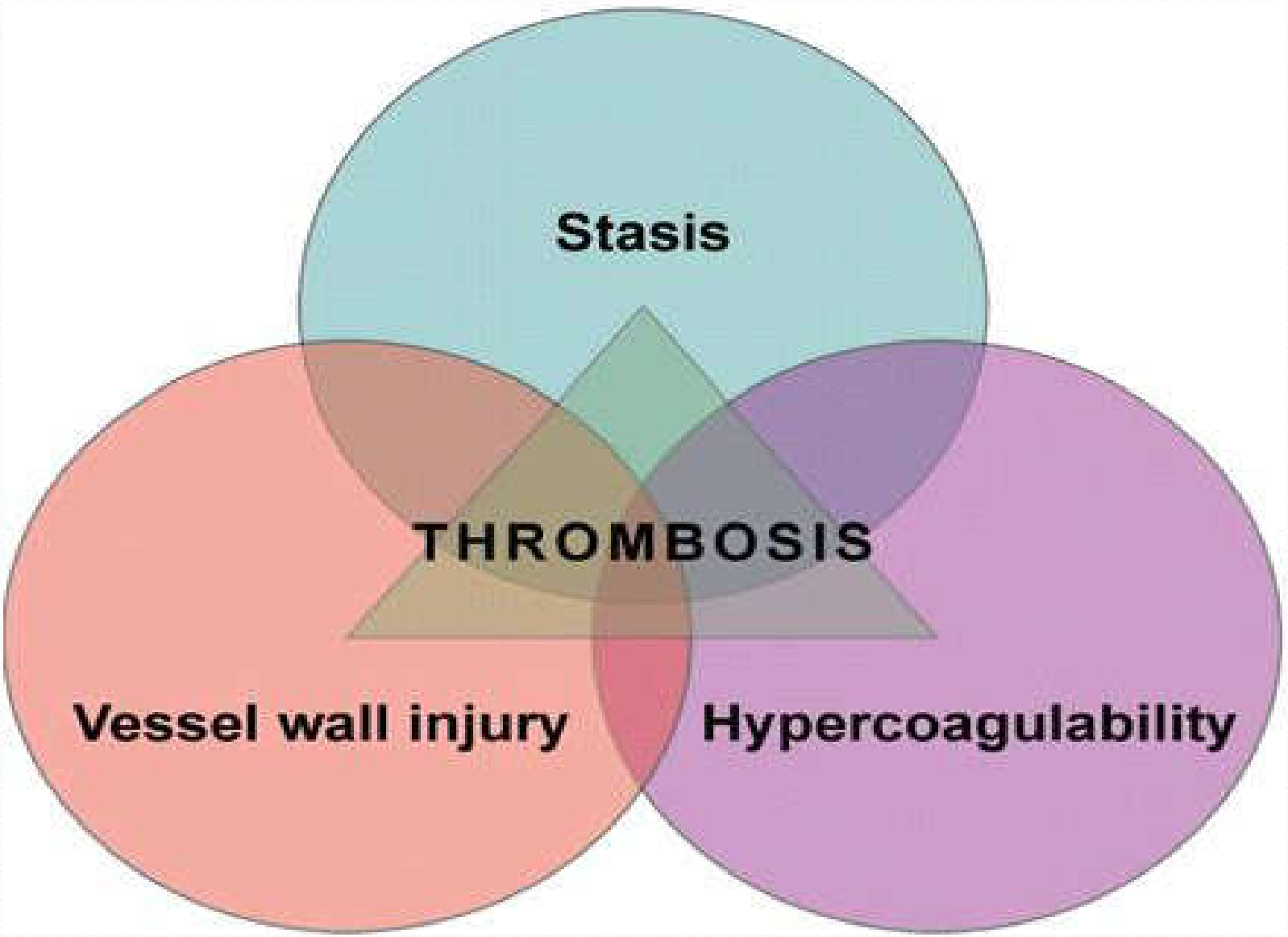
- Axillary vein thrombosis occasionally occurs, sometimes related to trauma, but usually for no obvious reason.



Epidemiology

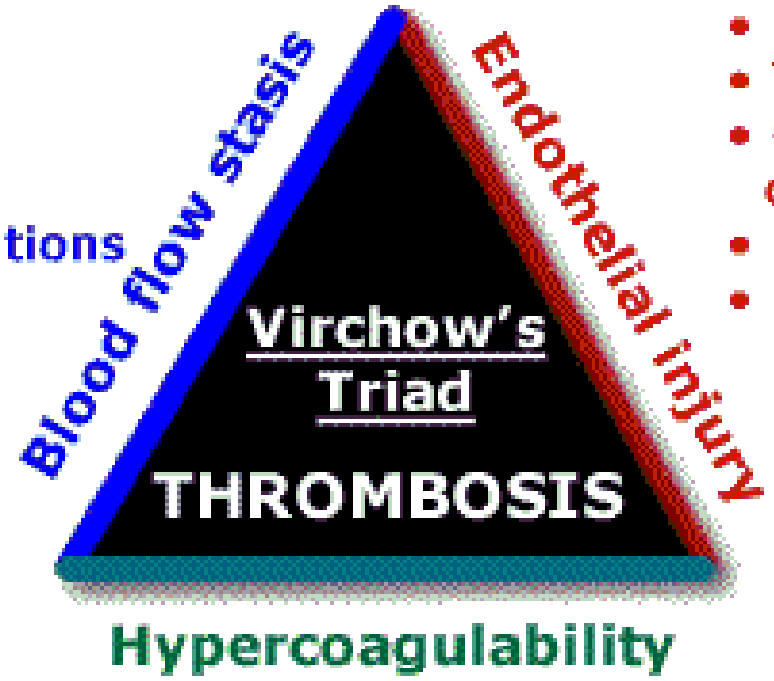
- The incidence of VTE in the community is unknown; it occurs in approximately 1% of all patients admitted to hospital and accounts for around 5% of in-hospital deaths. It is a common mode of death in patients with cancer, stroke and pregnancy.
- Post-mortem studies indicate that this is a very common condition (microemboli in the pulmonary arterial system are found in up to 60% of autopsies) but it is not usually diagnosed this frequently in life. Of clinical pulmonary emboli, 10% are fatal.

Causes are “ Virchow triad ”.



- **Endothelial damage**
  - Endothelium makes natural anticoagulants
- **Stasis of blood**
  - Normal blood flow prevents pooling of clotting factors
- **Hypercoagulability**
  - Conditions that increase clot formation

- Chronic medical conditions
  - Immobility
  - Advanced age
  - Obesity
  - Heart failure
- Acute medical conditions
  - Dehydration
- Spinal cord injury



- Ischemia
- Major surgery
- Trauma
- Central venous catheterization
- Drugs
- Radiation therapy

Inherited hypercoagulability

- Antithrombin deficiency
- Protein C deficiency
- Protein S deficiency
- Factor V Leiden
- Prothrombin gene mutation
- Dysfibinogenemia

Acquired hypercoagulability

- Cancer
- Pregnancy & Postpartum
- Oral contraceptives
- Hormone replacement therapy
- Polycythemia vera
- Smoking
- Antiphospholipid syndrome
- Chemotherapy
- Inflammation

Risk factors

A. Age >60.

B. Malignancy.

C. Prior history of deep venous thrombosis (DVT), PE, or varicose veins.

D. Hereditary hypercoagulable states (factor V Leiden, protein C and S deficiency, antithrombin III deficiency).

E. Prolonged immobilization or bed rest.

F. Cardiac disease, especially CHF.

G. Obesity.

H. Major surgery, especially surgery of the pelvis (orthopedic procedures).

I. Major trauma.

J. Pregnancy, oral contraceptives/estrogen use.

19.94 Risk factors for venous thromboembolism

Surgery

- Major abdominal/pelvic surgery
- Hip/knee surgery
- Post-operative intensive care

Obstetrics

- Pregnancy/puerperium

Cardiorespiratory disease

- COPD
- Congestive cardiac failure
- Other disabling disease

Lower limb problems

- Fracture
- Varicose veins
- Stroke/spinal cord injury

Malignant disease

- Abdominal/pelvic
- Advanced/metastatic
- Concurrent chemotherapy

Miscellaneous

- Increasing age
- Previous proven VTE
- Immobility
- Thrombotic disorders (p. 1054)
- Trauma

- **Post surgery ("post-op state"):**
  - Hypercoagulable (inflammation from surgery)
  - Stasis (immobile)
  - Endothelial damage (surgery)
- **Fall, fracture or trauma:**
  - Hypercoagulable (inflammation from trauma)
  - Stasis (immobility)
  - Endothelial damage (trauma)
- **Long plane flights:**
  - Stasis (immobility)

- **Malignancy**

  - Some tumors produce pro-coagulants (i.e., tissue factor)
  - Inflammation associated with tumor growth
  - Decreased activity, surgery, bed rest

- **Consider occult malignancy with unprovoked venous thrombosis**

  - Absence of surgery, trauma, immobilization or known cancer
  - Limited workup for occult malignancy often done
  - History, physical exam and age-appropriate cancer screening

- **Pregnancy**
  - Probably evolved to protect against blood loss at delivery.
  - Many clotting factor levels change
  - Fetus also obstructs venous return → DVTs common

- **Estrogen-containing oral contraceptives**
  - Estrogen increases production of coagulation factors

- **Nephrotic syndrome**
  - Loss of anti-clotting factors in urine (ATIII)
  - other mechanisms
- **Smoking**
  - Associated with atherosclerosis and MI/Stroke
  - Some data linking smoking to DVT/PE
  - Evidence that smoking increases fibrinogen levels

Common inherited disorders affecting blood coagulability :

- Inherited Thrombophilia.
- Factor V Leiden Mutation; the most common (excessive procoagulant proteins)
- Prothrombin Gene Mutation (excessive procoagulant proteins)
- Antithrombin III Deficiency.
- Protein C or S Deficiency (defective anticoagulant proteins)
- Antiphospholipid Syndrome.

(A) Deep Vein thrombosis (DVT)

- DVT: thrombus within a deep vein.
- Causes are Virchow's triad . . .
- Categories :

A- Upper extremity DVT

Higher risk to develop Pulmonary Embolism (PE)

B- Lower Extremity DVT

More Common than DVT of upper extremity and divided into:

1- Proximal vein thrombosis : In which thrombosis involves the popliteal, femoral, or iliac veins.

2- Distal (calf) vein thrombosis : In which thrombi remain confined to the deep calf veins.

- The rationale that patients with isolated distal DVT are at lower risk of embolization (approximately half the risk) than those with proximal DVT and that in some patients, the distal DVTs resolve spontaneously without therapy.

Clinical presentation

- DVT may be occlusive or non occlusive and the later being more serious.
- The classical features of DVT relate to occlusive thrombus.
- Most patients who die from PE have nonocclusive thrombus and the leg is normal on clinical examination.

- Often asymptomatic until PE (so careful monitoring of the leg, usually by ultrasound, is required).
- Calf pain, unilateral edema (worse with dependency/walking, better with elevation/rest).
- Palpable cord (thrombosed vein).
- Warmth, tenderness, erythema.
- Engorged superficial veins.
- Complete occlusion, particularly of a large vein, can lead to a cyanotic discoloration of the limb and severe edema, which can very rarely lead to venous gangrene.

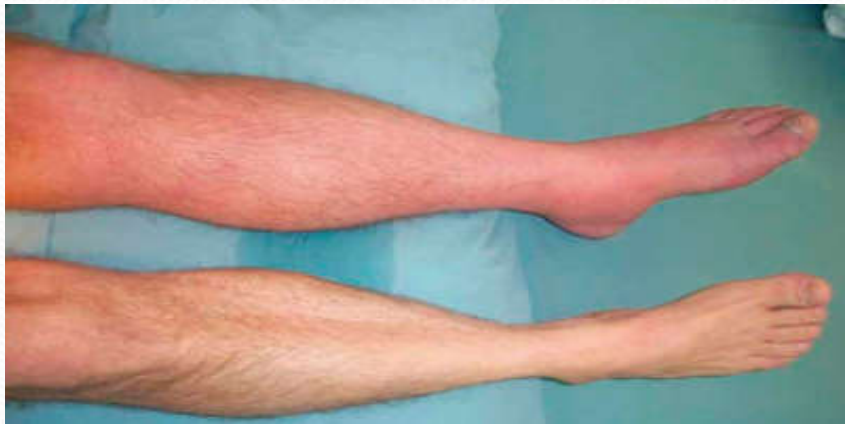
Physical examination

- Physical examination alone is insufficient & unreliable for making a diagnosis of DVT.

(1) The increase in the circumference of the affected leg as compared with the contralateral limb.

(2) Pratt's sign: Squeezing of posterior calf elicits pain.

(3) Homan's sign: calf pain with dorsiflexion of foot but it is not used now because the increase risk of dislocation of the thrombus



Differential diagnosis of a swollen limb:

1-Peripheral vascular disease (acute ischemia).

2-Lymphedema.

3- Baker's cyst.

4- Contusion of calf muscle.

5-Ceullitis.

6-Hematoma.

Investigations

Labs:

- Routine laboratory tests are not useful diagnostically, but may provide clues as to the underlying cause and may influence treatment decisions if DVT is confirmed.

1) Blood Tests:

Complete Blood Count(CBC), platelets count, Protein C and protein S levels, Antithrombin levels, Factor V Leiden mutation.

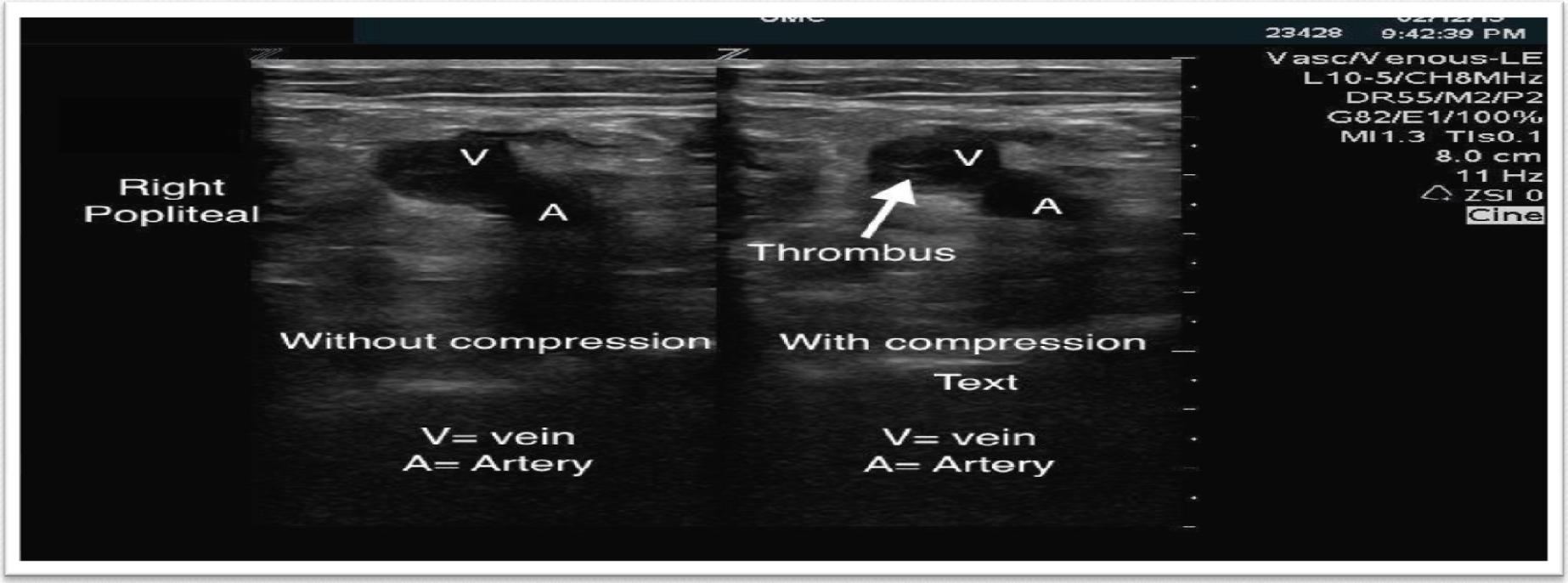
2) Coagulation studies (PT, aPTT).

3) Liver function test (LFT) & kidney function test (KFT).

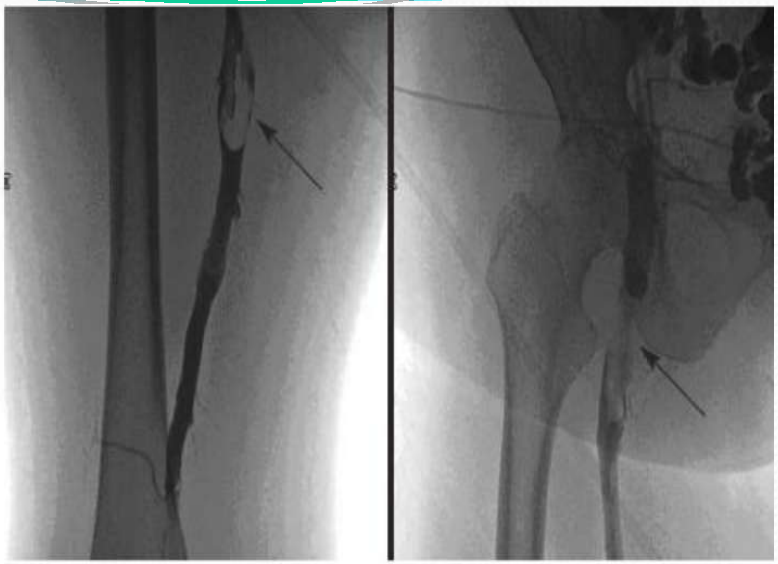
4) Urinalysis.

A. Doppler analysis and Duplex ultrasound.

- Initial test for DVT; noninvasive, but highly operator dependent.
- High sensitivity and specificity for detecting proximal thrombi (popliteal and femoral), not so for distal (calf vein) thrombi.



B. Venography.



- An x-ray test that involves injecting x-ray contrast material into a vein to shows how blood flows through the veins.
- Most accurate test for diagnosis of DVT of calf veins.
- Invasive and infrequently used.
- Allows visualization of the deep and superficial venous systems, and allows assessment of patency and valvular competence.

c. D-dimer testing.

- A small protein fragment present in the blood after a blood clot is degraded by fibrinolysis.
- Has a very high sensitivity (95%), but low specificity (50%); can be used to rule out DVT when combined with Doppler and clinical suspicion.
- It is nonspecific since elevated levels are found in many other conditions (e.g. malignancy, sepsis, recent surgery or trauma, pregnancy, renal failure).
- A negative result (e.g. <500 ng/ml) is useful for ruling out DVT, particularly in those with a low or moderate pre-test probability (PTP) for thrombosis.
- A positive result (e.g. ≥500 ng/ml) is not diagnostic and indicates the need for further investigation.

Causes of high plasma D-dimer

Condition	Mechanism
Thromboembolism: ▪ Arterial • Myocardial infarction • Stroke • Acute limb ischemia • Intracardiac thrombus ▪ Venous • Deep vein thrombosis • Pulmonary embolism ▪ Disseminated intravascular coagulation (DIC)	Intravascular thrombosis and fibrinolysis
Inflammation: ▪ COVID-19 ▪ Other severe infections ▪ Sepsis	Activation of the acute inflammatory response and coagulation pathway, intravascular thrombosis and fibrinolysis
Surgery/trauma	Tissue ischemia, tissue necrosis
Liver disease	Reduced clearance of fibrin degradation products
Kidney disease	Multiple, including renal vein thrombosis and nephrotic syndrome
Vascular disorders: ▪ Vascular malformations ▪ Sickle cell disease vaso-occlusion	Intravascular thrombosis and fibrinolysis
Malignancy	Multiple, including vascular abnormalities, cancer procoagulant, and microvascular thrombosis
Thrombolytic therapy	Fibrin breakdown
Pregnancy: ▪ Normal pregnancy ▪ Preeclampsia and eclampsia	Physiologic changes in the coagulation system Microvascular thrombosis and fibrin deposition

Plasma D-dimer is a product of clot breakdown, released upon degradation of polymerized, crosslinked fibrin (if non-crosslinked fibrinogen was degraded, D-monomers would be released). Elevated plasma D-dimer levels indicate that coagulation has been activated, fibrin clot has formed, and clot degradation by plasmin has occurred. There are many causes of elevated D-dimer; identification of the underlying cause requires correlation with other findings, including the clinical picture and other laboratory results. Refer to UpToDate for further explanation of fibrinogen domain structure and pathophysiology of the disorders listed here.

COVID-19: coronavirus disease 2019.

Modified Wells Score

Prior DVT	1
Active cancer	1
Recent immobilization or bedridden	1
Localized tenderness along venous distribution	1
Leg swelling	1
One leg swollen > other	1
Pitting edema	1
Superficial veins visible	1
Alternative diagnosis likely	-2

Score ≥ 3 High Probability
1-2 Mod Probability
0 Low Probability

A-Low to moderate probability

- D-dimer
- Elevated D-dimer → ultrasound
- If Doppler ultrasound is negative, there is no need for anticoagulation; observation is sufficient.
- Repeat ultrasound in 2 days.

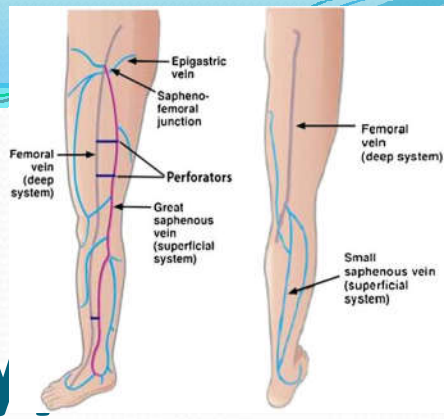
B-High probability

- Ultrasound
- If Doppler ultrasound is positive, begin anticoagulation.
- If Doppler ultrasound is nondiagnostic, repeat ultrasound every 2 to 3 days for up to 2 weeks.

Complications

1. Pulmonary embolus (PE): can originate from the iliofemoral, pelvic, calf, ovarian, axillary, subclavian, and internal jugular veins, as well as the inferior vena cava and cavernous sinuses of the skull.
2. Postthrombotic syndrome.
3. Phlegmasia cerulea.

Postthrombotic syndrome (Chronic Venous Insufficiency



Anatomy

A. The lower-extremity venous system consists of three systems: deep, superficial, and perforating systems.

Valves exist in all three systems, preventing retrograde blood flow.

B. The perforating veins connect the superficial and deep systems.

Valves allow flow from superficial to deep, but not vice versa.

Pathophysiology

A. History of DVT is the underlying cause in many cases, this has two major effects:

(1) It causes destruction of venous valves in the deep venous system. Valvular incompetence results in gravitational pressure of the blood column to be transmitted to ankles.

(2) Valves in the perforator veins are also damaged secondary to the chronically elevated deep venous pressure, inhibiting transmission of blood from superficial to deep, as normally occurs.

B. Leads to ambulatory venous HTN, which has two undesirable effects:

(1) Interstitial fluid accumulation, resulting in edema.

(2) Extravasation of plasma proteins and RBCs into subcutaneous tissues, resulting in brawny induration and pigmentation (a brown-black color) of skin.

C. Eventually leads to reduced local capillary blood flow and hypoxia of tissues.

Even mild trauma may precipitate tissue death and ulcer formation.

Clinical features

1. Swelling and pain of the lower leg. Symptoms are worsened by periods of sitting or inactive standing. Leg elevation provides relief of symptoms.
2. Chronic changes include:

a. Skin changes

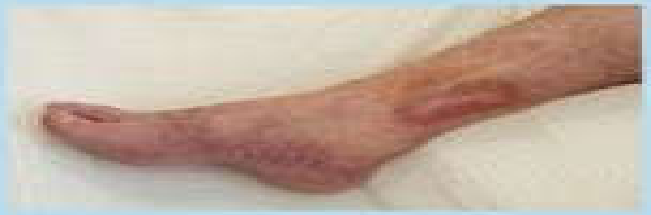
- Skin becomes thin, atrophic, shiny, and cyanotic.
- Brawny induration develops with chronicity.

b. Venous ulcers

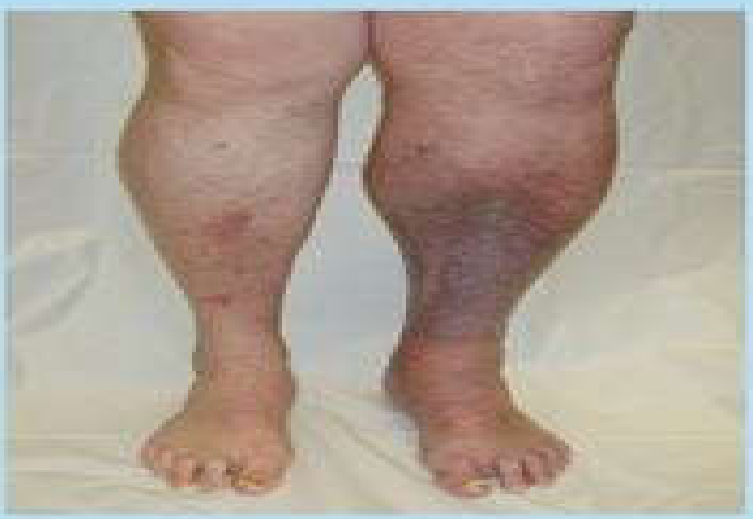
- Less painful than ulcers associated with arterial insufficiency
- Usually located just above the medial malleolus
- Often rapidly recur

Postthrombotic syndrome

Postthrombotic pigmentation

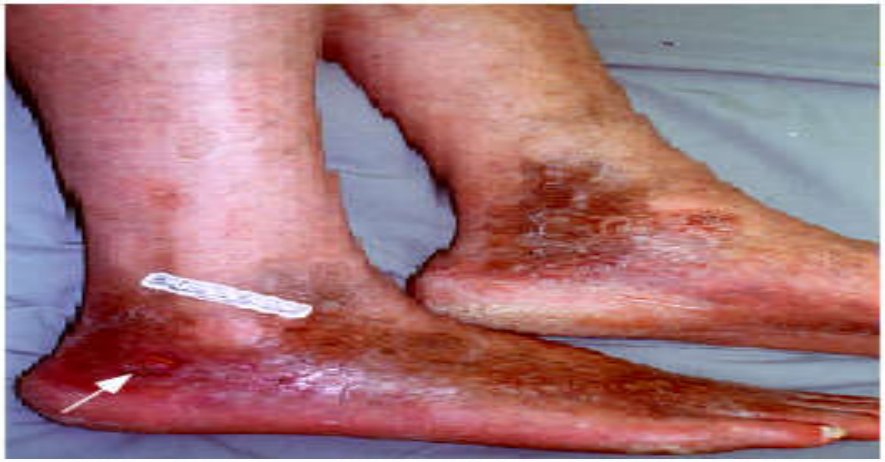


Healed skin ulcer and postthrombotic pigmentation



Chronic (left) leg swelling, skin hardening, and postthrombotic pigmentation

Skin changes of chronic venous insufficiency



Treatment

1. Before the development of ulcers, strict adherence to the following controls stasis sequelae in most patients:

a. Leg Elevation: Periods of leg elevation during the day and throughout the night to a level above the heart.

c. Avoiding long periods of sitting or standing.

d. Heavy-weight elastic stockings (knee-length) are worn during waking hours.

2. If ulcers develop, management also entails:

a. Wet-to-dry saline dressings (three times daily).

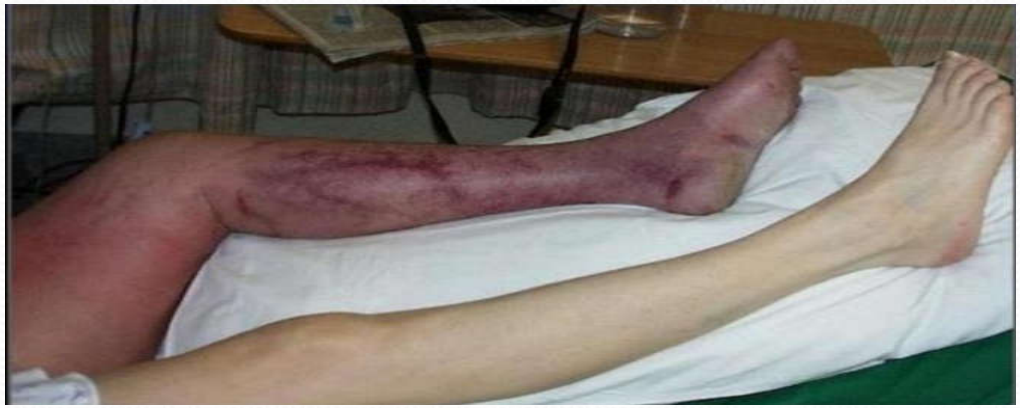
b. Unna venous boot (external compression stocking) — best changed every week to 10 days.

- Healing occurs in 80% of ulcers. Compliance reduces the rate of recurrence.
- For ulcers that do not heal with the Unna boot:

Apply split-thickness skin grafts with or without ligation of adjacent perforator veins.

Phlegmasia cerulean dolens (painful, blue ,swollen leg)

- Occurs in extreme cases of DVT : indicates that major venous obstruction has occurred.
- Sever leg edema compromises arterial supply to the limbs resulting in impaired sensory and motor function.
- Venous thrombectomy is indicated.



Treatment

- The main aim of therapy is to prevent pulmonary embolism, and all patients with thrombi above the knee(proximal DVT) must be anticoagulated.

- Anticoagulation of below-knee thrombi (distal DVT) is now recommended for 6 weeks, as 30% of patients will have an extension of the clot proximally.

- The indication to anticoagulant is stronger for patients with proximal DVT (popliteal, femoral, iliac vein) than with distal DVT (calf vein) because the risk of complications is higher, especially embolization and death.

- Bed rest is advised until the patient is fully anticoagulated.

- The patient should then be mobilized, with an elastic stocking giving graduated pressure over the leg.

1. Anticoagulation therapy.

A. Prevents further propagation of the thrombus.

B. Initial treatment with heparin or LMWH then Transition to oral anticoagulation: Dabigatran ,Rivaroxaban, apixaban or warfarin as the following:

1. Heparin bolus followed by a constant infusion and titrated to maintain the PTT at 1.5 to 2 times aPTT.

2. Start warfarin once the aPTT is therapeutic and continue for 3 to 6 months. Anticoagulate to INR at 2 to 3.

*** Patients with CKD (low GFR):

- Unfractionated heparin
- Warfarin or apixaban

3. Continue heparin until the INR has been therapeutic for 48 hours.

	Heparin	Warfarin
MOA	Inactivates thrombin and factor Xa	Inhibits synthesis of clotting factors
Route	IV or subQ	PO
Teratogenic	Does not cross placenta or into breast milk	Crosses placenta (**teratogenic**)
Onset	Rapid (minutes)	Slow (hours)
Duration	Brief (hours)	Prolonged (days)
Drug interactions	Few drug interactions	Many drug interactions
Elimination	Eliminated renally	Eliminated hepatically
Monitoring	aPTT	PT
Antidote	Protamine	Phytomenadione (Vitamin K)

2. Thrombolytic therapy (streptokinase, urokinase, tissue plasminogen activator [t-PA]).

A. Speeds up the resolution of clots.

B. Indicated mainly for patients with massive PE who are hemodynamically unstable *(hypotension with SBP <90 mm Hg)*, and with no contraindications for thrombolytic.

Thromboectomy

Surgical thrombectomy:

- clear thrombus surgically.

Pharmaco-mechanical thrombectomy (PMT)

- catheter-based devices.
- allow the thrombus to be isolated from the general venous circulation while being laced with thrombolytic. So, reducing systemic effects.

Indications:

- Insufficient response to anticoagulation and thrombolytics.
- Extensive thrombus.

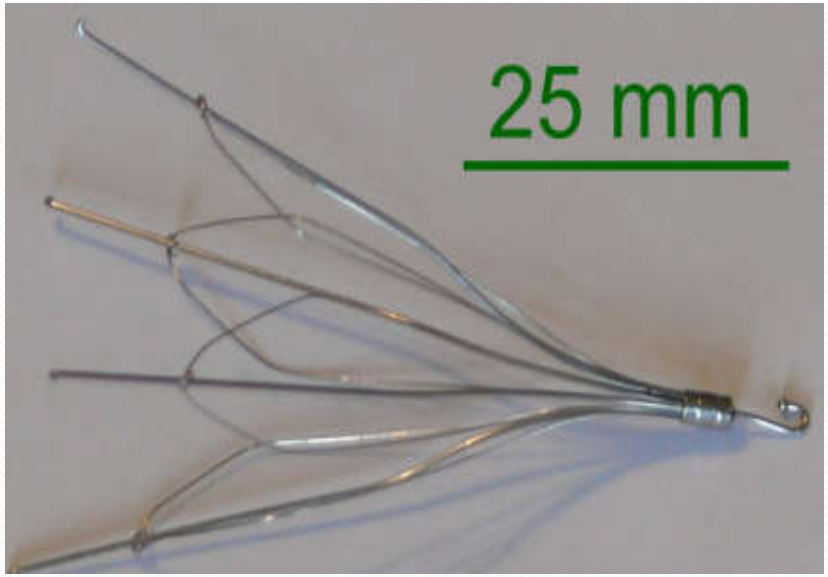
Massive proximal DVT: thrombolysis or surgical thrombectomy.

Inferior vena cava filter placement (Greenfield filter)

a. Indications for treatment of VTE

- If absolute contraindication to anticoagulation (bleeding)
- If failure of appropriate anticoagulation

b. Effective only in preventing PE, not DVT.



Prophylaxis

Methods of prophylaxis after surgery:

A. Mechanical:

- Leg elevation, graduated compression stockings, early ambulation.
- Pneumatic compression boots—intermittently inflate and deflate, causing compression of the limb, usually the calves; very effective.
- IVC filter for patients at high risk for DVT/PE who have an absolute contraindication to other forms of prophylaxis; for example, after trauma or spinal/ orthopedic surgery and have evidence of bleeding.

Prophylaxis (cont.)

B. Pharmacologic:

- Heparin or LMWH: Unfractionated heparin or LMWH postoperatively until patient is ambulatory.

- Combination of pneumatic compression devices and pharmacologic prophylaxis may provide the greatest protection.

(B) Pulmonary Embolism (PE)

- A PE occurs when a thrombus in another region of the body embolizes to the pulmonary vascular tree via the RV and pulmonary artery. Blood flow distal to the embolus is obstructed.

- Sources of Pulmonary emboli :

(1) Lower extremity DVT – the majority of pulmonary emboli.

(2) Septic emboli (from endocarditis affecting the tricuspid or pulmonary valves), tumour (especially choriocarcinoma), fat, air, amniotic fluid, placenta and foreign material during IV drug use.

Pathophysiology

A. Emboli block a portion of pulmonary vasculature, leading to increased pulmonary vascular resistance, pulmonary artery pressure, and right ventricular pressure. If it is severe (large blockage), acute cor pulmonale may result.

B. Blood flow decreases in some areas of the lung. Dead space is created in areas of the lung in which there is ventilation but no perfusion. The resulting hypoxemia and hypercarbia drive respiratory effort, which leads to tachypnea.

C. If the size of the dead space is large (large PE), clinical signs are more overt (SOB, tachypnea).

Course and prognosis

- Most often, PE is clinically silent. Recurrences are common, which can lead to development of chronic pulmonary HTN and chronic cor pulmonale.
- When PE is undiagnosed, mortality approaches 30%. A significant number of cases are undiagnosed (as many as 50%).
- When PE is diagnosed, mortality is 10% in the first 60 minutes. Treatment with anticoagulants decreases the mortality to 2% to 8%.
- Immediate morality is greatest in those with echocardiographic evidence of right ventricular dysfunction or cardiogenic shock. The risk of recurrence is highest in the first 6–12 months after the initial event, and at 10 years around one-third of individuals will have suffered a further event.

Clinical features

- **Symptoms:**

  Dyspnea, pleuritic chest pain, cough & hemoptysis.

  - Only 1/3 of patients with PE will have s/s of a DVT

  - Syncope seen in large PE

- **Signs:**

  Tachypnea, crackles, tachycardia ,loud S4 & increased p2.

  - Shock with rapid circulatory collapse in massive PE

  - other signs: low-grade fever, decreased breath sounds and dullness on percussion.

- Signs and symptoms are not a reliable indicators of the presence of PE. This often leads to confusion and delay in diagnosis and treatment. *If, however, a patient has symptoms of PE and a DVT is found, one can make the diagnosis of PE without further testing*.

- Clinical presentation varies, depending on number, size and distribution of emboli and on underlying cardiorespiratory reserve.

- Categories :

(1) *Small/medium pulmonary embolism*

(2) *Massive pulmonary embolism*

(3) *Multiple recurrent pulmonary emboli*

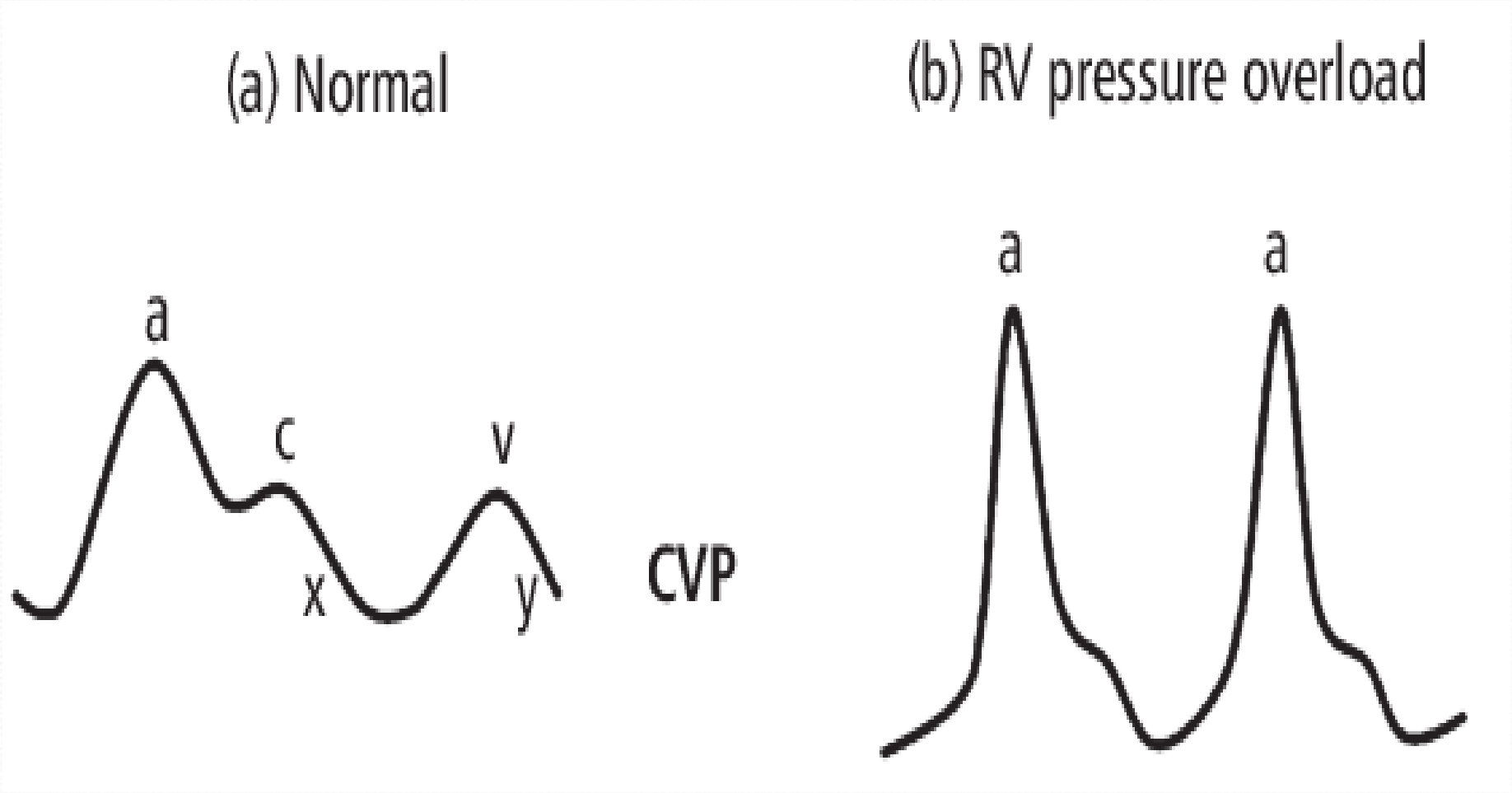
1- Small/medium pulmonary embolism

- In this situation an embolus has impacted in a terminal pulmonary vessel.
- Symptoms are pleuritic chest pain and breathlessness. Haemoptysis occurs in 30%, often ≥3 days after the initial event.
- **On examination**: the patient may be tachypneic with a localized pleural rub and often coarse crackles over the area involved. An exudative pleural effusion (occasionally blood-stained) can develop.

2- Massive pulmonary embolism

- This is a much rarer condition where sudden collapse occurs because of an acute obstruction of the right ventricular outflow tract.
- The patient has severe central chest pain (cardiac ischaemia due to lack of coronary blood flow) and becomes shocked, pale and sweaty.
- Syncope may result if the cardiac output is transiently but dramatically reduced, and death may occur.
- **On examination**: the patient is tachypneic, has a tachycardia with hypotension and peripheral shutdown. *The jugular venous pressure (JVP) is raised with a prominent 'a' wave. There is a right ventricular heave, a* gallop rhythm and a widely split S2.

JVP waveform



prominent '*a*' *wave*

3- Multiple recurrent pulmonary emboli

- This leads to increased breathlessness, often over weeks or months. It is accompanied by weakness, syncope on exertion and occasionally angina.
- The physical signs are due to the pulmonary hypertension that has developed from multiple occlusions of the pulmonary vasculature.
- **On examination:** there are signs of right ventricular overload with a right ventricular heave and loud pulmonary second sound.

19.93 Features of pulmonary thromboemboli

	Acute massive PE	Acute small/medium PE	Chronic PE
Pathophysiology	Major haemodynamic effects: ↓cardiac output; acute right heart failure	Occlusion of segmental pulmonary artery → infarction ± effusion	Chronic occlusion of pulmonary microvasculature, right heart failure
Symptoms	Faintness or collapse, crushing central chest pain, apprehension, severe dyspnoea	Pleuritic chest pain, restricted breathing, haemoptysis	Exertional dyspnoea. Late symptoms of pulmonary hypertension or right heart failure
Signs	Major circulatory collapse: tachycardia, hypotension, ↑JVP, RV gallop rhythm, loud P_2, severe cyanosis, ↓urinary output	Tachycardia, pleural rub, raised hemidiaphragm, crackles, effusion (often blood-stained), low-grade fever	May be minimal early in disease. Later: RV heave, loud P_2. Terminal: signs of right heart failure
Chest X-ray	Usually normal. May be subtle oligaemia	Pleuropulmonary opacities, pleural effusion, linear shadows, raised hemidiaphragm	Enlarged pulmonary artery trunk, enlarged heart, prominent right ventricle
ECG	$S_1Q_3T_3$ anterior T-wave inversion, RBBB	Sinus tachycardia	RV hypertrophy and strain
Arterial blood gases	Markedly abnormal with ↓PaO_2 and ↓$PaCO_2$. Metabolic acidosis	May be normal or ↓PaO_2 or ↓$PaCO_2$	Exertional ↓PaO_2 or desaturation on formal exercise testing
Alternative diagnoses	Myocardial infarction, pericardial tamponade, aortic dissection	Pneumonia, pneumothorax, musculoskeletal chest pain	Other causes of pulmonary hypertension

Investigations in pulmonary embolism

- VTE causing PE may be difficult to diagnose. It is helpful to consider:
  - Is the clinical presentation consistent with PE?
  - Does the patient have risk factors for PE?
  - Are there any alternative diagnoses that can explain the patient's presentation?
- Why PE and DVT are problematic for physicians?
  - Clinical findings are sometimes subtle in both.
  - Noninvasive imaging tests do not always detect either condition.
  - Anticoagulation carries significant risk.

CLINICAL PEARL 2-14

Workup of PE

It is often difficult to definitively diagnose or rule out PE. The following tests provide an adequate basis for treating PE with anticoagulation:

- Intraluminal filling defects in central, segmental, or lobular pulmonary arteries on CTA
- DVT diagnosed with ultrasound and clinical suspicion
- Positive pulmonary angiogram (definitely proves PE)

The following can essentially rule out PE:

- Low-probability V/Q scan (*or* normal helical scan) **and** low clinical suspicion
- Negative pulmonary angiogram (definite)
- Negative D-dimer assay plus low clinical suspicion

Adapted from PIOPED data. *JAMA* 1990;263:2753.

CLINICAL PEARL 2-15

Dichotomized Clinical Decision Rule for Suspected Acute Pulmonary Embolism (Modified Wells Criteria)

Factor	Points
Symptoms and signs of DVT	3.0
Alternative diagnosis less likely than PE	3.0
Heart rate >100 beats/min	1.5
Immobilization (>3 days) or surgery in previous 4 wks	1.5
Previous DVT or PE	1.5
Hemoptysis	1.0
Malignancy (current therapy, or in previous 6 months, or palliative)	1.0

Score ≤4 indicates that PE is unlikely, score >4 indicates that PE is likely.

Investigations include:

- Chest X-ray
- ECG
- Blood test
- Plasma D-dimer
- Arterial blood gases
- Radionuclide ventilation/perfusion scanning
- Doppler ultrasound
- CT Angiography
- MRI
- Pulmonary Angiography (DSA)

- ***Chest X-ray is often normal, but linear atelectasis* or blunting of a costophrenic angle (due to a small effusion) is not uncommon**.
- These features develop only after some time. A raised hemidiaphragm is present in some patients. More rarely, a wedge-shaped pulmonary infarct (Hampton's hump), the abrupt cut-off of a pulmonary artery or a translucency of an underperfused distal zone is seen. Previous infarcts may be seen as opaque linear scars.
- CXR is most useful in excluding key differential diagnoses, e.g. Pneumonia or pneumothorax.
- Normal appearances in an acutely breathless and hypoxemic patient should raise the suspicion of PE, as should bilateral changes in a patient presenting with unilateral pleuritic chest pain.

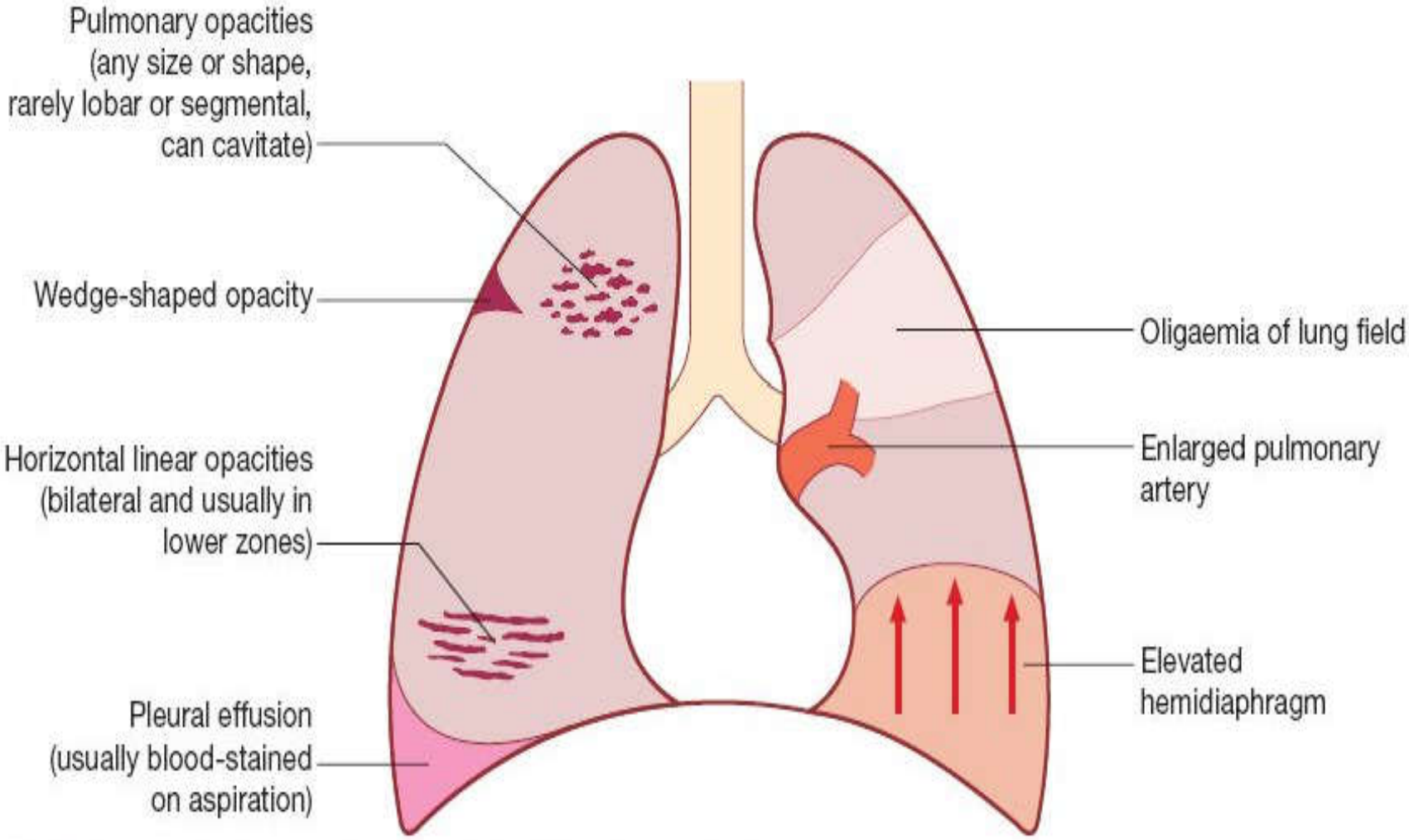
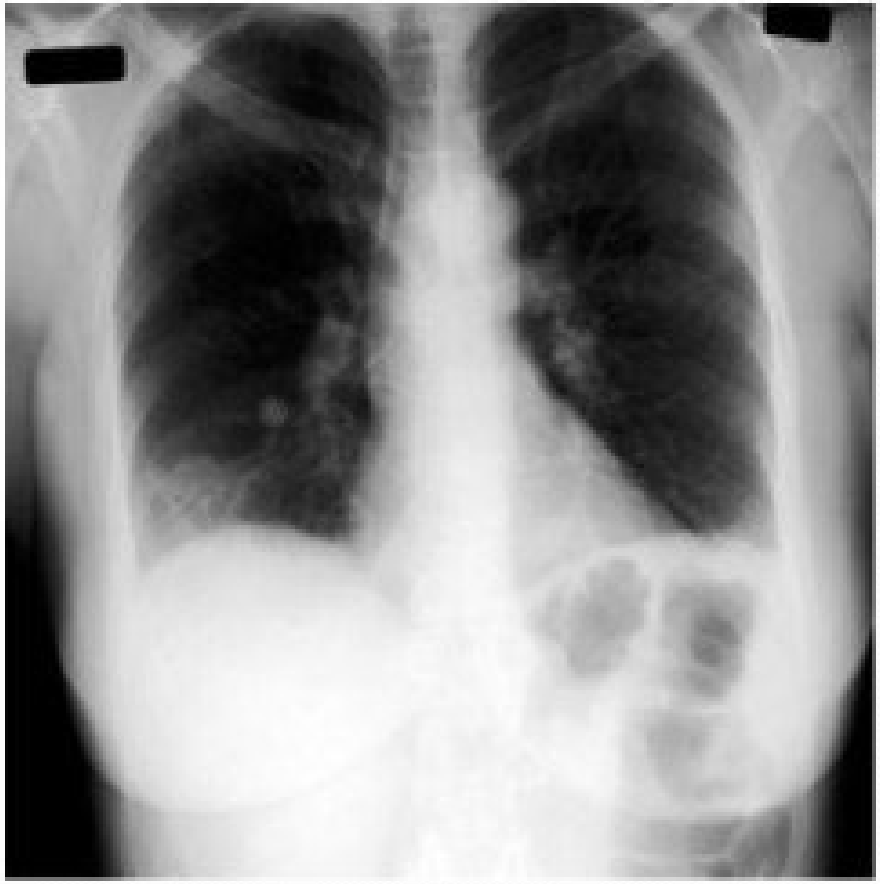


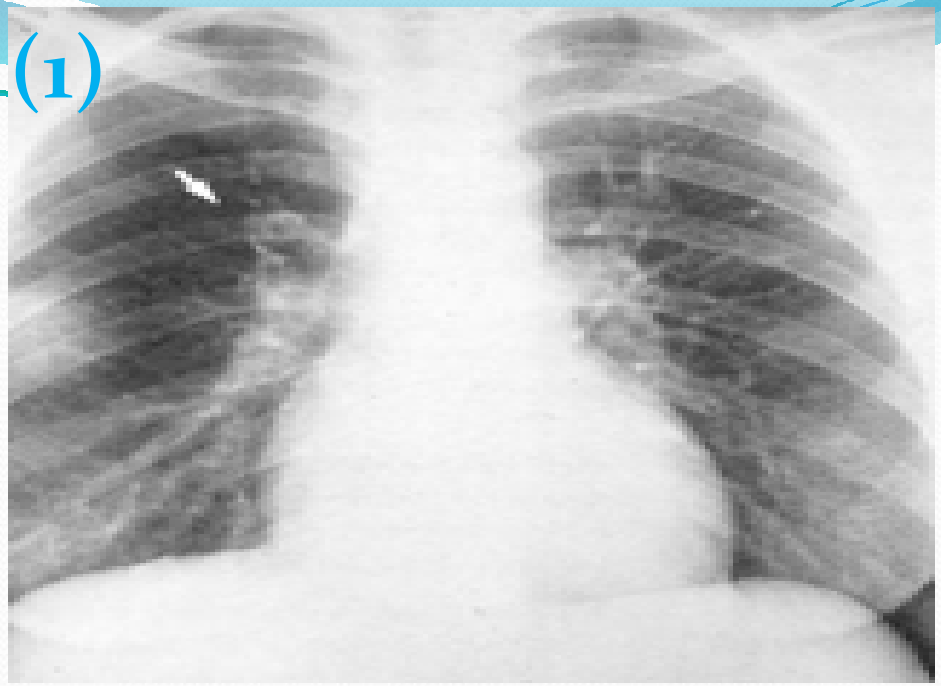
Fig. 19.67 Features of pulmonary thromboembolism/infarction on chest X-ray.

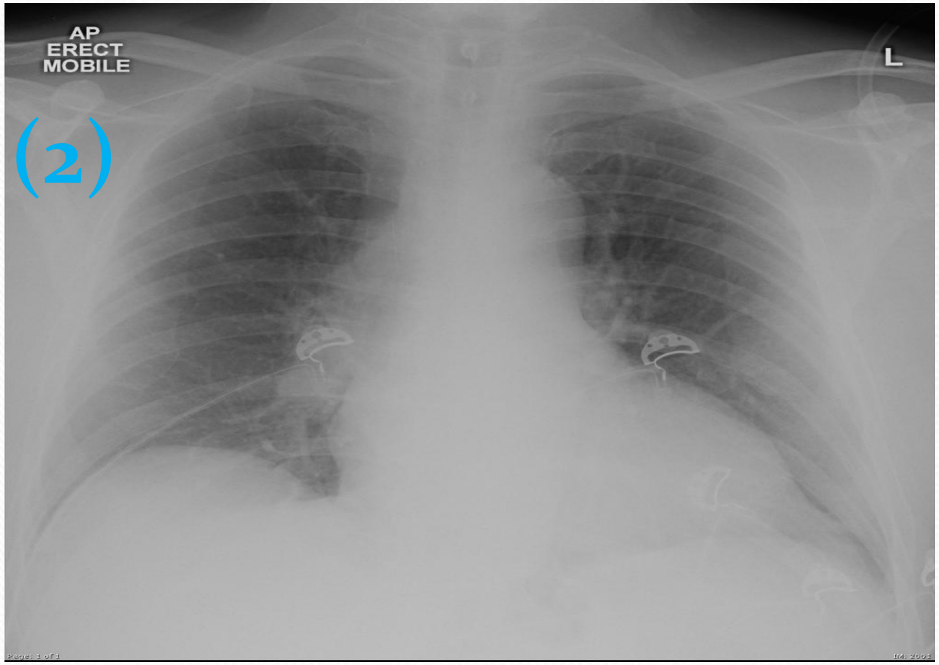
Figure 5. Hampton's hump.

Hampton's hump is a wedge-shaped pleural-based infiltrate that is occasionally seen with PE. Note the density at the right costophrenic angle in this film.



(1)

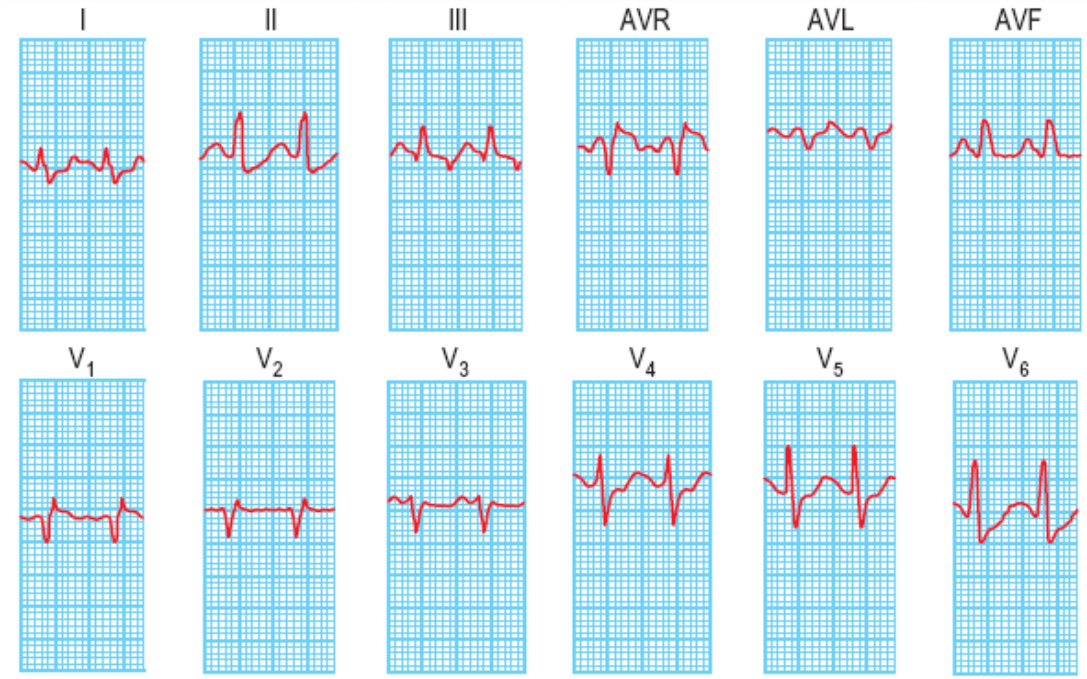




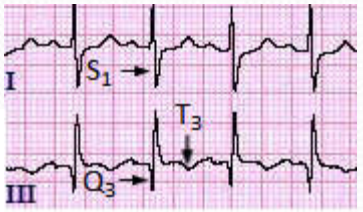
(2)

(1) Westermark's sign: decreased vascularization at the lung periphery due to reflex vasoconstriction in PE.
(2) Fleishner's sign: enlarged right inferior pulmonary artery.

- ***ECG is usually normal, except for sinus tachycardia***, but sometimes atrial fibrillation , anterior T-wave inversion or another tachyarrhythmia occurs. Larger emboli may cause right ventricular strain revealed by an S1Q3T3 pattern, ST-segment and T-wave changes, or the appearance of right bundle branch block.



S1 Q3 T3 pattern



The $S_1Q_3T_3$ pattern

A large S wave in lead I, a Q wave in lead III and an inverted T wave in lead III together indicate acute right heart strain

Figure 14.99 Acute pulmonary embolism shown by a 12-lead ECG. There is an S wave in lead I, a Q wave in lead III and an inverted T wave in lead III (the S1, Q3, T3 pattern). There is sinus tachycardia (160 b.p.m.) and an incomplete right bundle branch block pattern (an R wave in AVR and V1 and an S wave in V_6).

- ***Blood tests.***

  Pulmonary infarction results in a polymorphonuclear leucocytosis, an elevated ESR and increased lactate dehydrogenase levels in the serum. Immediately prior to commencing anticoagulants a thrombophilia screen should be checked.

- ***Plasma D-dimer.***

  A specific degradation product released into the circulation when cross-linked fibrin undergoes endogenous fibrinolysis.

- *If this is undetectable and the clinical suspicion of PE is low, **it excludes a diagnosis of pulmonary embolism***. However, the D-dimer result should be disregarded in high-risk patients, as further investigation is mandatory even if it is normal.
- Low specificity, of limited value (elevated in MI, CHF, sepsis or pneumonia).

  If pretest probability of PE is low, D-dimer test is a good noninvasive test to rule out PE. So if D-dimer is negative, you can rule out a clot.

  But if it is positive, this is not enough to diagnose a PE!

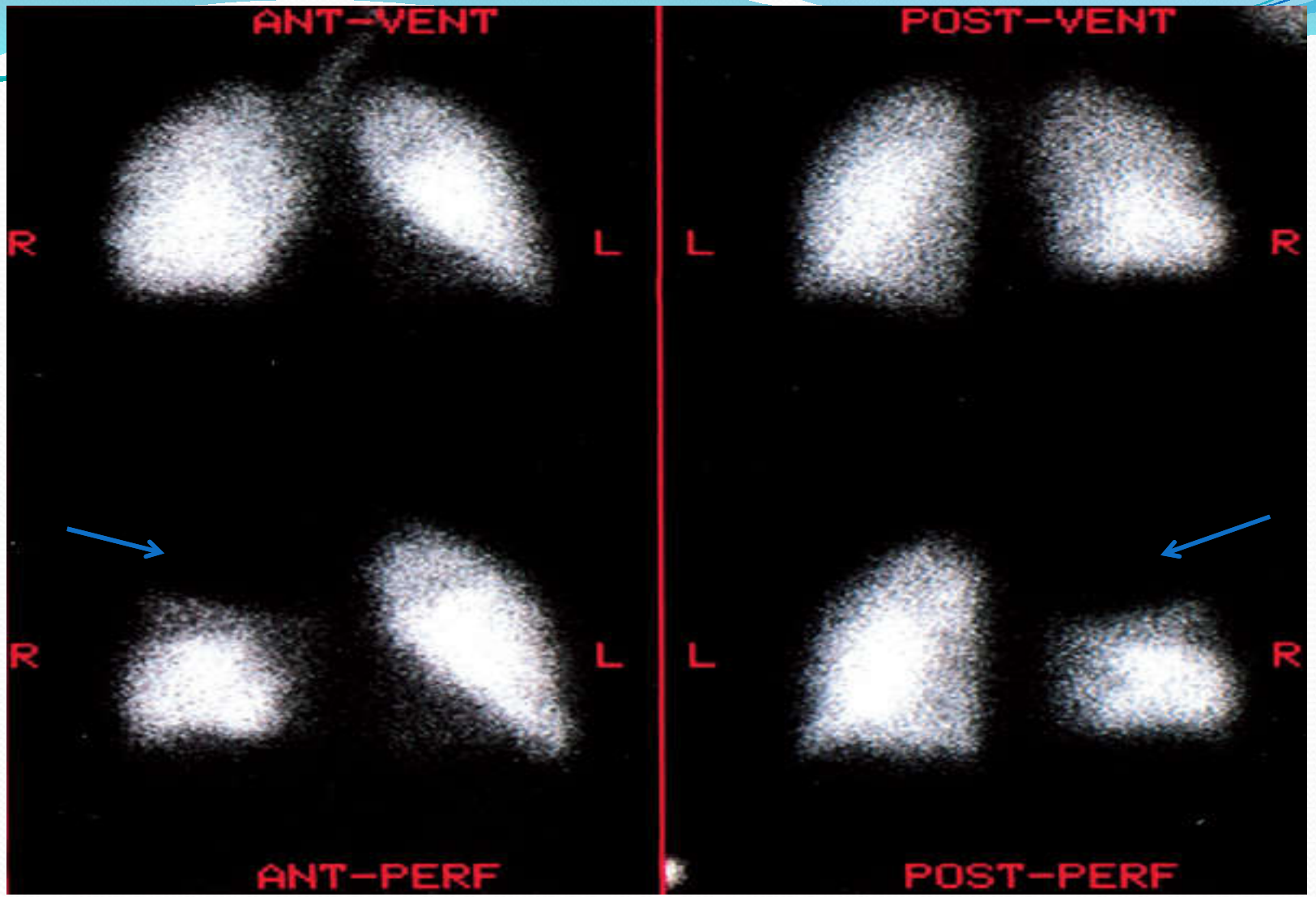
- ***ABG.***

  Typically show a reduced *PaO_2 (hypoxemia)* and a normal or low *$PaCO_2$, and an increased alveolar–* arterial oxygen gradient (↑A-a gradient), but may be normal in a significant minority. A metabolic acidosis ,as a result of lactates accumulation and persistent hypoxemia, may be seen in acute massive PE with cardiovascular collapse. (A – a gradient = P_AO_2 - P_aO_2, a normal value for a young adult non-smoker breathing air, is between 5–10 mmHg)

- ***Radionuclide ventilation/perfusion scanning (V/Q scan) is a good and widely available diagnostic* investigation.**

  Pulmonary 99mTc scintigraphy demonstrates underperfused areas which, if not accompanied by a ventilation defect on a ventilation scintigram performed after inhalation of radioactive xenon gas, is highly suggestive of a pulmonary embolus.

  This test is therefore conventionally reported as a probability (low, medium or high) of pulmonary embolus and should be interpreted in the context of the history, examination and other investigations.



Ventilation (top) and perfusion (bottom) lung scans which demonstrate absence of perfusion in the right upper lobe that isn't accompanied by a ventilation defect, i.e. probably pulmonary embolism (arrows).

- ***Ultrasound scanning.***

  Doppler ultrasound can be performed for the detection of clots in pelvic or iliofemoral veins.

- ***CTA is the first-line diagnostic test.***

  - *Contrast-enhanced CT* angiograms (CTA) is very sensitive and specific and visualize very small clots (as small as 2 mm); may miss clots in small subsegmental vessels (far periphery).

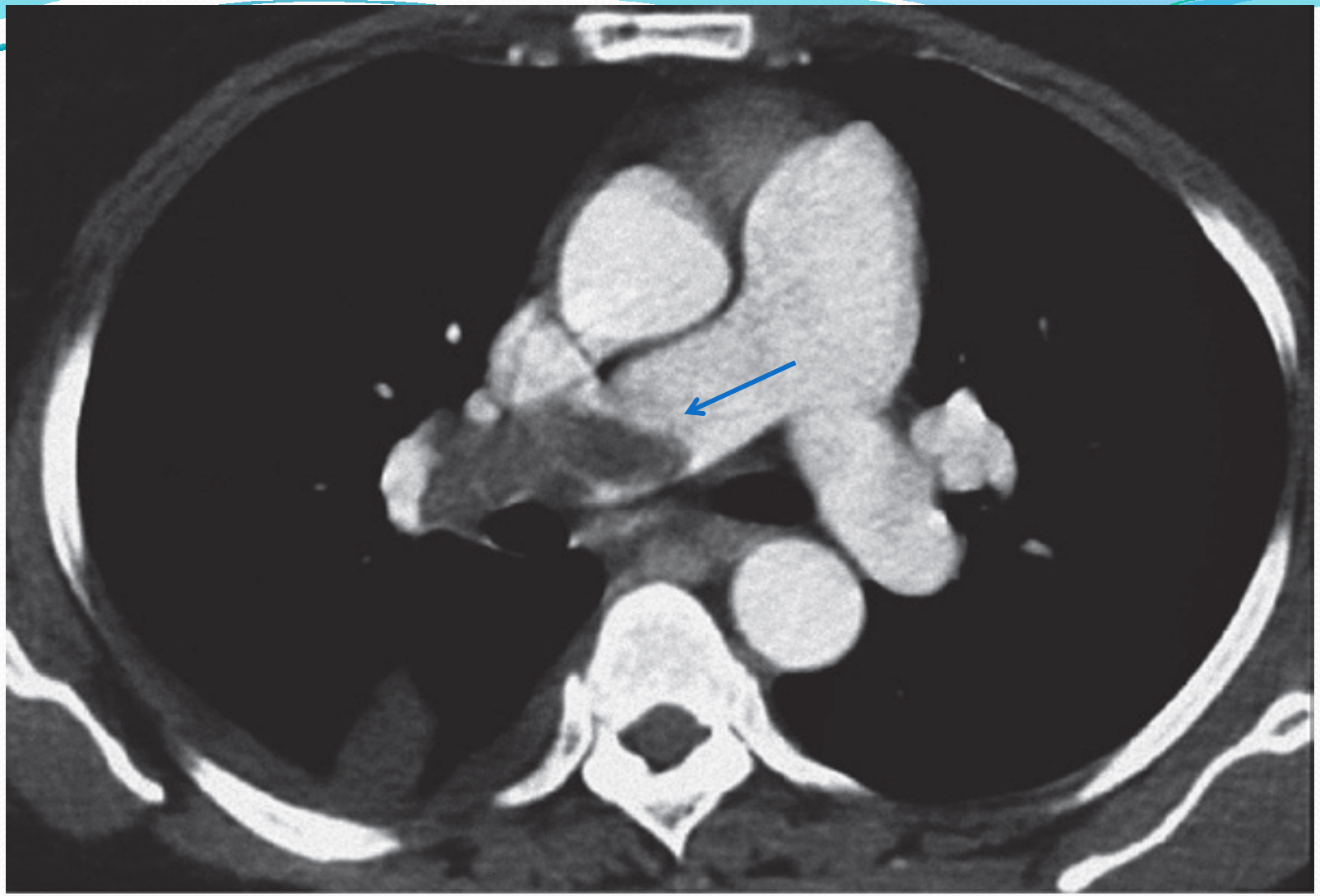
  - The test of choice in most medical centres.

  - In combination with clinical suspicion, guides treatment (see below).

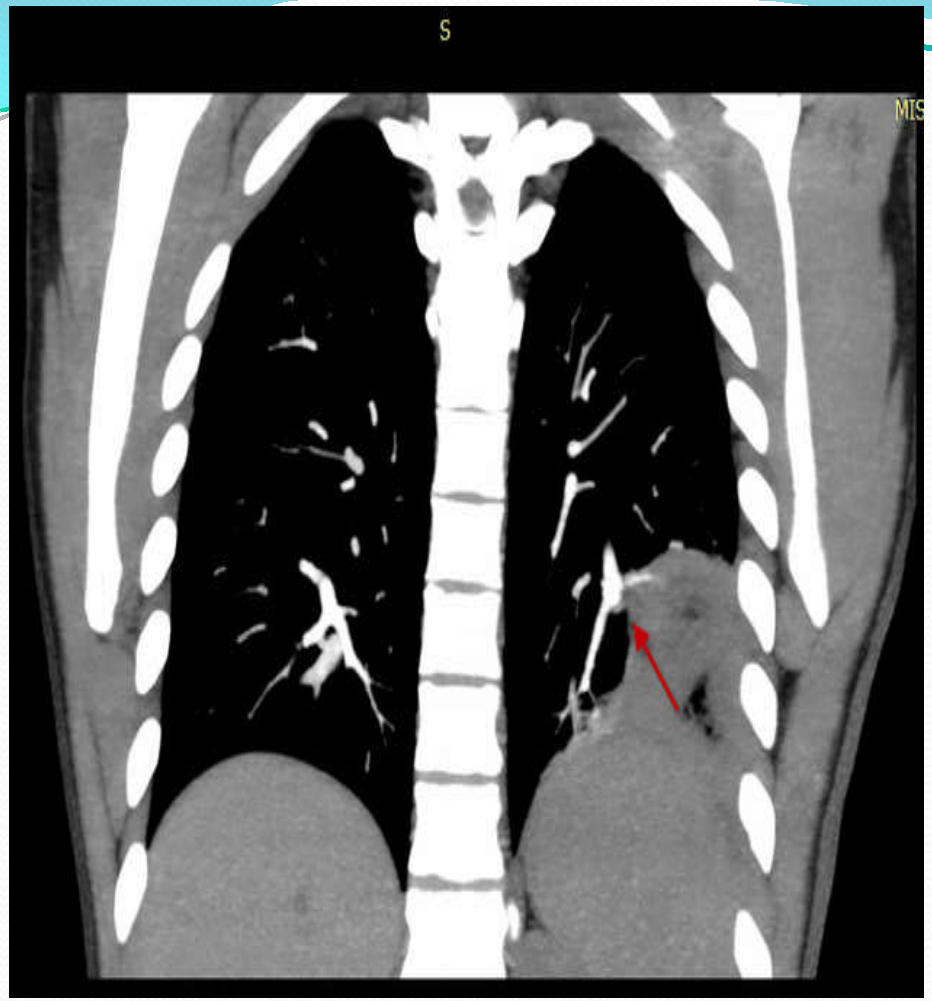
  - CTA cannot be performed in patients with significant renal insufficiency because of the nephrotoxicity of IV contrast. CTPA avoided in those with a history of allergy to iodinated contrast media.

  - If CTA is negative for PE, and clinical probability of PE is high, there is a 5% incidence of PE. So negative results should be interpreted with caution, if the patient has a high clinical probability of PE.

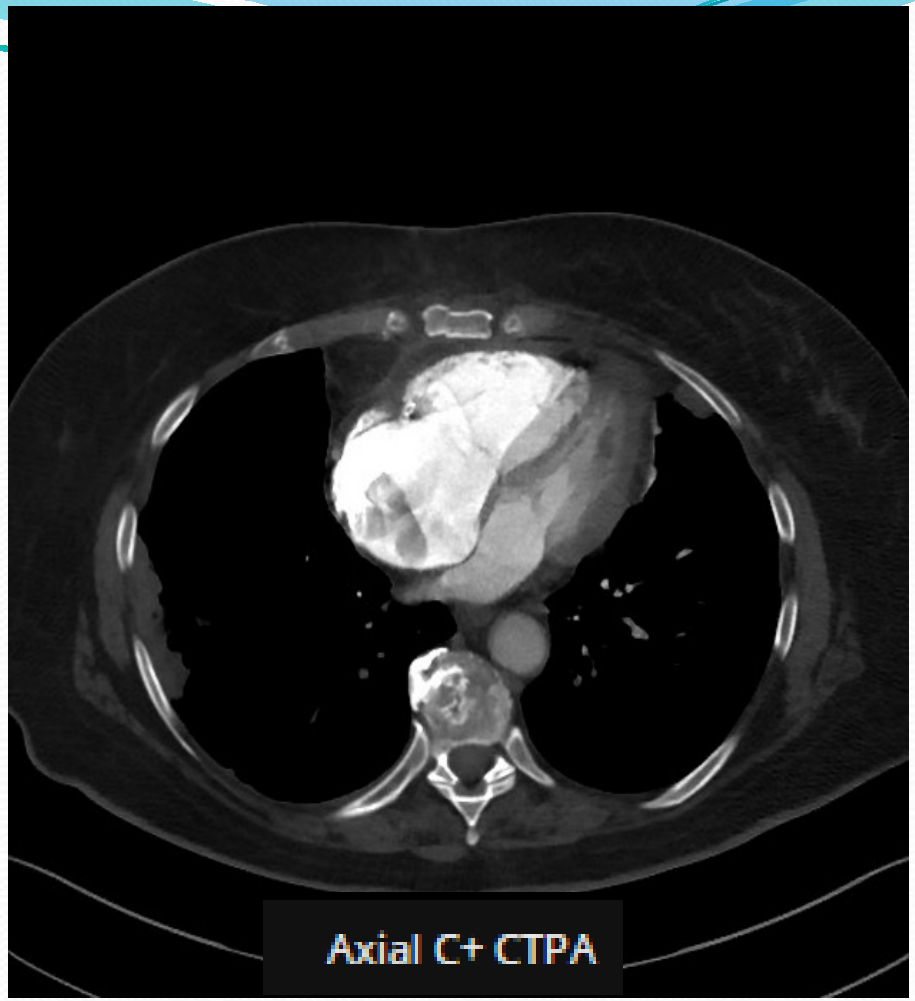
- ***MR imaging gives similar results and is used if CT* angiography is contraindicated.**



CT Pulmonary Angiographic image (CTPA) at level of the main right and left pulmonary arteries showing a large thrombus (arrow) in the right pulmonary artery.



segmental thrombosis: red arrows illustrate the defect of segmental artery occlusion which supplies the infarcted lateral basal segment of left lower lobe



Extensive acute bilateral pulmonary emboli nearly filling both right and left pulmonary arteries and involving all lobes. Dilated right heart with flattening/bowing of the interatrial septum.

- ***Conventional pulmonary angiography.***

  - Definitively diagnoses or excludes PE, but is invasive.

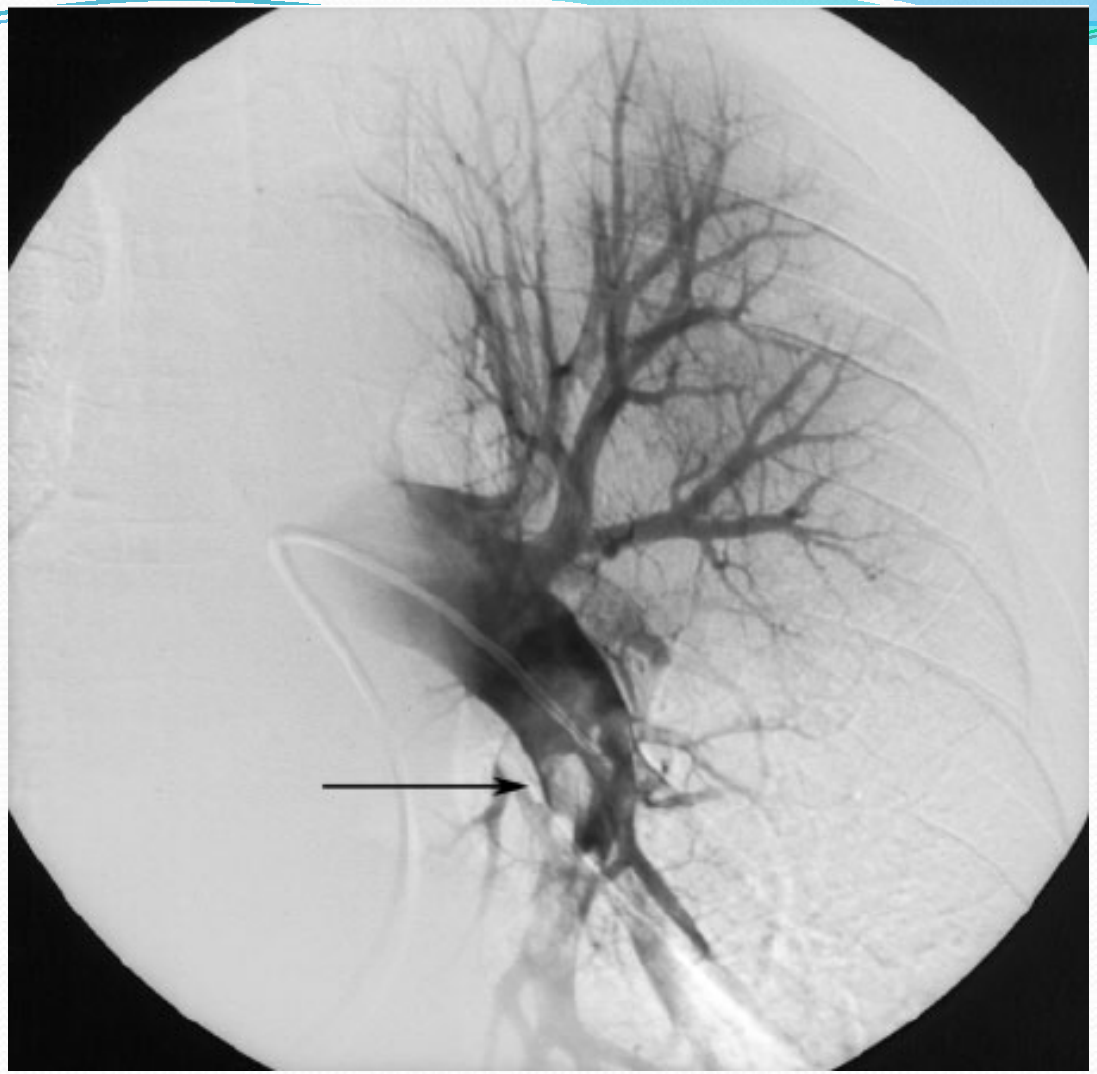
  - Has been replaced by the newer, less invasive, faster and safer CT pulmonary angiography (CTPA).

  - Contrast injected into the pulmonary artery branch after percutaneous catheterization of the femoral vein and fluoroscopy is used to visualize the pulmonary artery.

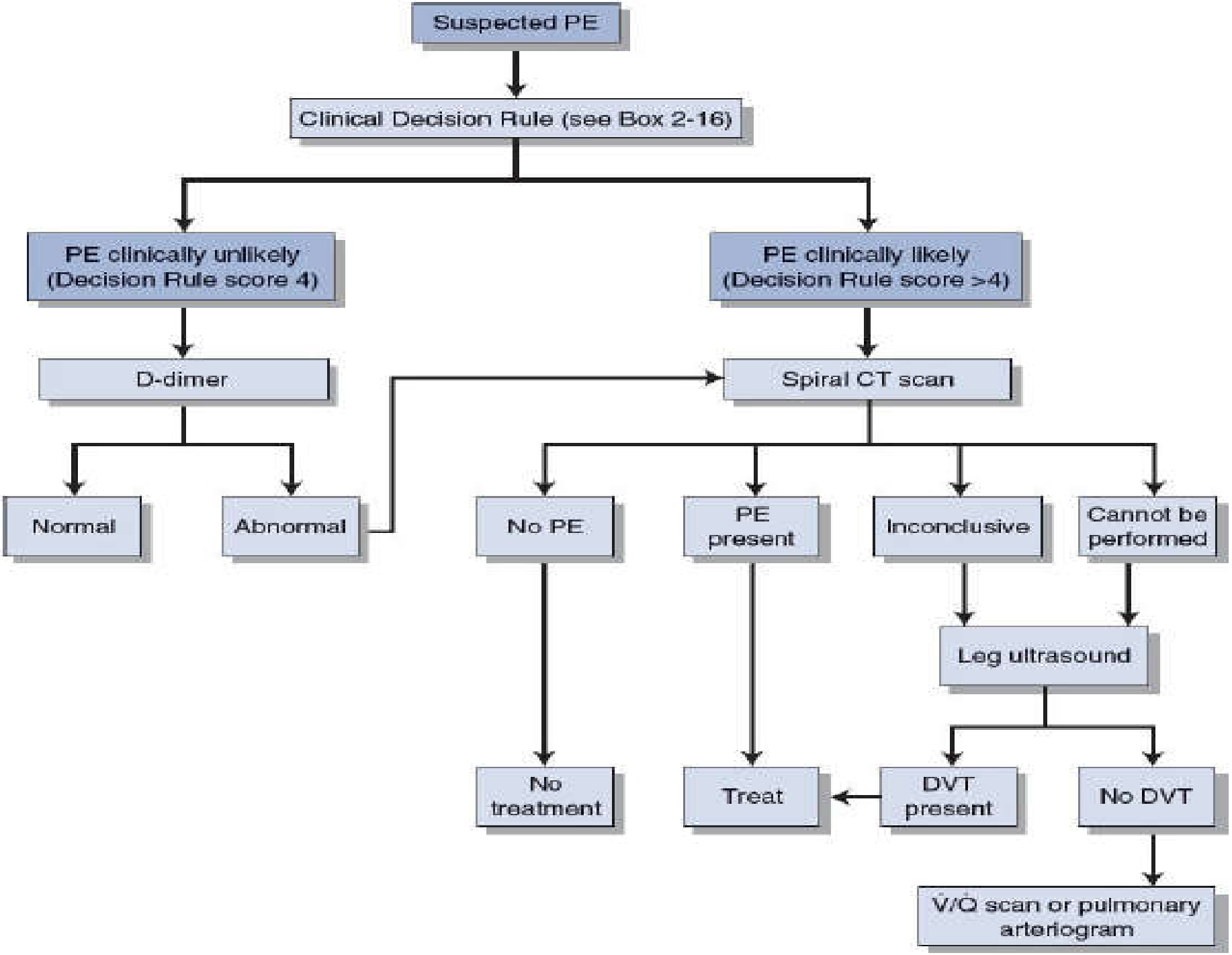
  - Consider when:

    * noninvasive testing is equivocal, and
    * risk of anticoagulation is high, or
    * if the patient is hemodynamically unstable and embolectomy may be required.

  - Angiography is rarely performed because it carries a 0.5% mortality.



Pulmonary angiogram (digital subtraction angiography) revealing large pulmonary embolus (indicated by arrow) in right lower lobe main pulmonary artery.


Suspected PE
Clinical Decision Rule (see Box 2-16)
PE clinically unlikely (Decision Rule score 4)
PE clinically likely (Decision Rule score >4)
D-dimer
Spiral CT scan
Normal
Abnormal
No PE
PE present
Inconclusive
Cannot be performed
Leg ultrasound
No treatment
Treat
DVT present
No DVT
V/Q scan or pulmonary arteriogram

Treatment

1. **Supplemental oxygen** to correct hypoxemia. Severe hypoxemia or respiratory failure requires intubation and mechanical ventilation.
2. Acute **anticoagulation therapy** with either unfractionated or low–molecular-weight heparin to prevent another PE.

   Anticoagulation prevents further clot formation, but does not lyse existing emboli or diminish thrombus size.

- Start immediately on the basis of clinical suspicion. ***Do not wait for studies to confirm PE if clinical suspicion is high*** **!**
- For unfractionated heparin, give one bolus, followed by a continuous infusion for 5 to 10 days. The goal is an aPTT of 1.5 to 2.5 times control. It acts by promoting the action of antithrombin III.
- Contraindications to heparin include: active bleeding, uncontrolled HTN, recent stroke, and heparin-induced thrombocytopenia(HIT).
- Low–molecular-weight heparin has better bioavailability and lower complication rates than unfractionated heparin. It has been shown to be at least as effective or more effective than unfractionated heparin.

3. Oral anticoagulation with warfarin or one of the novel oral anticoagulants (e.g. rivaroxaban) for long-term treatment.

- Can start warfarin with heparin on day 1. Target INR with warfarin for PE treatment is 2 to 3.
- If using a novel oral anticoagulant (e.g. rivaroxaban or apixaban), concurrent treatment with heparin during initiation is not necessary as these medications are effective immediately.
- Continue for 3 to 6 months or more, depending on risk factors.
- Some patients at significant risk for recurrent PE (e.g., malignancy, hypercoagulable state) may be considered for lifelong anticoagulation.

4. **Thrombolytic therapy** — for example, **streptokinase** or **tPA**.

- Speeds up the lysis of clots.
- There is no evidence that thrombolysis improves mortality rates in patients with PE. Therefore, its use is not well defined at this point.
- Situations in which thrombolysis should be considered:

  (1) Patients with massive PE who are hemodynamically unstable (persistent hypotension).

  (2) Patients with evidence of right heart failure (thrombolysis can reverse this).
- Catheter-directed thrombolysis has lower systemic side effects and should be considered in patients at high risk for systemic fibrinolysis or surgery.

5. Inferior vena cava interruption (IVC filter placement).

- Use has become more common but reduction in mortality has not been conclusively demonstrated.
- Patients who have IVC filter placed are at higher risk of recurrent DVT but lower risk of recurrent PE.
- Indications include:

(1) Contraindication to anticoagulation in a patient with documented DVT or PE.

(2) A complication of current anticoagulation.

(3) Failure of adequate anticoagulation as reflected by recurrent DVT or PE.

(4) A patient with low pulmonary reserve who is at high risk for death from PE.

- Complications of IVC filter placement are rare including: filter migration or misplacement, filter erosion and perforation of IVC wall, and IVC obstruction due to filter thrombosis.

6. Surgical thrombectomy.

Consider in patients with hemodynamic compromise, a large, proximal thrombus, and who are poor candidates for fibrinolytics.

Thank You