Pulmonary embolism

Objectives:

- To know etiology & risk factors for pulmonary embolism
- How to diagnose pulmonary embolism & its major clinical presentations
- Lines of treatment of pulmonary embolism

[Color index : Important | Notes | Extra]

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The doctor didn't talk about the different type of PE he only mention the massive PE although they are mentioned in details in the books.

Resources:

- 435 slides
- Step-up to medicine, Kumar, Davidson
- 434 Teamwork

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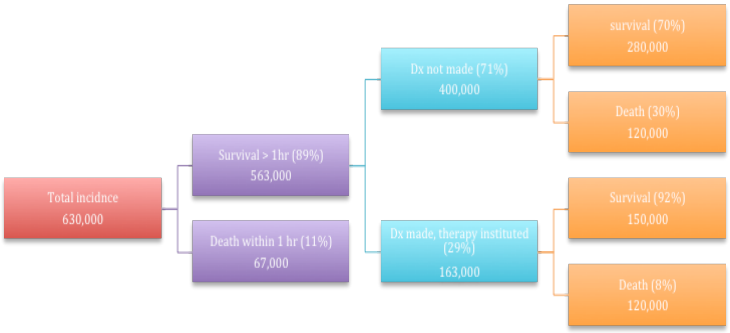
"Medicine is an art, nobody can deny it."

To know etiology & risk factors for pulmonary embolism

- **Overview:** 1: 23 minutes
  - **Pulmonary embolism (PE)** and **deep venous thrombosis (DVT)** are considered as a continuum of one clinical entity **(venous thromboembolism)** diagnosing either PE or DVT is an indication for treatment.
  - A **PE** occurs when a **thrombus** "usually formed in the systemic veins or *rarely* in the right heart (<10% of cases)" in another region of the body dislodges and embolizes to the **pulmonary vascular tree** (pulmonary arterial system) via the right ventricle (RV) and pulmonary artery.
    - ➔ Blood flow **distal** to the embolus is obstructed.

  - **Epidemiology[1]:**
    - 10% of clinical pulmonary emboli are fatal.
    - Over **317,000** deaths were related to VTE in six countries of the European Union (with a total population of **454.4** million) in 2004 Of these cases:
      - **34%** presented with sudden fatal PE
      - **59%** were deaths resulting from PE that remained undiagnosed[2]
      - Only **7%** of the patients who died early were correctly diagnosed with PE before death.



    - **Incidence of pulmonary embolism per year in the united states[3]:**

      50,000 individuals die from PE each year in USA, the incidence of PE in USA is 500,000 per year.

- **Risk factor for venous thrombosis[4]:** here
  - **Stasis,**
  - **Injury to venous intima**
  - **Alterations in the coagulation-fibrinolytic system.** Hypercoagulable state : inherited conditions (Protein c, antithrombin 3, factor V leiden deficiency) > if patient is young or recurrent DVT you need to investigate these.

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[1] **Graph explanation**: 11% of PE patients die within 1 hr because of massive PE. (Note: Massive PE= SHOCK + HYPOTENSION, the rest (89%) survive after 1 hr: 71% of the later are misdiagnosed with mortality rate of 30%" and 29% are diagnosed with mortality rate of 8%

[2] Undiagnosed = you give them the treatment then they go home & develop another clot and die because of it

[3] Dx: diagnosis

[4] **Put in mind not only PE**

- **Risk factors for DVT:** here

U've to ask the PT. about all of these when PE is suspected

Patient factors	Surgical conditions	Medical conditions	Haematological disorders
- Advanced age >60 **- Obesity** **- Pregnancy** **- Oral contraceptive pills** **- Postpartum** **-Prolonged immobility:** bed rest, long-distance travel **-Varicose veins.** **-previous Hx of DVT or PE.**	**- General anesthesia** Muscle relaxants > muscles do not contract **- Major surgery:** especially pelvic surgery (orthopedic procedures) and **Lower limb.**	**- Cardiac and respiratory diseases:** especially Congestive heart failure. Because of stasis **- Malignancy,** **- Nephrotic syndrome** **- Major trauma.**	**- Coagulation problems:**[5][6] Protein C and S deficiency, Antithrombin III deficiency , factor V leiden - Thrombophilia[7]: It needs an insult to trigger PE as smoking or being pregnant. - Antiphospholipid antibody/ lupus anticoagulant.

Source of emboli:

Lower extremity DVT	Upper extremity DVT	Other sources
PE is the major complication of DVT(>95%). - **Most** pulmonary emboli arise from thromboses in the **deep veins of lower extremities** above the knee (iliofemoral DVT). - Pulmonary emboli can also arise from the **deep veins of the pelvis.** - **calf vein thrombi** have a **low incidence** of embolizing to the lungs.[8]	"**Axillary thrombosis**" is a **rare** source of emboli. - (it may be seen in **IV drug abusers** due to foreign material).	**- Thrombus in other vein:** Renal, Uterine, Right cardiac chamber **- Other sources of emboli :** - Fat embolism (due long-bone fractures) - Amniotic fluid embolism (during delivery) - Air embolism (due to trauma to thorax) - Septic embolism (IV drug use) -In lupus anticoagulant PE can be caused from an artery.

Objective: How to diagnose pulmonary embolism & its major clinical presentations

Clinical features:

★ **Most often, PE is clinically silent.**

- **Sudden onset of unexplained dyspnea,** is the most common,and often the only symptom of pulmonary embolism.
- **Pleuritic chest pain** (Sharp & can be Pinpointed with one finger) and **Hemoptysis** "Not diagnostic" are present only when infarction has occurred.

Table 3 Clinical characteristics of patients with suspected PE in the emergency department (adapted from Pollack et al. (2011)).

Feature	PE **confirmed** Feature (n= 1880)	PE **not confirmed** (n= 528)
Dyspnea	50%	51%
Pleuritic chest pain	39%	28%
Cough	23%	23%
Substernal chest pain	15%	17%
fever	10%	10%
Hemoptysis	8%	4%
Syncope	6%	6%
Unilateral leg pain	6%	5%
Signs of DVT (unilateral 18% extremity swelling)	24%	18%

DVT: deep vein thrombosis.

★ Clinical clues are not specific that means we cannot make the diagnosis of PE based on them; their main value lies in suggesting the diagnosis which must be confirmed or rejected by the investigations.

[5] **(inherited conditions),**"you need to investigate these"
[6] if patient is young or recurrent DVT.
[7] is a condition where the blood has an increased tendency to form clots
[8] But in many patients these thrombi progress into the proximal veins, increasing the incidence of PE.

★ **there are three typical clinical presentations of pulmonary embolism:** here

1. **Acute Small/Medium Pulmonary Embolism:**

pathophysiology:	DVT or any thrombus that embolizes through the **systemic circulation** into the **RA → RV → pulmonary artery**[9] **→ Occlusion of segmental (terminal) pulmonary artery → infarction**[10] **+\- effusion**[11].
Symptoms:	**- pleuritic chest pain , - breathlessness, - hemoptysis**[12].
Signs:	- tachypnea , - sinus tachycardia , - localized pleural rub , - coarse crackle , - low grade fever.

2. **Acute Massive Pulmonary Embolism:**[13]

massive means major hemodynamic effect (shock & hypotension), not referred to the size.

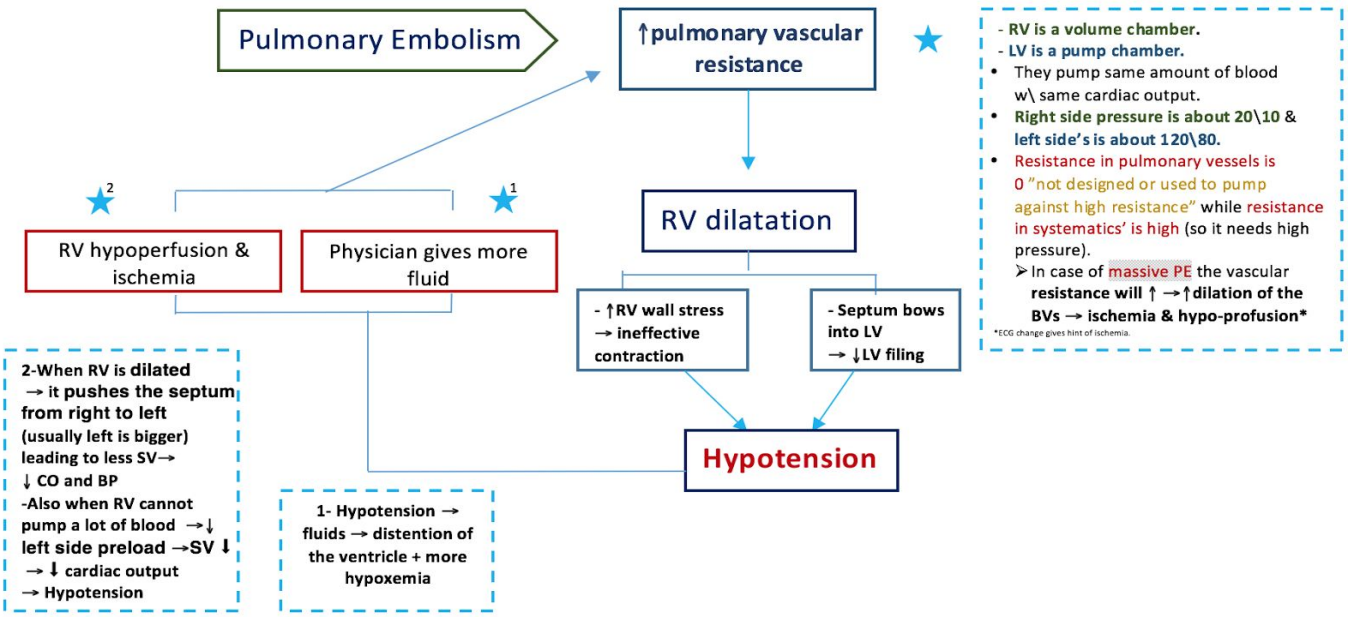
pathophysiology:	DVT or any thrombus that embolizes through the **systemic circulation** into the **RA → RV → pulmonary artery → occlusion of the vascular bed**[14]**→ ↑ pulmonary resistance and pressure → ↑ RV pressure → acute obstruction of RV outflow → ↓ preload → ↓ cardiac output → acute right ventricular failure → death** see below "PE death spiral" ◆ **Hypoxemia ensues stimulating vasoconstriction increase in PAP** - In patients without cardiopulmonary disease, occlusion of **25-30** % of the vascular bed **increase in Pulmonary artery pressure (**PAP) - **More than 50%** of the vascular bed has to be occluded before PAP becomes substantially elevated - When **obstruction approaches 75%,** the **RV** must generate systolic pressure in excess of 50mmHg to preserve pulmonary circulation - The normal RV is unable to accomplish this acutely and eventually fails.[15]
Symptoms:	**- crushing central chest "ischemic**[16]**" pain, - severe dyspnea, - shocked**[17]**, -Faintness or syncop**
Signs:	- tachypnea , - severe cyanosis, **- hypotension,** - ↑ JVP, - widely split loud P2 , - RV gallop rhythm with heave, - ↓ urinary output.

3. **Multiple recurrent (chronic) Pulmonary Embolism:**

pathophysiology:	**Multiple chronic occlusions of pulmonary vasculature → pulmonary hypertension → right heart failure.**
Symptoms:	**- exertional dyspnea, -weakness, - late symptoms of HF and pulmonary HTN: angina and syncope.**
Signs:	- RV heave, - loud P2, - at the end stage: signs of right ventricular overload[18].

[9] This highlighted sequence constant in all the 3 presentation.
[10] **There is ventilation but there is no perfusion → dead space "infarction" → impaired gas exchange →hypoxemia. After some hours NO surfactant → alveolar collapse.**
[11] If there was it will be **blood-stained.**
[12] often 3 or more days after the initial event.
[13] **Fatal PE typically leads to death within one to two hours of the event.**
[14] **↓ cross-sectional arterial bed.**
[15] rapid RV dilatation and dysfunction which is clinically manifest as hypotension and cardiogenic shock.
[16] due to lack of coronary blood flow.
[17] apprehensive, pale and sweaty.
[18] - ↑ JVP, - widely split loud P2 , - RV gallop rhythm with heave

◆ **Pulmonary Embolism death spiral:**



- **Diagnosis:**
  - The symptoms and signs of **small/medium PE** are often subtle and nonspecific, so the diagnosis is often **delayed** or even **completely missed**.
  - The diagnosis of **Acute massive PE** should be explored whenever **oxygenation** or **hemodynamic** parameters are severely compromised without explanation.

Arterial blood gas (ABG)[19]:	★ levels are **NOT** diagnostic for PE. ◆ **Massive EP:** - Markedly abnormal with ↓ PaO2 "arterial **hypoxaemia**[20]" and ↓ PaCO2[21]. - pH is high, Metabolic acidosis. ◆ **small/medium PE: normal** or ↓ PaO2 or ↓ PaCO2 ◆ **Multiple recurrent PE: Exertional** ↓ PaO2
Chest X-ray (CXR): here	★ usually **NORMAL[22] so it's Not diagnostic,** but it is the most useful in **excluding alternative diagnoses[23].** ◆ **Massive EP:** Usually normal, but sometimes there are **oligaemia and dilatation (enlargement) of the pulmonary artery[24].** ◆ **small/medium PE: here** ◆ **linear shadow (opacity)→ "refers to previous scars", and Atelectasis,** ◆ **Hampton's hump[25] (pleural based peripheral Wedge shaped opacity due to infarction[26]) and Westermark's sign (focal peripheral hyperlucency 2ry to regional oligaemia), both are rarely seen,** ◆ **signs of pleural effusion: blunted costophrenic angle,**

[19] test measures the acidity (pH) and the levels of oxygen and carbon dioxide in the blood from an artery.

[20] Significant hypoxemia is almost uniformly present when there is a hemodynamically significant PE. **Hemodynamically PE** = unstable **PE** ("massive" **PE**). so The diagnosis of massive PE should be explored whenever oxygenation or hemodynamic parameters are severely compromised without explanation

[21] Due to hyperventilation.

[22] You may see some ischemic changes. However Normal appearances in an symptomatic patient should raise the suspicion of PE, as should bilateral changes in a patient presenting with unilateral pleuritic chest pain

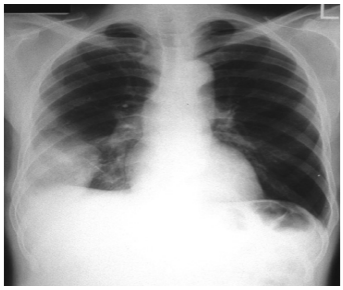
[23] pneumonia or pneumothorax

[24] Fleischner sign

[25] E.g. Pleural-Pulmonary opacities.

[26] **Infarction is not usual in PE..WHY?**
The Lung has: 1- **Dual blood supply**: pulmonary artery (Main supply) & bronchial artery (which comes from the systemic circulation, from the aorta). 2- **lower Oxygen consumption** than that in the heart.

- Raised hemidiaphragm. Atelectasis elevate the diaphragm.
- Multiple recurrent PE: may be NORMAL, but sometimes there might be:
- Enlarged pulmonary artery trunk,
- Enlarged heart, prominent right ventricle
- Oligemic lung.



E.g. of CXR showing pulmonary infarction in right lower lobe:

A patient had **low-grade fever**, **hemoptysis**, and **pleuritic chest pain. ventilation-perfusion scan** was done and the read shows **high probability** for pulmonary embolism.

On CXR: A signifies pulmonary infarction in the right lower lobe seen as A **pleural-based density** in the lower lobe with the convexity directed toward the hilum **"Wedge shaped"**.

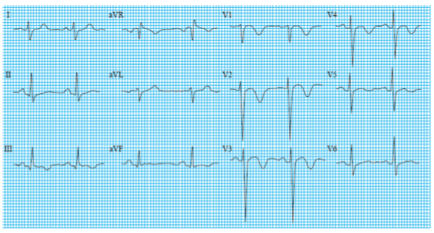
- **This sign is also known as ? "Hampton's hump."**

ECG[27]:

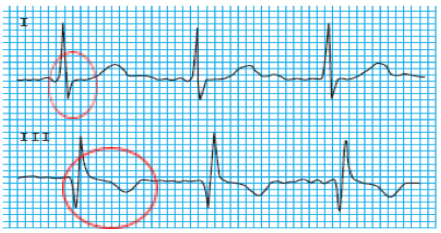
★ often **NORMAL** but is useful in **excluding alternative diagnoses**[28].

◆ **Massive EP[29]:**

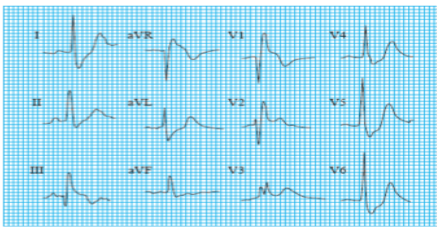
- The 'classic' ECG pattern **(S_1 , Q_3, T_3 anterior T-wave inversion[30])**[31] is **rare** and it's only suggestive NOT diagnostic
- **Right Bundle Branch Block (RBBB).**



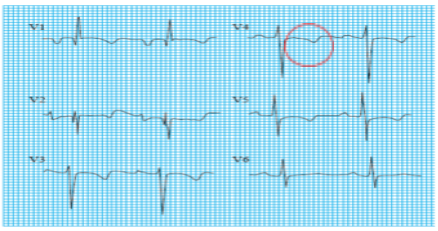
T-wave inversion



S_1, Q_3, T_3 pattern



Right Bundle Branch Block (RBBB).



right ventricular strain

- S wave (Lead I), **Narrowed QRS** (incomplete right bundle branch block.), **Wide QRS** (Complete bundle branch block.)

- Normal duration of QRS = 0.02

- small/medium PE: sinus tachycardia.
- Multiple recurrent PE: can be NORMAL or show signs of:
- Pulmonary hypertension,
- RV hypertrophy and strain.

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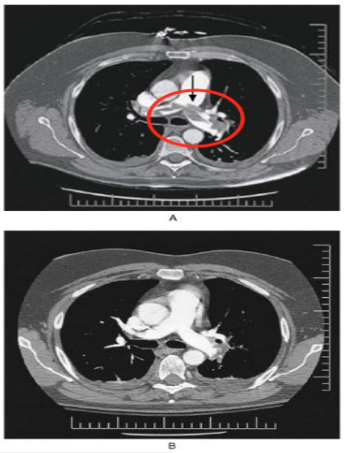
[27] Non-specific findings.
[28] E.g. Acute myocardial infarction and pericarditis.
[29] These findings are an evidence of right ventricular strain due to larger emboli
[30] Due to Ischemic changes (Right side is dilated).
[31] The number represent the number of lead where u can see the change.

D-dimer[32]: here	- fairly sensitive test (90% to 98%) with low Specificity. - An **elevated** D-dimer is of limited value,as it may be raised in a variety of conditions including PE.[33] (**negative**, you can rule out a clot. but if it is **positive**, this does not help you.) - If results are **NORMAL OR LOW** (< 500 ng/mL, measured by ELISA) and **clinical suspicion (risk) is low**, have a high negative predictive value **(PE is very unlikely)** and further investigation is usually unnecessary - **Disregarded** the result if it is **NORMAL** in **high-risk patients,** and further investigation is mandatory even.[34]
★ **CT pulmonary angiography (CTPA):**	Helical (spiral) computed tomography scan of the chest with IV contrast[35], **is the first-line diagnostic test + Has replaced V/Q scan.** ◆ Its advantages: - have a sensitivity of **83%** and specificity of **96%**, with a positive predictive value of **92%**.[36] - Visualising the distribution and extent of the emboli[37], - Highlighting an alternative diagnosis[38], ◆ Its disadvantages: - As the contrast media may be **nephrotoxic**, care should be taken in patients with renal impairment, - Should be avoided in those with a history of **allergy** to iodinated contrast media.  **A-** PE "Saddle clot." **B-** after treatment "thrombolytics" ★ In combination with clinical suspicion, guides treatment: - Data suggest that a **negative Spiral CT** is an adequate criterion for excluding PE in patients with a **non-high clinical probability of PE.** - If **negative** with **high** clinical probability (there is a 5% incidence of PE) so, do V\Q scan. **What if there wasn't a CT?** **Treat with your clinical suspicion,** Start with anticoagulation & do the CT when it avaliable (Stop the anticoagulation if negative).
Colour Doppler ultrasound of the leg veins:	Remains the investigation of choice in patients with suspected **DVT[39]** (performed for the detection of **clots in pelvic or iliofemoral veins**), but can be used in patients with **suspected PE**[40]. ◆ **Interpretation of results:** 1. If there is **a positive result,** treat with **IV anticoagulation** (heparin); treatment of DVT is the same as for PE. - Keep in mind that with this approach, a false positive ultrasound will result in anticoagulation of some patients who do not have DVT or PE. Also, a negative result is not helpful, as patient may still have a PE despite no DVT on ultrasound. 2. This test is very helpful when positive, but of **little value when negative** (negative results occur in 50% of patients with proven PE).

[32] is a specific degradation product released into the circulation when cross-linked fibrin undergoes endogenous fibrinolysis, levels can be elevated in patients with PE and DVT.
[33] Any cause of clot or increased bleeding can elevate the d -dimer level. E.g. myocardial infarction, CHF, pneumonia, sepsis and postoperative.
[34] Other circulating markers that reflect right ventricular micro-infarction, such as troponin I and brain natriuretic peptide, are under investigation.
[35] Dark color = clot.
[36] **increased by simultaneous visualisation of the femoral and popliteal veins.**
[37] Can visualize very small clots (as small as 2 mm)
[38] E.g. consolidation, pneumothorax or aortic dissection.
[39] Not PE
[40] particularly if there are clinical signs in a limb, as many will have identifiable proximal thrombus in the leg veins.

Ventilation-perfusion lung scan (V/Q):

- Traditionally, this **was** the **most common** test used when PE is suspected, but it has been replaced by helical CT as the initial study of choice.. WHY we stop using it in the same way that we used to do? Because: it is Time consuming, Requires patient cooperation and it is Not available (in all hospitals).
  - Plays an important role in diagnosis when there is a **contraindication to helical CT** (spiral CT scan) or in centers which are inexperienced in performing helical CT scans:
    - Radiation is much less than the CT more safe in pregnancy,
    - May be particularly useful when the chest x-ray is clear and when there is no underlying cardiopulmonary disease.
- To know how it performed see here: investigation of lung diseases , but in short:

1. Patient will **inhale radioactive** → take a photo →OK all the areas are **ventilated** now.
2. Then they give them **contrast** → see if there is match or mismatch*.

*If area is ventilated but not perfused → **mismatch** (clot).

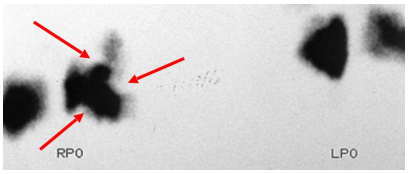
- **Interpretation of results:** can be either **NORMAL**, **low-probability, intermediate probability, or HIGH-PROBABILITY** (treatment guidelines based on PIOPED study):

Prospective investigation of pulmonary embolism diagnosis results

Scan category	PE present	PE absent	PE uncertain	No angiogram	Total
High probability	102	14	1	7	124
Intermediate probability	105	217	9	33	364
Low probability	39	199	12	62	312
Near normal or normal	5	50	2	74	131
Total	251	480	24	176	931

- A **NORMAL** V/Q scan virtually rules out PE, **no** further testing is needed, **but** a scan is almost **never "normal" in anyone**.
- A **HIGH PROBABILITY** V/Q scan has a very high sensitivity for PE; **treat with heparin.**
- If there is **low or intermediate probability, clinical suspicion** determines the next step:
  - ★ If **clinical suspicion is high**, → **pulmonary angiography** is indicated. Alternatively, perform a **lower extremity duplex ultrasound** to avoid pulmonary angiography.
  - If the **duplex is positive**, treatment for DVT is the same as for PE[41].
  - If the **duplex is negative/uncertain**, then pulmonary angiography is indicated to exclude PE.

Pic: High-probability ventilation-perfusion scan. →

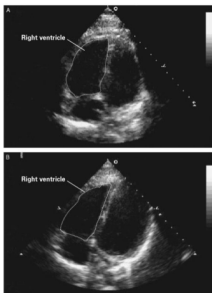


Bedside echocardiography:

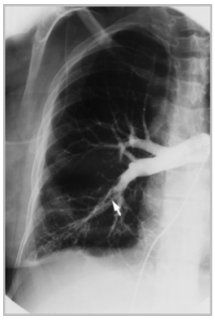
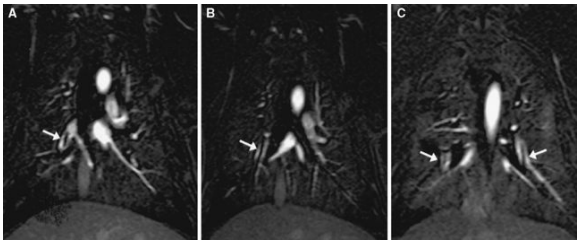
is extremely **helpful in the differential diagnosis**[42] and assessment of acute circulatory collapse .

- ★ **In massive PE:**
- **Acute dilatation of the right heart** is usually present,
- A clot in the right ventricular outflow tract.may be visible,
- Vigorously contracting left ventricle.

Pic: Trans esophageal Echo: One of the investigations that we use in ICU patients. **A-**before **B-** after treatment



[41] It will be discussed later.
[42] E.g. left ventricular failure, aortic dissection and pericardial tamponade, can also be identified.

Conventional pulmonary angiography:	**It is the is the gold standard test in detecting PE, but it has been largely superseded by CTPA[43] or MRI.** - Definitively diagnoses or excludes PE**, but is invasive[44].** - **Contrast** injected into pulmonary artery branch after percutaneous **catheterization** of femoral vein. (Catheter internal jugular > RA > RV > pulmonary artery > contrast) - The diagnosis is confirmed by persistent filling defect or abrupt cut-off of flow.  ◆ Consider when: - noninvasive testing is equivocal and risk of anticoagulation is high, or - if the patient is hemodynamically unstable and embolectomy may be required. Pic: **Abrupt cut-off of flow** to the right and left upper lobe vessels is seen in this patient.
MR imaging: here	**MR imaging CT is better, but can be used if CT angiography is contraindicated.** 

Objective: Lines of treatment of pulmonary embolism

- **Treatment:**
  - **General measures:**

Start treatment immediately in high suspicion you don't need to confirm the PE.

★ **All patients should receive high-flow oxygen (60-100%)[45] to correct hypoxemia.** Patients with pulmonary infarcts require bed rest and analgesia[46].

★ Circulatory shock[47] should be treated with intravenous fluids or plasma expander[48], but inotropic agents[49] are of limited value.

[43] but is still useful in selected settings or to deliver catheter-based therapies.
[44] Angiography is rarely performed because it carries a 0.5% mortality.
[45] unless they have significant chronic lung disease.
[46] should be used with caution in the hypotensive patient.
[47] very ill patients will require care on the intensive therapy unit.
[48] Diuretics and vasodilators should also be avoided, as they will reduce cardiac output.
[49] As the hypoxic dilated right ventricle is already close to maximally stimulated by endogenous catecholamines. Even that, sometimes they're required improve the pumping of the right heart are sometimes required.

- **Anticoagulation**:

Anticoagulation should be commenced immediately in patients with a high or intermediate probability of PE[50]

★ Acute anticoagulation therapy with **HEPARIN** (either unfractionated or low-molecular-weight) **to prevent another PE.**

- Heparin acts by promoting the action of antithrombin III.
- The dose is based on the patient's weight.
- should continue for **at least 5 days** (usually continued for 5–7 d), during which time an oral anticoagulant is commenced.
- **Platelet count** should be monitored at **least every 3 d** during initial heparin therapy[51],
- **Therapeutic APTT** should correspond to plasma heparin level of **0.2–0.4 IU/mL**.
- After initiating heparin therapy, **repeat APTT every 6 h** for first 24 h and then **every 24 h** when therapeutic APTT is achieved **(The goal is an APTT of 1.5 to 2.5 times control).**

★ **Oral anticoagulant (WARFARIN[52] – a vitamin K antagonist –)** is usually begun immediately and the heparin is tapered off as the oral anticoagulant becomes effective (Heparin can be stopped[53] after 4–5 d of warfarin therapy when **INR is in 2.0–3.0 range** for at least 24 hours).

- **Warfarin 5 mg/d** can be started on **day 1 of therapy;** there is no benefit from higher starting doses,
- Oral anticoagulants are **continued for 6 weeks to 6 months,** depending on the likelihood of recurrence of venous thrombosis or embolism. In some situations, such as after **recurrent embolism**, lifelong treatment is indicated.
- Regular measurement of the INR is required throughout the duration of anticoagulation.

Drugs that decrease warfarin requirement	Drugs that increase warfarin requirement
Phenylbutazone	Barbiturates
Metronidazole	Carbamazepine
Trimethoprim-sulfamethoxazole	Rifampin
Amiodarone	Penicillin
Second- and third-generation cephalosporins	Griseofulvin
Clofibrate	Cholestyramine
Erythromycin	
Anabolic steroids	
Thyroxine	

Why?

1-narrow therapeutic index of warfarin and 2- its propensity to interact with other drugs and food (table: Important drug interactions with warfarin: u don't have to memorise it).

★ **Complications of anticoagulation:**

	Complication	Management
Heparin	**Bleeding**	- Stop heparin infusion. - in **severe bleeding**, the anticoagulant effect of heparin can be reversed with **IV protamine sulfate** **1 mg/100 units of heparin bolus** or 0.5 mg for the number of units given by constant infusion over the past hour[54]; provide supportive care including transfusion and clot evacuation from closed body cavities as needed.
	Heparin-induced thrombocytopenia and thrombosis[55]	- Carefully **monitor platelet count during therapy.** **(after 3 days of initiating therapy and repeat it after 6 days)** - Stop-heparin for platelet counts <75,000.

[50] may be safely withheld in those with low clinical probability, pending investigation.
[51] Due to HIT syndrome
[52] Newer thrombin or activated factor X inhibitors offer more predictable dosing and have no requirement for coagulation monitoring; they may ultimately replace warfarin. here
[53] LMWH should be continued for at least 6 months before switching to warfarin In patients with cancer associated VTE.
[54] Fractionated > ⬇ half life. LMW > ⬆ half life > predicted dose response
[55] idiosyncratic reaction: Immune , Not dose dependent.

		- Replace heparin with **direct inhibitors of thrombin**-like **desirudin** if necessary. These agents do not cause heparin-induced thrombocytopenia. Avoid platelet transfusion because of the risk for thrombosis.
	Heparin-induced osteoporosis (therapy >1 mo)	**LMWHs** may have **lower propensity** to cause osteoporosis as compared with **unfractionated heparin**; consider LMWH if prolonged heparin therapy is necessary.
Warfarin	**Bleeding**	- Stop therapy. - **Administer vitamin K and fresh-frozen plasma** for **severe bleeding**; provide supportive care including transfusion and clot evacuation from closed body cavities as needed.
	Skin necrosis (rare)	Supportive care.
	Teratogenicity	Do not use in pregnancy or in patients planning to become pregnant.

(Anticoagulation **(Heparin\warfarin)** prevents further clot formation, but **does not lyse existing emboli or diminish thrombus size.**)**Thrombolytics = dissolve already formed.**

- **Approved thrombolytics for pulmonary embolism:**[56]

MASSIVE PE = THROMBOLYTICS

★ **Recombinant tissue-plasminogen activator: Thrombolytics = dissolve already formed clots**

100 mg as a continuous peripheral intravenous infusion administered **over 2 h**

★ **Streptokinase:**

250,000 IU as loading dose **over 30 min**, followed by 100,000 U/h **for 24 h**

★ **Urokinase:**

4400 IU/kg as a loading dose **over 10 min**, followed by 4400 IU/kg/h **for 12-24 h.**

◆ **Indications:**

- Hemodynamically unstable patient. (Patients with massive PE with persistent hypotension).
- Hypoxia on 100% oxygen
- Right ventricular dysfunction by echocardiography (thrombolysis can reverse this).

◆ **Contraindications:**

Relative:

- **Recent surgery** within **last 10 d** or **Previous arterial punctures** within **10 d,**
- **Neurosurgery** within **6 months** ,
- **Ophthalmologic surgery** within **6 weeks ,**
- **Bleeding disorder** (thrombocytopenia, renal failure, liver failure)[57],
- **Hypertension >200 mmHg systolic** or **110 mmHg diastolic ,**
- **Placement of central venous catheter** within **48 h,**
- **Hypertensive retinopathy** with **hemorrhages** or **exudates Intracerebral aneurysm** or **malignancy,**
- **Cardiopulmonary resuscitation** within **2 weeks,**
- **Cerebrovascular disease,**

[56] 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**.

[57] patients must be screened carefully for haemorrhagic risk, as there is a high risk of intracranial haemorrhage.

- **Major internal bleeding** within the **last 6 months**,
- **Pregnancy** and the **1st 10 days postpartum,**
- **Infectious endocarditis** or **Pericarditis,**
- **Severe trauma** within **2 months,**

Absolute:

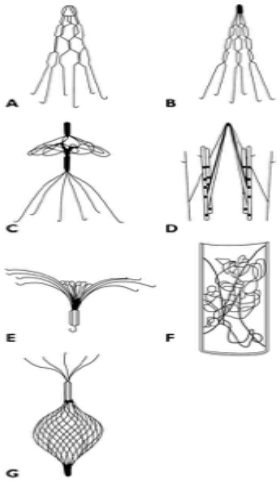
- **Active internal bleeding**

  - **Other Treatment Modalities:** If thrombolytics have failed

★ Surgical embolectomy,

★ Percutaneous catheter-directed treatment[58]:

◆ **Various inferior vena caval filters:**



- 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:**

- **Anticoagulation contraindicated** (eg, patients with multiple trauma, active bleeding)
- **Failure of antithrombotic therapy**
- **Complications from anticoagulant** therapy preclude further use
- **Prophylaxis against embolism** from preexisting DVT in patients with poor cardiopulmonary reserve or in patients at high risk to develop DVT.
- Patients with **recurrent PE** undergoing thromboendarterectomy.

- **Complications of IVC filter placement (rare):**

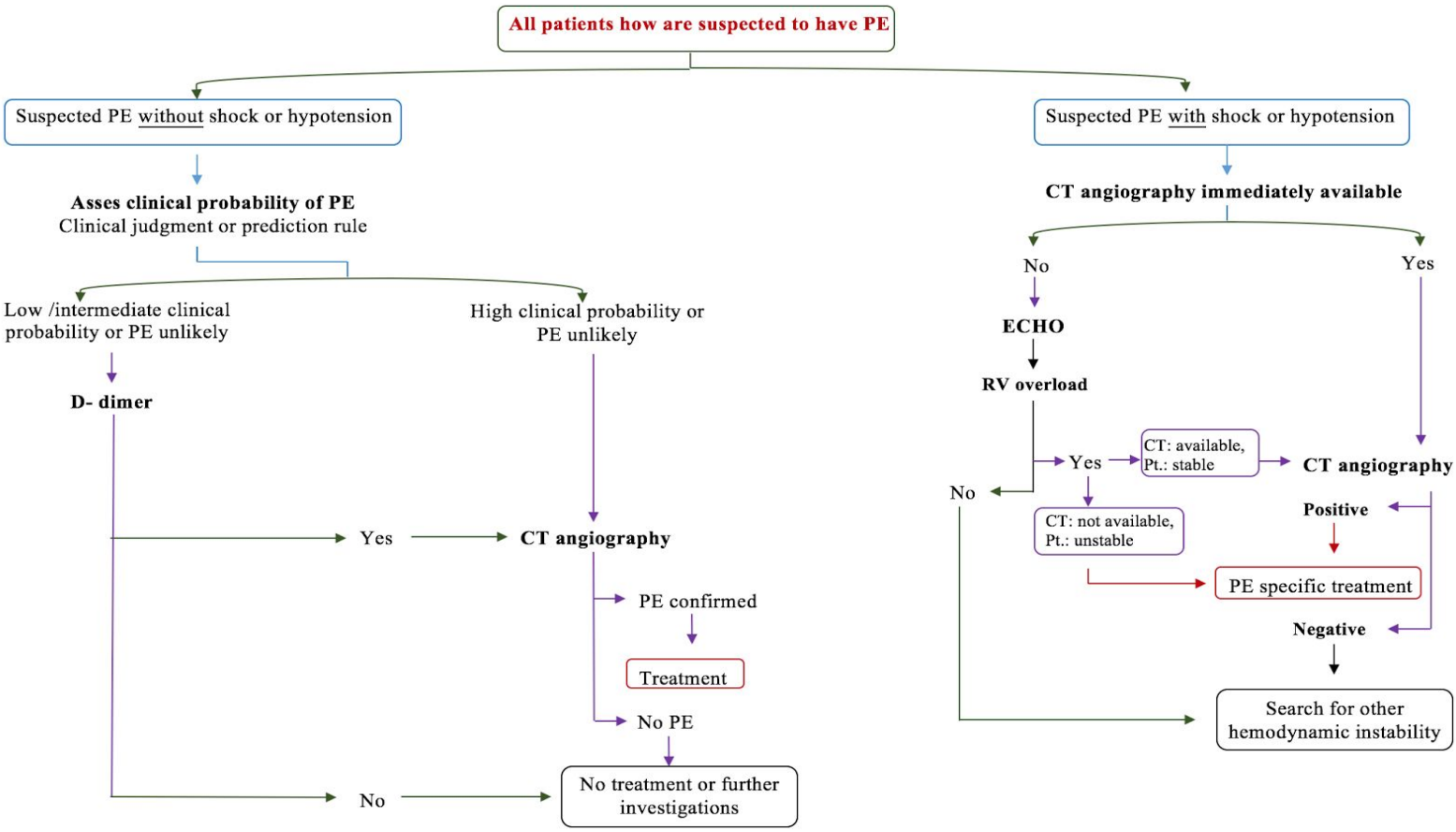
- filter migration or misplacement,
- filter erosion and perforation of IVC wall, and IVC obstruction due to filter thrombosis.

Conclusions:

- PE is common and under-recognized serious medical problem
- Early diagnosis and treatment is essential for good outcome
- High index of suspicion is needed in high risk patients.

[58] Either they suck it or fragment it.

- **HELPFUL summary:**



- Risk factors for venous thromboembolism:

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

- Factors predisposing to venous thrombosis:

24.17 Factors predisposing to venous thrombosis

Patient factors
- Increasing age
- Obesity
- Varicose veins
- Previous DVT
- Family history, especially of unprovoked VTE when young
- Pregnancy/puerperium
- Oestrogen-containing oral contraceptives and HRT
- Immobility, e.g. long-distance travel (> 4 hrs)
- IV drug use (femoral vein)

Surgical conditions
- Major surgery, especially if > 30 mins' duration
- Abdominal or pelvic surgery, especially for cancer
- Major lower limb orthopaedic surgery, e.g. joint replacement and hip fracture surgery

Medical conditions
- Myocardial infarction/heart failure
- Inflammatory bowel disease
- Malignancy
- Nephrotic syndrome
- Pneumonia
- Neurological conditions associated with immobility, e.g. stroke, paraplegia, Guillain–Barré syndrome

Haematological disorders
- Polycythaemia rubra vera
- Essential thrombocythaemia
- Deficiency of anticoagulants: antithrombin, protein C, protein S
- Paroxysmal nocturnal haemoglobinuria
- Gain-of-function prothrombotic mutations: factor V Leiden, prothrombin gene *G20210A*
- Myelofibrosis

Antiphospholipid syndrome
- Lupus anticoagulant (more strongly associated with thrombosis than anticardiolipin antibodies)
- Anticardiolipin antibody

- typical clinical presentations of PE:

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

(JVP = jugular venous pressure; PE = pulmonary embolism; RBBB = right bundle branch block; RV = right ventricular)

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

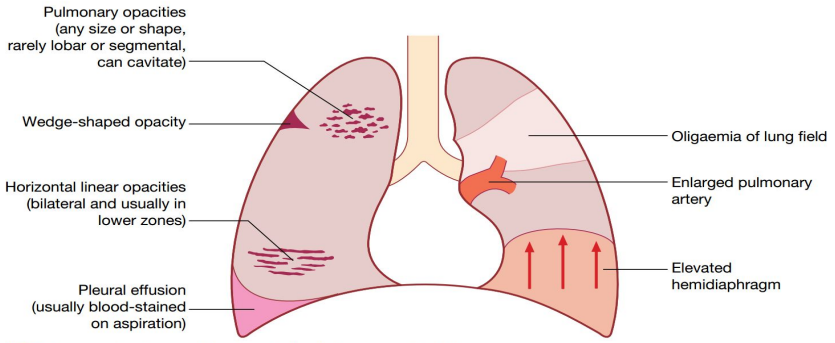


Fig. 19.67 Features of pulmonary thromboembolism/infarction on chest X-ray.

- D- dimer assay:

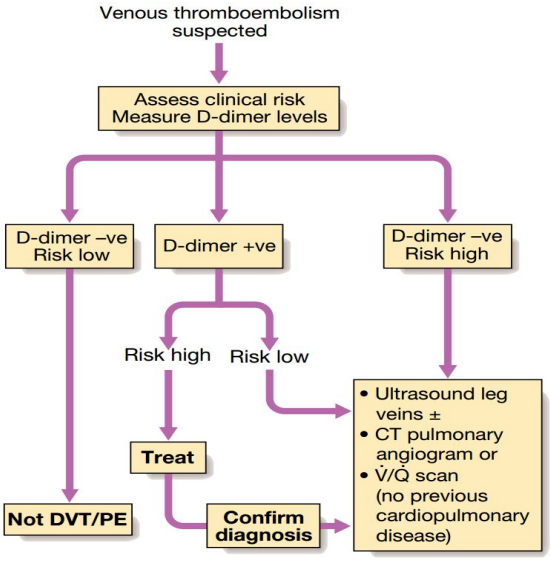


Fig. 19.68 Algorithm for the investigation of patients with suspected pulmonary thromboembolism. Clinical risk is based on the presence of risk factors for venous thromboembolism and the probability of another diagnosis.

- CXR findings in patients with PE

Chest radiographic findings in patients with pulmonary embolism

	COPD, % (n= 21)	No prior cardiopulmonary disease, % (n= 117)
Atelectasis or pulmonary parenchymal abnormality	76	68
Pleural effusion	52	48
Pleural-based opacity	33	35
Elevated diaphragm	14	24
Decreased pulmonary vascularity	38	21
Prominent central pulmonary artery	29	15
Cardiomegaly	19	12
Westermark's sign*	5	7
Pulmonary edema	14	4

- Sensitivity of spiral CT, MRI angiography, real-time MRI angiography, for detecting pulmonary emboli:

Cases

1- A 66-year-old woman presents to accident and emergency with a 2-day history of shortness of breath. The patient notes becoming progressively short of breath as well as a sharp pain in the right side of the chest which is most painful when taking a deep breath. The patient also complains of mild pain in the right leg, though there is nothing significant on full cardiovascular and respiratory examination. Heart rate is 96 and respiratory rate is 12. The patient denies any weight loss or long haul flights but mentions undergoing a nasal polypectomy 3 weeks ago. The most likely diagnosis is:

A. Muscular strain
B. Heart failure
C. Pneumothorax
D. Angina
E. Pulmonary embolism

2- A 60-year-old man presents to accident and emergency with a 3-day history of increasingly severe chest pain. The patient describes the pain as a sharp, tearing pain starting in the centre of his chest and radiating straight through to his back between his shoulder blades. The patient looks in pain but there is no pallor, heart rate is 95, respiratory rate is 20, temperature 37°C and blood pressure is 155/95mmHg. The most likely diagnosis is:

A. Myocardial infarction
B. Myocardial ischaemia
C. Aortic dissection
D. Pulmonary embolism
E. Pneumonia

3- A 41-year-old woman is referred for assessment after suffering a second pulmonary embolus within a year. She has not been travelling recently, has not had any surgery, does not smoke and does not take the oral contraceptive pill. She is not currently on any medication as the diagnosis is retrospective and she is now asymptomatic. What should be the next step in her management?

A. Initiation of warfarin therapy
B. ECG
C. Thrombophilia screen
D. Insertion of inferior vena cava filter
E. Duplex scan of lower limb veins and pelvic ultrasound

4- You are discussing a patient with your registrar who has become acutely short of breath on the ward. After performing an arterial blood gas, you have high clinical suspicion that the patient has a pulmonary embolism. Which of the following is the investigation of choice for detecting pulmonary embolism?

A. Magnetic resonance imaging (MRI) of the chest
B. High-resolution CT chest (HRCT)
C. Chest x-ray
D. Ventilation/perfusion scan (V/Q scan)
E. CT pulmonary angiogram (CT-Pa)

5- A 68-year-old woman has presented with acute onset shortness of breath 24 hours after a long haul flight. Her blood results show a raised D-dimer level and the arterial blood gas shows a *P*O2 of 8.3kPa and *P*CO_2 of 5.4kPa. Your consultant suspects a pulmonary embolism and the patient needs to be started on treatment while a CT-PA is awaited. From the list below, please select the most appropriate treatment regime.

A. Commence loading with warfarin and aim for an international normalized ratio (INR) between 2 and 3
B. Thromboembolic deterrent stockings
C. Aspirin 75mg daily
D. Prophylactic dose subcutaneous low molecular weight heparin+ loading with warfarin and aim for INR between 2 and 3
E. Treatment dose subcutaneous low molecular weight heparin + loading with warfarin and aim for INR between 2 and 3

Answers

1)E This patient is most likely suffering from a pulmonary embolism (E), defined as an occlusion of the pulmonary vasculature by a thrombus causing an area of lung that is ventilated but not perfused. Patients most often complain of shortness of breath, pleuritic chest pain and haemoptysis. Clinical signs can include a pleural rub, coarse crackles and atrial fibrillation. In massive pulmonary embolism there can be a raised JVP, respiratory rate, heart rate and hypotension. The Geneva scoring system (see below) is useful for predicting the risk of a pulmonary embolism: a score of ≤3 (mild), 4–10 (moderate) and ≥11 (high). Muscular strain (A) typically occurs on movement and is not associated with shortness of breath or leg pain and there is usually an indicator of injury or a preceding stressor. Heart failure (B) is unlikely due to the acute presentation of symptoms which tend to occur more insidiously and can be associated with bilateral leg oedema, murmurs, orthopnoea or hepatomegaly, among others. A pneumothorax (C) can present with a similar pleuritic chest pain that occurs in an embolism, however, there is no association with limb pain and a respiratory examination is likely to reveal hyper-resonance. Angina (D) is typically described as a dull or crushing chest pain in the centre of the chest, patients have risk factors such as diabetes, hyperlipidaemia, obesity, smoking and hypertension.

2)C All of the answer options can present as central chest pain, however the patient describes a very typical description of an aortic dissection (C), usually a severe, tearing pain that radiates toward the back though this can be to the jaw depending on the location of the dissection. An MI (A) is typically described as severe, crushing chest pain with an acute onset, this patient has been suffering from a 3-day history of chest pain which makes an infarction unlikely. Although myocardial ischaemia (B), i.e. angina, can occur for a longer period of time they tend not radiate to the back but more toward the jaw, arms or epigastrium, and again are described as crushing in nature rather than tearing. A pulmonary embolism (D) typically presents with pleuritic chest pain, cough and haemoptysis which are not present in this patient, or preceding risk factors such as long haul travel or surgery. Pneumonia (E) is associated with fever and productive coughing.

3)C As the history strongly suggests a thrombophilic trait, e.g. the presence of factor V Leiden, the correct option is a thrombophilia screen (C). This should be completed as rapidly as possible before starting warfarin (A) therapy, which would prevent a proper screen. In fact, a duplex scan (E) would probably be carried out at the same time as the screening, to exclude the presence of thrombus and of pelvic masses. An ECG (B) is irrelevant, while an inferior vena cava filter (D) may be considered later if anticoagulation is ineffective or not tolerated.

4)E CT-Pa (E) is regarded as the investigation/diagnostic tool of choice for the detection of pulmonary embolisms (being the most readily available, sensitive and specific test). CT-Pa is able to detect PEs down to the 5th order pulmonary arteries and is readily obtainable out of hospital hours. Although V/Q scans (D) have high sensitivity/specificity, they are unlikely to be available out of hours and results are reported as low, moderate or high probability. Low probability V/Q scan results may require follow up with CT-Pa for exclusion/diagnosing PEs. Chest x-rays (C) may be normal or may show decreased vascular markings, atelectasis or a small pleural effusion. An occasional late sign on chest x-ray may be a homogenous wedge-shaped area of pulmonary infarction in the lung periphery. High resolution CT-chest (B) may not accurately detail the pulmonary vasculature but will confirm atelectasis and pleural effusion. MRI chest (A) is not used for the exclusion/diagnosis of PEs due to inaccurate imaging of pulmonary vasculature, lengthy scan times and difficulty obtaining a scan out of hours.

5)E Once pulmonary embolism is suspected, anticoagulation must be commenced with treatment dose subcutaneous low molecular weight heparin (e.g. Dalteparin) and warfarin loading (E). Once the INR has stabilized, usually between a therapeutic range of 2–3, the low molecular weight heparin may be stopped and the patient is to continue on warfarin for a minimum of three months. If this is a first presentation of pulmonary embolism, treatment usually ranges from three to six months. If there is a recurrent history of pulmonary embolism, the patient will usually stay on warfarin for life. Patients who have pulmonary emboli secondary to a malignant process (e.g. ovarian carcinoma, bronchogenic carcinoma) will usually be on life-long treatment dose low molecular weight heparin as studies have shown improved anticoagulation when compared to warfarin. Therefore, answers A–D are incorrect here.