PULMONARY HYPERTENSION

- pulmonary artery pressure is > 30 with exercise mean > 25 mm Hg

- respiratory failure due to intrinsic pulmonary disease is the most common cause of pulmonary hypertension

- severe pulmonary hypertension :
  - a primary disorder
  - a complication of connective tissue disease (e.g. systemic sclerosis)
  - a result of chronic thromboembolic events.

19.98 Classification of pulmonary hypertension

Pulmonary arterial hypertension

- Primary pulmonary hypertension: sporadic and familial
- Related to: connective tissue disease (limited cutaneous systemic sclerosis), congenital systemic to pulmonary shunts, portal hypertension, HIV infection, exposure to various drugs or toxins, and persistent pulmonary hypertension of the newborn

Pulmonary venous hypertension

- Left-sided atrial or ventricular heart disease
- Left-sided valvular heart disease
- Pulmonary veno-occlusive disease
- Pulmonary capillary haemangiomatosis

Pulmonary hypertension associated with disorders of the respiratory system and/or hypoxaemia

- COPD
- DPLD
- Sleep-disordered breathing
- Alveolar hypoventilation disorders
- Chronic exposure to high altitude
- Neonatal lung disease
- Alveolar capillary dysplasia
- Severe kyphoscoliosis

Pulmonary hypertension caused by chronic thromboembolic disease

- Thromboembolic obstruction of the proximal pulmonary arteries
- In situ thrombosis
- Sickle cell disease

Miscellaneous

- Inflammatory conditions
- Extrinsic compression of central pulmonary veins

Primary Pulmonary Hypertension

- ❑ idiopathic change in arterial walls :
  hypertrophy of both the media and intima of the vessel & observed in situ thrombosis

- ❑ commonly complain of dyspnea, fatigue, syncope, chest pain

- ❑ disease of young women (20-40 years)

- physical exam :
  - elevation of the JVP
  - a parasternal heave (RV hypertrophy)
  - accentuation of the pulmonary component of the second heart sound and a right ventricular third heart sound.

- ❑ positive serology (ANA) > 30%
- ❑ patients frequently have Raynaud's syndrome

- ❑ may be associated with the use of anorexic drugs (e.g. aminorex, fenfluramine)

Investigations

- **ECG : a right ventricular 'strain' pattern**
- **chest X-ray : enlarged pulmonary arteries, peripheral pruning and right ventricle enlargement.**
- **Confirmation : echocardiography**

treatment:

- **All patients should be anticoagulated with warfarin**
- **oxygen, diuretics and digoxin prescribed as appropriate.**
- **high-dose calcium channel blockers**
- **prostaglandins such : epoprostenol (prostacyclin)**
- **the PDE5 inhibitor : sildenafil**
- **oral endothelin antagonist: bosentan.**
- **transplantation**

prognosis

- poor, with 2-3 year mean survival from time of diagnosis

Secondary Causes of Pulmonary Hypertension

Cardiac Disease (Passive)

- ❑ increased LAP (e.g. chronic LVF, mitral stenosis)
- ❑ increased pulmonary vascular flow
  - as with a L —> R shunt (ASD, VSD, PDA)
  - as right sided pressure increases due to increased flow, pressure eventually becomes greater than left sided pressure resulting in a R —> L shunt and cyanosis (irreversible Eisenmenger's complex)

Pulmonary Vasoconstriction (Reactive)

- primary response to hypoxia but also to acidosis from hypercapnia (i.e. with chronic lung disease)

- note: chronic hypoxia also causes polycythemia which will increase viscosity and increase pulmonary arterial pressure

Loss of Pulmonary Vessels (Destructive)

- loss of vascular bed surface area as with interstitial lung disease/pulmonary fibrosis, emphysema, scleroderma, pneumonectomy, multiple lobectomies, bronchiectasis, CF

- pulmonary arterial pressure may be normal at rest but increased with exercise

Pulmonary Vascular Occlusion (Obstructive)
Chronic thromboembolic disease

Clinical Presentation

- symptoms
  - dyspnea
  - fatigue
  - substernal chest pain
  - syncope
  - symptoms of underlying disease

- signs
  - loud, palpable P2
  - RV heave
  - right sided S4 (due to RVH)
  - if RV failure: right sided S3, increased JVP, peripheral edema, TR

Investigations

- CXR
  - enlarged central pulmonary arteries
  - cardiac changes due to RVH/failure (filling of retrosternal air space)
- ECG
  - RVH/strain and RA enlargement, rightward axis deviation
- 2-D echo doppler assessment of RVSP
- cardiac catheterization: direct measurement of pulmonary artery pressures
- spiral CT and PFTs to rule out lung disease
- V/Q scan +/– pulmonary angiogram to rule out thromboembolic disease

Management

- O2 if hypoxic
- treat underlying condition
- phlebotomy for polycythemia (rarely required)
- treatment of exacerbating factors
  - smoking
  - sedatives
  - obesity
  - infection
- anti-coagulation +/– vasodilators (prostacyclin)
- lung transplant

PULMONARY EMBOLI (PE)

- thrombi usually start in calf, but must propagate into proximal veins (i.e. thigh) to create a sufficiently large thrombus for a clinically significant PE
- only 50% of patients have previous clinical evidence of DVT (i.e. tenderness, swelling of lower extremity)
- always suspect PE if patient suddenly collapses 1-2 weeks after surgery

Risk Factors (Virchow's Triad)

- **stasis**
  - **immobilization: bed rest, prolonged sitting during travel, immobilization of an extremity after fracture**
  - **obesity, CHF**
  - **chronic venous insufficiency**
- ***endothelial cell damage***
  - **post-operative complications, trauma**
- ***hypercoagulable states***
  - **underlying CA (particularly adenocarcinoma)**
  - **high dose exogenous estrogen administration**
  - **pregnancy, post-partum**
  - **coagulopathies: inherited deficiencies of antithrombin III, protein C, protein S, activated protein C resistance, antiphospholipid antibody, hyperhomocysteinemia, factor V Leiden mutation**
  - **prior history of DVT/PE, family history**

Other Causes (all rare)

- tumour cells/fragments
- fat
- amniotic fluid
- foreign bodies
- air

- **A recognised risk factor is present in between 80% and 90% of patients**

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 (Ch. 24)
- Trauma

Clinical Presentation

- respiratory symptoms/signs (neither sensitive nor specific)
  - tachypnea
  - SOB +/– wheeze
  - pleuritic chest pain or non-pleuritic non-central chest pain
  - hemoptysis
  - SaO2 < 92%
  - pleural rub

- other (neither sensitive nor specific)
  - tachycardia +/– hypotension
  - syncope
  - +/– fever, elevated white count
  - leg symptoms

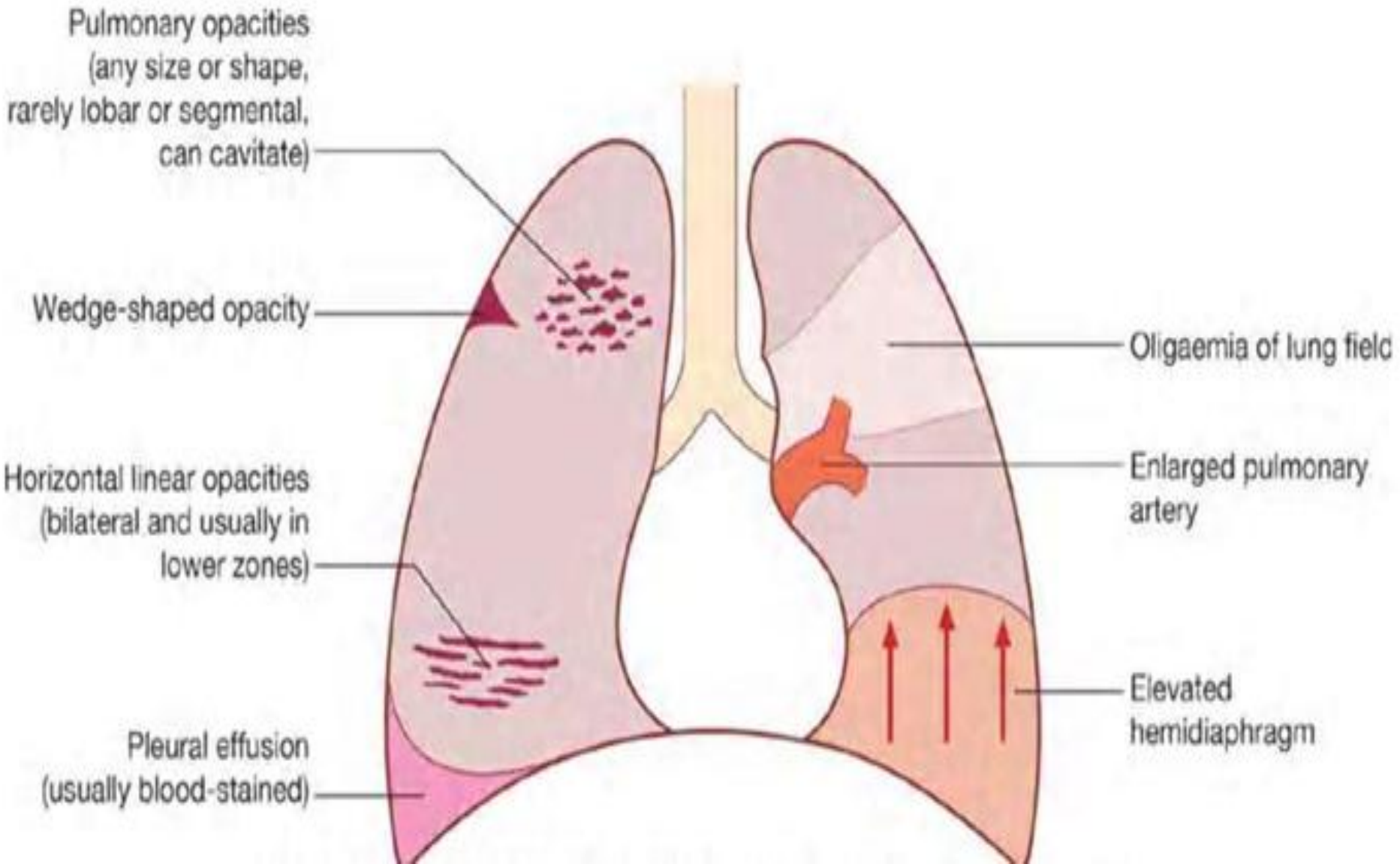
Clinical Presentation

- in severe hemodynamic compromise:
  - increased pulmonary arterial pressure, RVH (RV heave, loud/palpable P2, right-sided S4)
  - if RV failure (right sided S3, distention of jugular veins), TR
  - decreased LV filling (decreased cardiac output, syncope, shock)

Investigations

- **CXR**
  - **frequently normal**
  - **Hampton's hump- cone-shaped area of opacification representing atelectasis/infarction**
  - **Westermark's sign- area of oligemia/decreased vascular markings (difficult to assess without prior films)**
  - **rarely - dilatation of proximal PA**
  - **often nonspecific (e.g. areas of atelectasis, elevation of a hemidiaphragm, pleural effusion)**

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



Investigations

❑ *ECG*

- **often normal**
- *sinus tachycardia most common* **& anterior T-wave inversion**
- *RAD, S1Q3T3 with large embolus* **(right heart strain)**

❑ *ABG*

- *PaO2 usually decreased, PaCO2 decreased (due to increase in overall minute ventilation)*
- *increased A-a gradient*

❑ *D-dimers (products of thrombotic/fibrinolytic process)*

- *ELISA better than latex agglutination*
- *D-dimer results alone do not rule in or out DVT/PE*
- **high negative predictive value and further investigation is unnecessary**
- *need to use in conjunction with leg dopplers, other investigations*

elevated D-dimer

- PE
- myocardial infarction
- pneumonia
- Sepsis
- Surgery (2 weeks)
- Pregnancy
- Inpatient
- Malignancy

Investigations

- ❑ venous duplex ultrasound or doppler (high specificity)

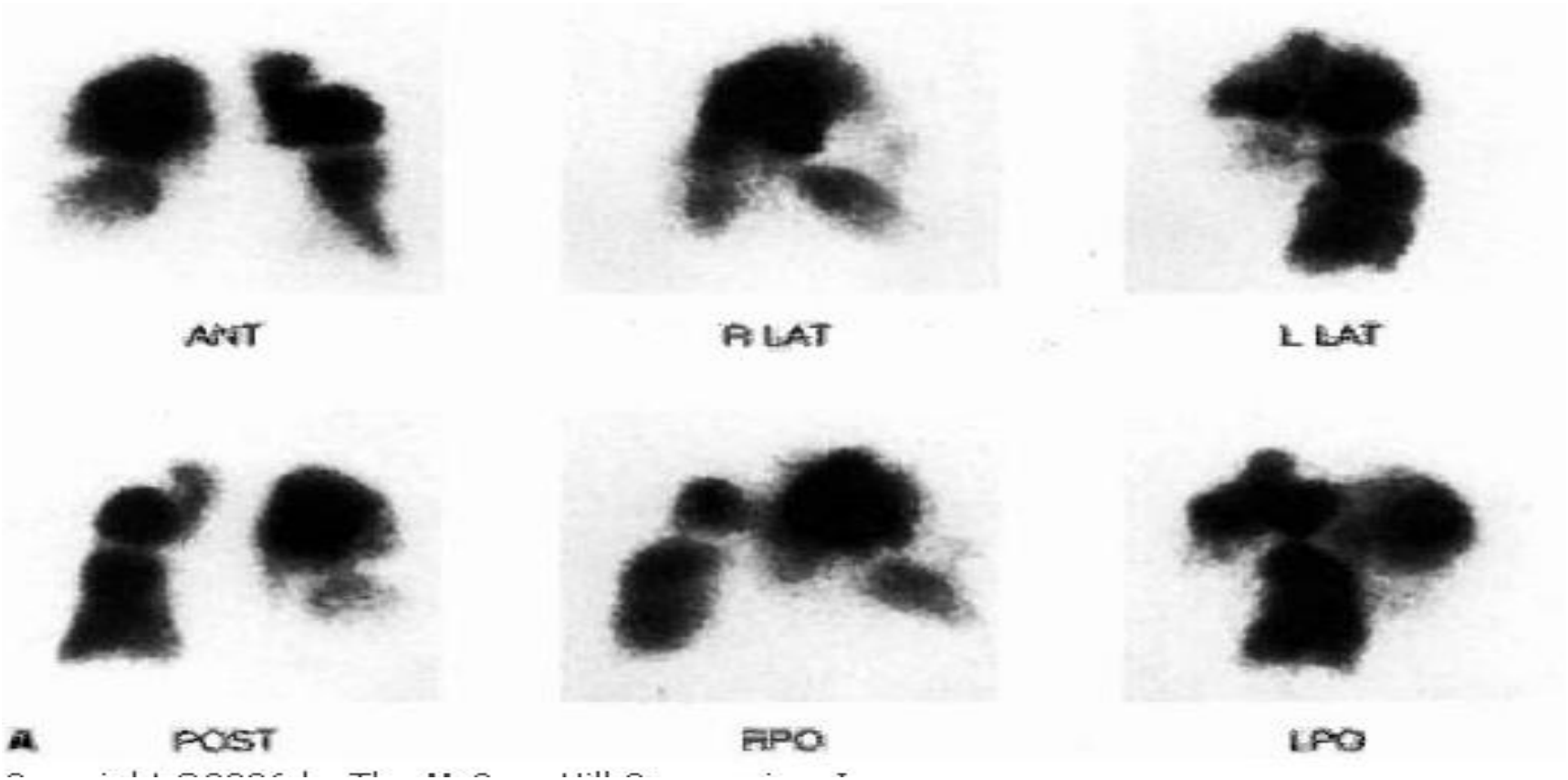
- with leg symptoms
  - positive test can rule in a proximal or distal DVT
  - negative test can only rule out a proximal DVT
- without leg syptoms
  - positive test rules in proximal DVT
  - negative test does not rule out a DVT (a possible non-occlusive DVT?)

- ❑ V/Q scan (very sensitive but low specificity) :

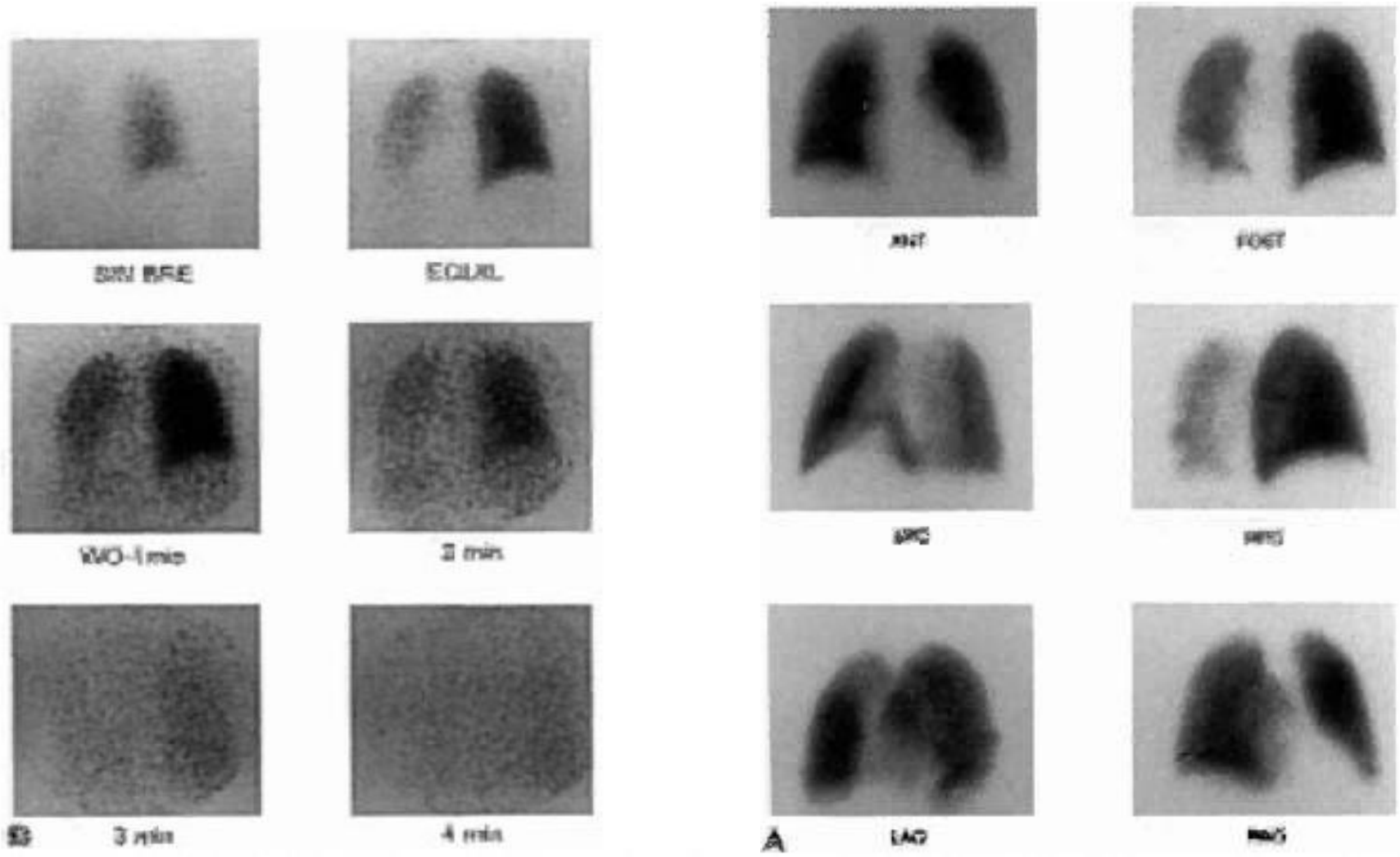
order scan if :
  - CXR normal/mild abnormalites, no COPD
  - normal leg dopplers but abnormal D-dimers

avoid scan if :
  - CXR very abnormal or COPD
  - leg dopplers and D-dimers are normal

ومضان التهوية / تروية



ومضان التهوية / تروية



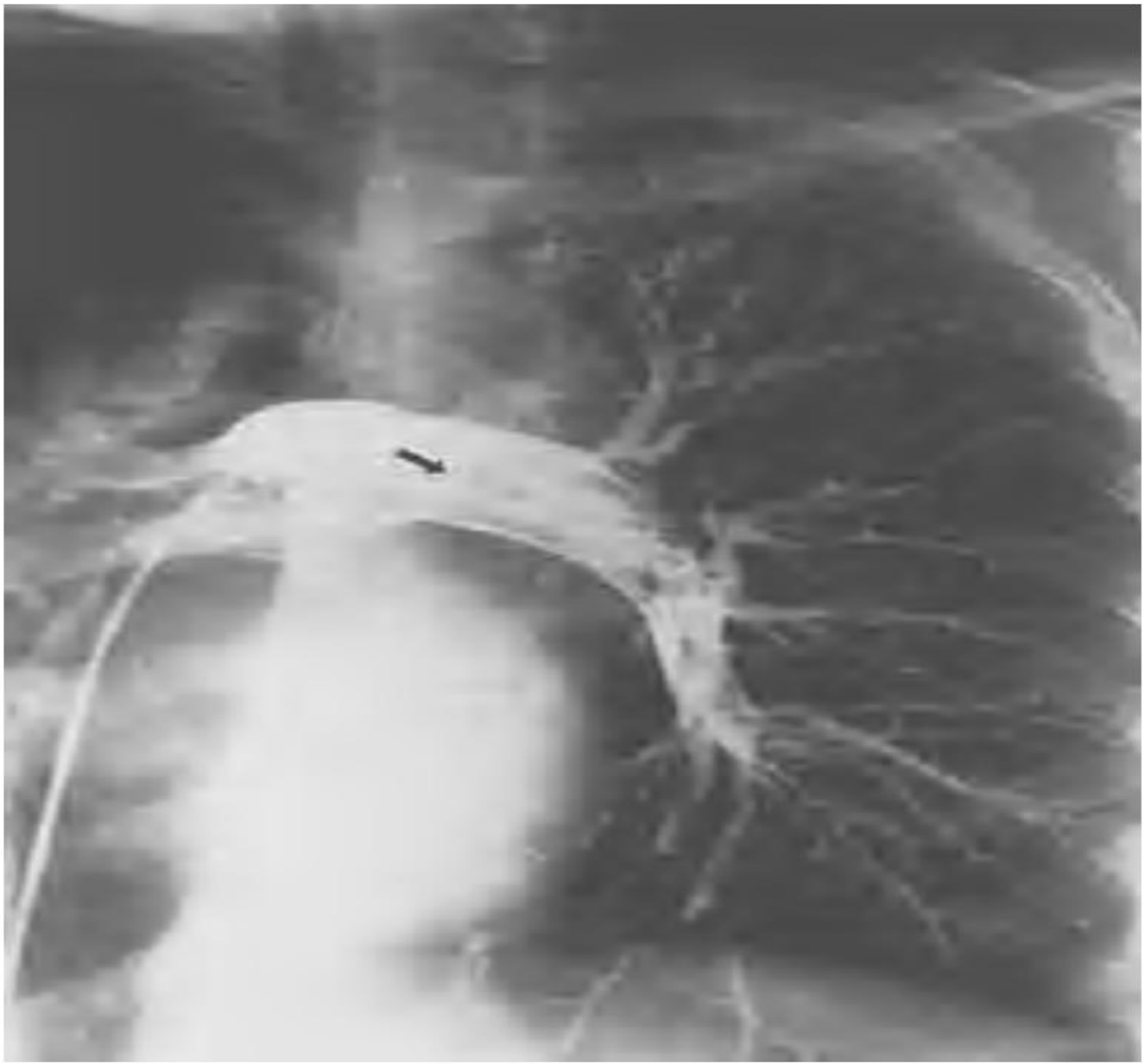
Bedside echocardiography

- extremely helpful in the differential diagnosis
- Acute dilatation of the right heart is usually present in massive PE

Investigations

- pulmonary angiogram is gold standard but more invasive
- spiral CT scan with contrast
- ECHO

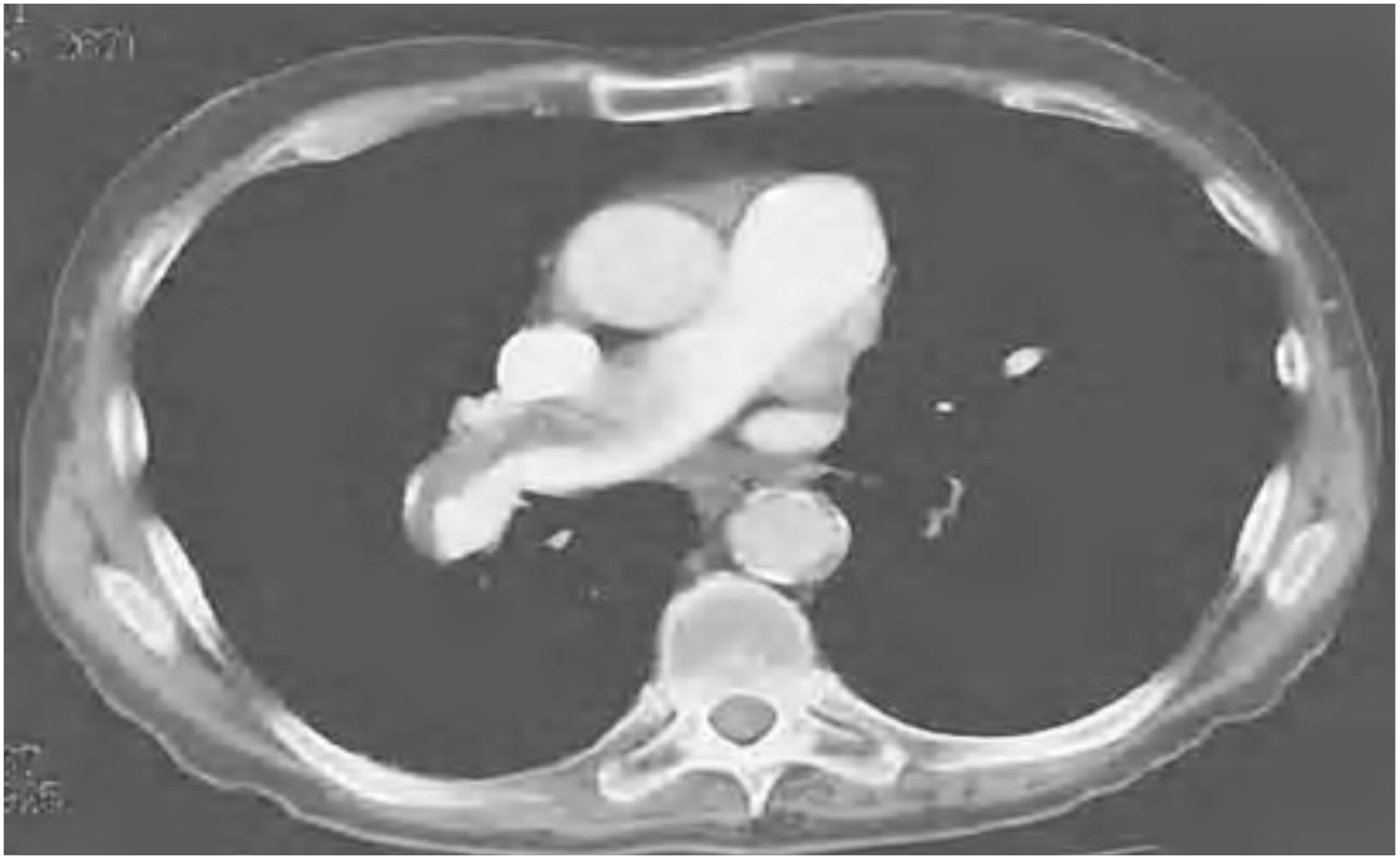
Figure 48.7 Left-sided pulmonary angiogram showing extensive filling defects within the left pulmonary artery (*arrows*) and the upper lobe, lingula, and lower lobe arteries consistent with the diagnosis of pulmonary embolism.



CT pulmonary angiography (CTPA)

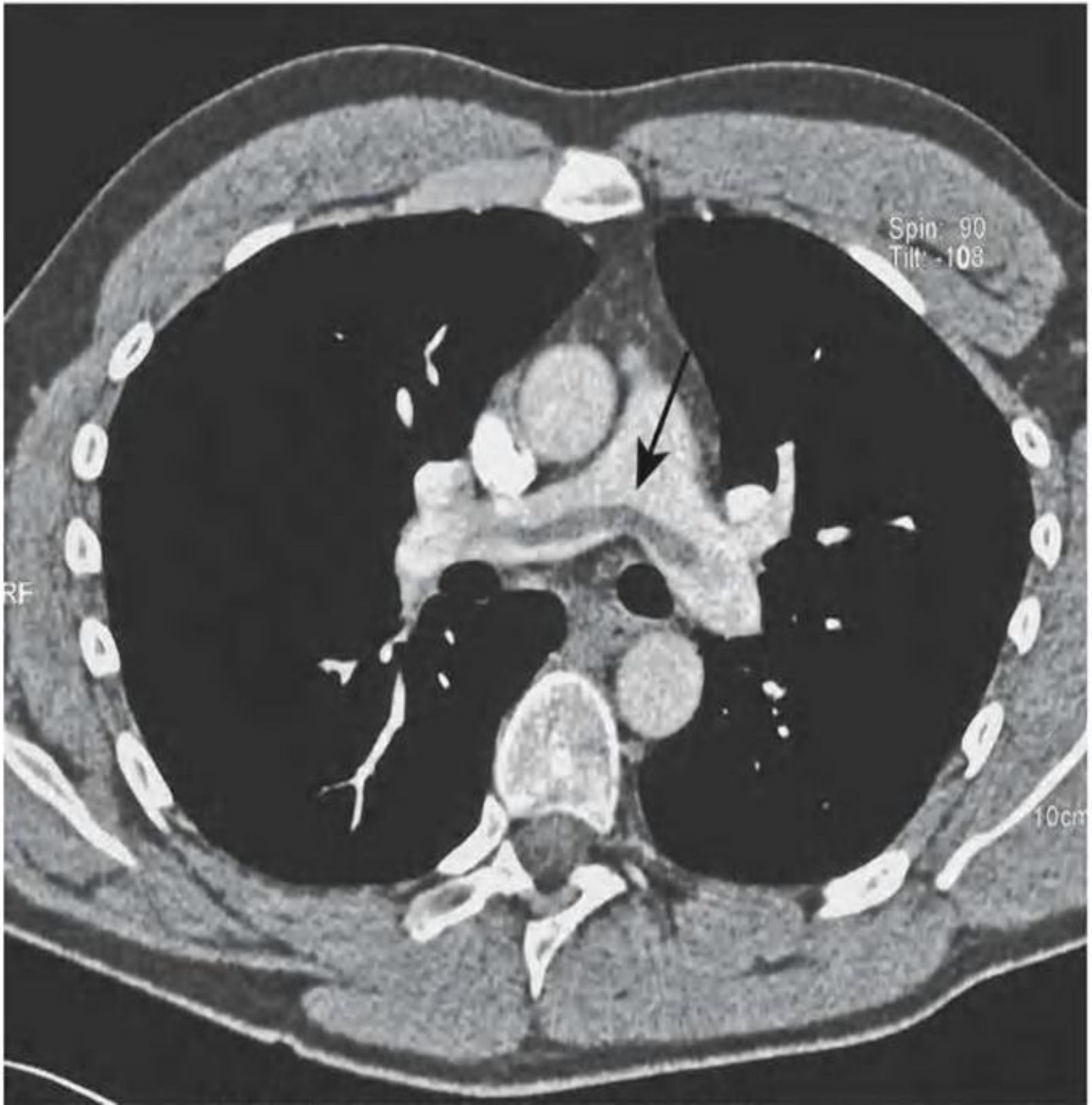
- most commonly sought first-line diagnostic test.
- visualising the distribution and extent of the emboli
- highlighting alternative diagnoses such as consolidation or pneumothorax
- renal impairment and the use of iodinated contrast media should be avoided

Figure 48.6 Chest computed tomography scanning demonstrating extensive embolization involving the right main, upper lobe, and lower lobe pulmonary arteries.



CT pulmonary angiogram.

The arrow points to a saddle embolism in the bifurcation of the pulmonary artery.



الفحوص المشخصة

- ومضان التهوية / تروية Ventilation/perfusion lung scan :
  حساسيته : 98 % لكن نوعيته سيئة و عادةً لا يجرى إذا كانت صورة الصدر غير طبيعية

- دوبلر لأوردة الطرفين السفليين : كشف خثار وريدي عميق

- تصوير الشرايين الرئوية :
  في حال الشك القوي و كل الفحوص سلبية و هو نوعي و حساس 100 %

- التصوير الطبقي المحوري الوعائي الرئوي :
  نوعي للتشخيص و كثيرون يعتمدون عليه لوحده وبالمشاركة مع D-Dimer

- D-Dimer بطريقة ELISA:
  الحساسية 100 % و يمكن إجراؤها لنفي الصمة الرئوية إذا ما كانت سلبية

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, right ventricular 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 RV
ECG	$S_1Q_3T_3$ anterior T-wave inversion, right bundle branch block (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

معايير Well في تقدير الخطورة للإصابة بالصمة الرئوية Pre-test probability (PTP)

- علامات التهاب وريد خثري : 3 نقاط
- الصمة الرئوية هي التشخيص الأكثر احتمالاً : 3 نقاط
- الخباثة : 1.5 نقطة
- البقاء في الفراش لمدة طويلة (3< أيام) أو قصة كسر من أسبوعين أو عملية جراحية خلال 3 أسابيع : 1.5نقطة
- تسرع قلب : 1 نقطة
- نفث دموي : 1 نقطة

مجموع النقط : > 6 مرتفع الخطورة ، 3 – 6 متوسط الخطورة ، <2نقطة منخفض الخطورة

TABLE 244-1 Wells Diagnostic Scoring System[a] for Suspected PE

	Points
• Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3.0
• An alternative diagnosis is less likely than PE	3.0
• Heart rate >100 beats/min	1.5
• Immobilization or surgery in the previous 4 weeks	1.5
• Previous DVT/PE	1.5
• Hemoptysis	1.0
• Malignancy (on treatment, treated in the past 6 months, or palliative)	1.0

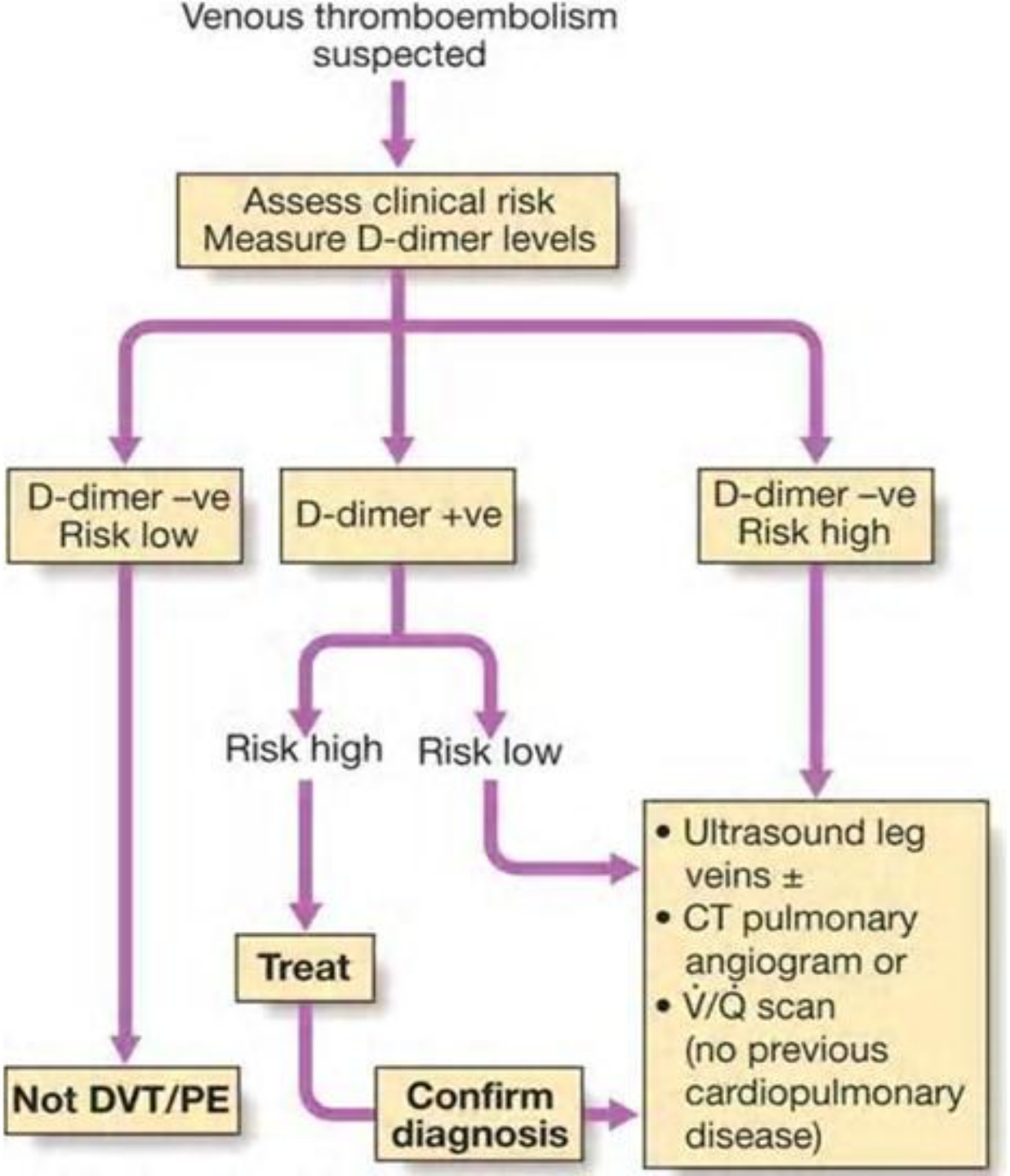
[a] The Wells Scoring System has a maximum of 12.5 points. If the score is ≤ 4 points, the likelihood of PE is only 8%.

التسلسل المنطقي للتشخيص

- PTP < 6 & D-Dimer سلبي : ينفيان الصمة
- صورة صدر طبيعية : يجرى ومضان تهوية /تروية
- صورة صدر غير طبيعية : يجرى التصوير الطبقي المحوري للأوعية الرئوي CTPA
- PTP< 2 مع ومضان تهوية/ تروية سلبي أو CTPA طبيعي : ينفي الصمة
- ومضان تهوية/ تروية ايجابي مع PTP > 3 : وضع تشخيص صمة رئوية

Algorithm for the investigation of patients with suspected pulmonary thromboembolism.

Clinical risk is based on the presence of risk factors for VTE and the probability of another diagnosis.



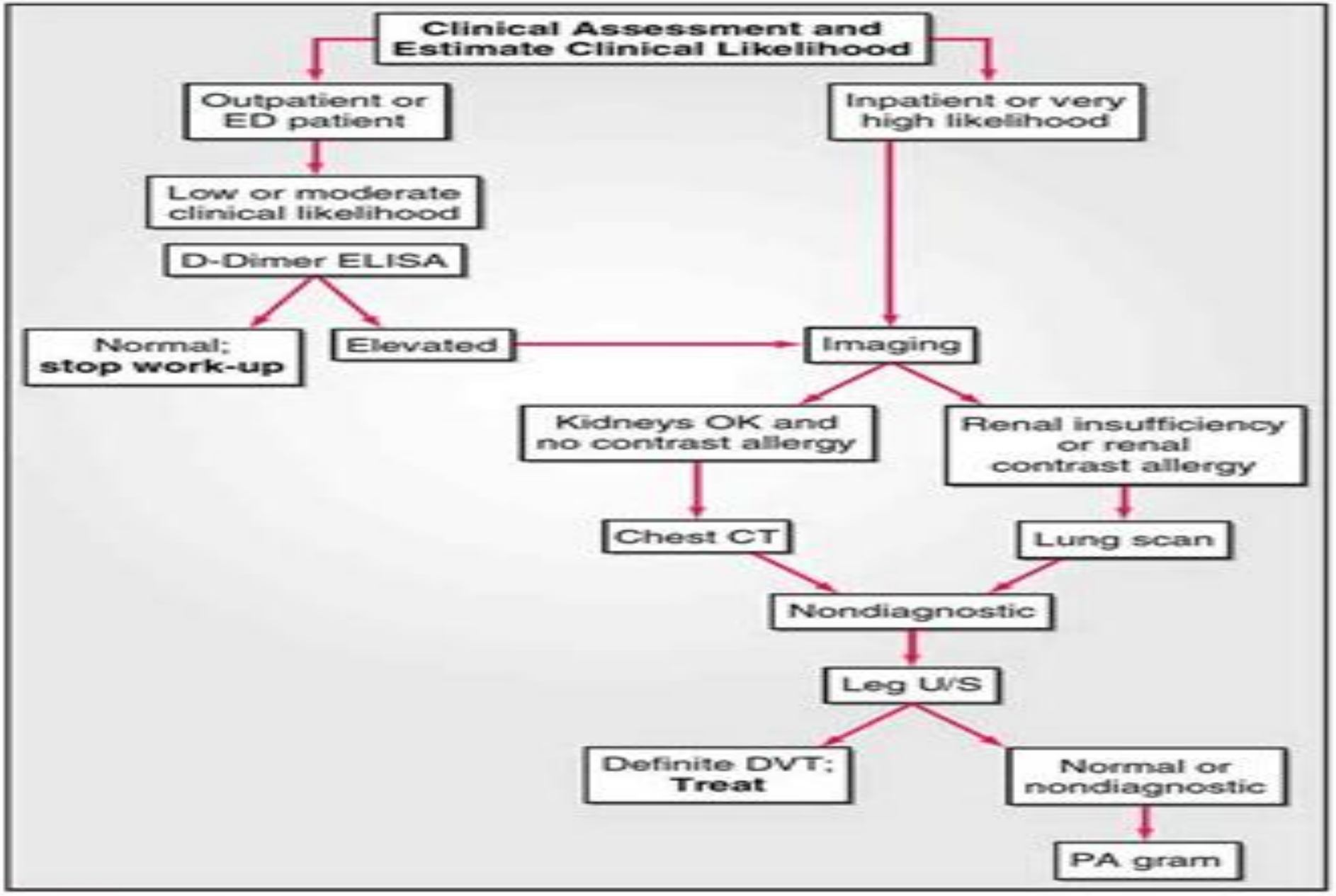


FIGURE 244-3 Diagnosis strategy for pulmonary thromboembolism: An integrated diagnostic approach. ED, emergency department; ELISA, enzyme-linked immunosorbent assay; CT, computed tomography; U/S, ultrasound; DVT, deep vein thrombosis; PA gram, pulmonary arteriogram.

Prevention

- early mobilization of peri-operative patients, in-patients
- prophylactic anticoagulation: limited mobility, chronically ill (e.g. heparin 5,000 units SC BID)
- peri-operative anticoagulation:

  heparin or LMWH (enoxaparin)

Treatment

- have patient sit up as it aids respiration
- O2
- thrombolysis for large, hemodynamically significant emboli (ICU) or right ventricular dilatation and hypokinesis or severe hypoxaemia.

- anticoagulation to prevent further emboli
  - LMWH initial treatment (fragmin) (reliable dose-response curve at a given weight, so don't need to monitor PTTs with LMWH)
  - IV heparin

- 6-24+ weeks oral warfarin (started one day after heparin started)
- IVC filter if
  - anticoagulant therapy contraindicated or fails
  - pulmonary vascular reserve is such that another PE would be fatal

Treatment

- Heparin reduces further propagation of clot, the risk of further emboli, and lowers mortality.
- duration of LMWH treatment should be at least 5 days
- LMWH should not be discontinued until the international normalised ratio (INR) is greater than 2.
- Patients with a persistent prothrombotic risk or a history of previous emboli should be anticoagulated for life
- reversible risk factor usually require only 3 months of therapy.
- If the condition is idiopathic or risk factors are weak, anticoagulation for 6 months is recommended

Treatment

- shock : intravenous fluids or plasma expander, but inotropic agents are of limited value
- Diuretics and vasodilators should also be avoided
- Opiates may be necessary

العلاج

- يلزم البدء بالعلاج عند الشك
- الهيبارين : 5000 وحدة دولية وريدي و من ثم 800-1600 وحدة / ساعة بالتسريب المستمر
- الهيبارين المنخفض الوزن الجزيئي : نفس الفعالية
- الوارفارين : من اليوم الثاني و لمدة 6 أشهر و يراقب زمن البروترومبين PT (<25 %)
- حالات الخثار : في الصدمة الدورانية

Table 9–24. Selected low-molecular-weight heparin anticoagulation regimens.

Drug	Suggested Treatment Dose [1] (Subcutaneous)
Dalteparin	200 units/kg once daily (not to exceed 18,000 units/dose)
Enoxaparin	1.5 mg/kg once daily (single dose not to exceed 180 mg)
Nadroparin	86 units/kg twice daily for 10 days, or 171 units/kg once daily (single dose not to exceed 17,000 units)
Tinzaparin	175 units/kg once daily

Prognosis

- **greatest in those with echocardiographic evidence of right ventricular dysfunction or cardiogenic shock.**
- **persisting pulmonary hypertension :**
  4% of patients by 2 years.
- **A minority progress to overt right ventricular failure.**

VTE and pregnancy

- **Maternal mortality:** VTE is the leading cause.

- **CTPA:**

  may be performed safely with fetal shielding (0.01-0.06 mGy). It is important to consider the risk of radiation to breast tissue (particularly if family history of breast carcinoma) and the risk of iodinated contrast media to mother and fetus (neonatal hypothyroidism).

- **V/Q scanning:**

  greater radiation dose to fetus (0.11-0.22 mGy) but less to maternal breast tissue.

- **In utero radiation exposure:**

  estimated incidence of childhood malignancy is about 1 in 16 000 per mGy.

- **Warfarin:**

  teratogenic, so VTE should be treated with LMWH during pregnancy.

Thromboembolic disease in old age

- **Risk:** rises by a factor of 2.5 over the age of 60 years.

- **Prophylaxis for VTE:**
  should be considered in all older patients who are immobile as a result of acute illness, except when this is due to acute stroke.

- **Association with cancer:**
  the prevalence of cancer among those with DVT increases with age but the relative risk of malignancy with DVT falls; therefore intensive investigation is not justified if initial assessment reveals no evidence of an underlying neoplasm.

- **Warfarin:**
  older patients are more sensitive to the anticoagulant effects of warfarin, partly due to the concurrent use of other drugs and the presence of other pathology. Life-threatening or fatal bleeds on warfarin are significantly more common in those aged over 80 years.

- **Chronic immobility:**
  long-term anticoagulant therapy is not required as there is no associated increase in thromboembolism