Pulmonary embolism (PE) is a medical emergency. It may present with very few clinical signs and/or symptoms, making it easy to miss, and a high index of suspicion is warranted.

PE results from obstruction within the pulmonary arterial tree. The emboli can be caused by:

- Thrombosis - accounts for the majority of cases and has usually arisen from a distant vein and travelled to the lungs via the venous system.
- Fat - following long bone fracture or orthopaedic surgery.
- Amniotic fluid[1].
- Air - following neck vein cannulation or bronchial trauma.

The rest of this article deals with thrombotic PE.

Epidemiology

The incidence of venous thromboembolism (VTE) varies from 1-1.5 per 1,000 person-years[2].

Risk factors

Clots form when one or more of the following factors are present: increased blood coagulability, reduced mobility or blood vessel abnormalities. These correspond to some of the risk factors for VTE (see below). A number of patients may not have any risk factors, making the diagnosis difficult.
**Risk factors for venous thromboembolism**

<table>
<thead>
<tr>
<th>Major risk factors: relative risk of 5-20</th>
<th>Minor risk factors: relative risk of 2-4</th>
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</thead>
<tbody>
<tr>
<td><strong>Surgery:</strong></td>
<td><strong>Cardiovascular:</strong></td>
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<tr>
<td>Major abdominal/pelvic surgery</td>
<td>Congenital heart disease.</td>
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<td>or hip/knee replacement</td>
<td>Congestive cardiac failure.</td>
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<td>(risk lower if prophylaxis used)</td>
<td>Hypertension.</td>
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<td>Postoperative intensive care.</td>
<td>Paralytic stroke.</td>
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<tr>
<td><strong>Obstetrics:</strong></td>
<td><strong>Oestrogens:</strong></td>
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<tr>
<td>Late pregnancy.</td>
<td>Pregnancy (but see major risk factors for late pregnancy and puerperium).</td>
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<tr>
<td>Puerperium.</td>
<td>Combined oral contraceptive.</td>
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<td>Caesarean section.</td>
<td>Hormone replacement therapy.</td>
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<tr>
<td><strong>Lower limb problems:</strong></td>
<td><strong>Haematological:</strong></td>
</tr>
<tr>
<td>Fracture.</td>
<td>Thrombotic disorders (a detailed list is available)</td>
</tr>
<tr>
<td>Varicose veins - previous varicose vein surgery. superficial thrombophlebitis; varicose veins per se are not a risk factor.</td>
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<tr>
<td></td>
<td>Consider this in cases of PE aged &lt;40 years, recurrent VTE or a positive family history.</td>
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<tr>
<td></td>
<td>Memeloproliferative disorders.</td>
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<tr>
<td><strong>Malignancy:</strong></td>
<td><strong>Renal:</strong></td>
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<tr>
<td>Abdominal/pelvic.</td>
<td>Nephrotic syndrome.</td>
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<tr>
<td>Advanced/metastatic.</td>
<td>Chronic dialysis.</td>
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<td></td>
<td>Paroxysmal nocturnal haemoglobinuria.</td>
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<tr>
<td><strong>Reduced mobility:</strong></td>
<td><strong>Miscellaneous:</strong></td>
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<tr>
<td>Hospitalisation.</td>
<td>Chronic obstructive pulmonary disease (COPD).</td>
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<td>Occult malignancy.</td>
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<tr>
<td><strong>Previous proven VTE:</strong></td>
<td>Long-distance sedentary travel.</td>
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<tr>
<td>Intravenous (IV) drug use</td>
<td>Obesity.</td>
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<tr>
<td>(could be major or minor risk factor; no data on relative risk).</td>
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<tr>
<td></td>
<td>Other chronic diseases: inflammatory bowel disease, Behçet's disease.</td>
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<tr>
<td><strong>Other:</strong></td>
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<tr>
<td>Major trauma.</td>
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<tr>
<td>Spinal cord injury.</td>
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<td>Central venous lines.</td>
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</table>

**Presentation**

The symptoms and signs of PE are not specific. Severe cases of PE can lead to collapse or sudden death. Some PEs are rapidly fatal. In the majority of the fatal cases the PE is not clinically diagnosed prior to death.

**Symptoms include**:

- Dyspnoea.
- Pleuritic chest pain, retrosternal chest pain.
- Cough and haemoptysis.
- Any chest symptoms in a patient with symptoms suggesting a deep vein thrombosis (DVT).
- In severe cases, right heart failure causes dizziness or syncope.

**Signs include**:

- Tachypnoea, tachycardia.
- Hypoxia, which may cause anxiety, restlessness, agitation and impaired consciousness.
- Pyrexia.
- Elevated jugular venous pressure.
- Gallop heart rhythm, a widely split second heart sound, tricuspid regurgitant murmur.
- Pleural rub.
- Systemic hypotension and cardiogenic shock.

**Differential diagnosis**

Other causes of collapse, chest pain or dyspnoea - importantly:

- **Acute coronary syndromes**.
- **Aortic dissection** - especially as anticoagulation might be fatal.
- **Cardiac tamponade**.
- **Pneumonia**.
- **Pneumothorax**.
Sepsis.

Assessment[4]

NB: treatment may precede investigations if the patient is very ill (see 'Initial management' below).

National Institute for Health and Care Excellence (NICE) recommendations

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and CXR to exclude other causes.
- If PE is suspected, use the two-level PE Wells’ score to estimate the clinical probability of PE (see below).
- Offer patients in whom PE is suspected and with a likely two-level PE Wells’ score either an immediate computed tomography pulmonary angiogram (CTPA) or immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately. Consider a proximal leg vein ultrasound scan if the CTPA is negative and DVT is suspected.
- Offer patients in whom PE is suspected and with an unlikely two-level PE Wells’ score a D-dimer test and, if the result is positive, offer either an immediate CTPA or immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately.
- For patients who have an allergy to contrast media, or who have renal impairment, or whose risk from irradiation is high:
  - Assess the suitability of a ventilation/perfusion single-photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.
  - If offering a V/Q SPECT or planar scan that will not be available immediately, offer immediate interim parenteral anticoagulant therapy.
- Diagnose PE and treat patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan.
- Consider alternative diagnoses in the following two groups of patients:
  - Patients with an unlikely two-level PE Wells’ score and either a negative D-dimer test, or a positive D-dimer test and a negative CTPA.
  - Patients with a likely two-level PE Wells’ score and both a negative CTPA and no suspected DVT.
  - Offer all patients diagnosed with unprovoked PE who are not already known to have cancer the following investigations for cancer:
    - Physical examination guided by a full and thorough history.
    - CXR.
    - Blood tests (FBC, serum calcium and LFTs).
    - Urinalysis.
  - Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked PE who do not have signs or symptoms of cancer based on initial investigation.
  - Consider testing for antiphospholipid antibodies in patients who have had unprovoked PE if it is planned to stop anticoagulation treatment.
  - Consider testing for hereditary thrombophilia in patients who have had unprovoked PE and who have a first-degree relative who has had DVT or PE, if it is planned to stop anticoagulation treatment.

Risk score

Assessment of the clinical probability of VTE is recommended, as it is relevant when interpreting clinical findings and deciding how to investigate. NICE recommends the Wells’ score but other scoring systems have also been developed.

<table>
<thead>
<tr>
<th>Wells’ Two-level PE Score</th>
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<tbody>
<tr>
<td><strong>Clinical feature</strong></td>
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<tr>
<td>Clinically suspected DVT</td>
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<tr>
<td>Alternative diagnosis</td>
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<tr>
<td>Tachycardia</td>
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<tr>
<td>Immobilisation</td>
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<tr>
<td>Haemoptysis</td>
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<tr>
<td>Malignancy (on treatment</td>
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Clinical probability

- 4 points or less = PE unlikely.
- More than 4 points = PE likely.
Investigations

General investigations[3]

- **Baseline investigations** - as for any ill patient: oxygen saturation, FBC, biochemistry, baseline clotting screen. Troponin and brain natriuretic peptide levels may also be elevated.
- **ECG** - may be normal, or show any of these changes: sinus tachycardia, atrial fibrillation, nonspecific ST or T-wave abnormalities, right ventricular strain pattern V1-3, right axis deviation, right bundle branch block (RBBB), or deep S-waves in I with Q waves in III and inverted T waves in III (‘S1,Q3,T3’ pattern). A large PE can show ECG features of acute cardiac ischaemia (eg, ST depression)[6].
- **CXR** - mainly useful to exclude other chest disease, and is needed for interpreting V/Q scans. It is usually normal, but may show: decreased vascular markings, atelectasis or a small pleural effusion. An occasional late sign may be an homogeneous wedge-shaped area of pulmonary infarction in the lung periphery (Hampton's hump) with its base contiguous to a visceral pleural surface and its rounded convex apex directed toward the hilum.
- **Arterial blood gases** - may show reduced PaO₂, reduced PaCO₂ due to hyperventilation or acidosis.
- **Echocardiography** - may show thrombus in proximal pulmonary arteries and, if normal, can exclude haemodynamically important PE. It cannot exclude smaller PEs. It may show signs of right ventricular strain or right ventricular hypokinesia.
- **Cardiac troponins** - can be indicative of right heart strain.
- **D-dimers** - fibrin D-dimer is a degradation product of cross-linked fibrin. The concentration increases in patients with acute VTE and provides a very sensitive test to exclude acute DVT or PE. D-dimer tests have less specificity and are less useful in some groups of patients - eg, those with high clinical probability; those admitted to hospital for another reason, in whom the suspicion of PE is raised during their hospital stay; individuals older than 65 years; pregnant women[2].

Specific investigations for VTE[3]
The choice and order of investigations will depend on the clinical likelihood of PE, how ill the patient is and availability of the test. The 'gold standard' test is conventional pulmonary angiography, but this is invasive and usually unavailable urgently. Investigation strategies are detailed as part of the initial management and pregnancy sections below. An explanation of the scope of each test helps in understanding these strategies:

- **Leg ultrasound**: in patients with co-existing clinical DVT, lower limb ultrasound as the initial imaging test is often sufficient to confirm VTE and hence to start anticoagulation. However, a single normal leg ultrasound cannot exclude DVT.
- **Isotope lung scanning (V/Q scan)**: although there have been controversies about the accuracy of isotope scans, they are reliable enough to exclude or confirm PE, if performed according to UK protocols. However, if the result is 'indeterminate', further imaging is needed. V/Q scanning is unlikely to be available out-of-hours. Also the results will be reported as low, moderate or high probability.
- **CTPA** has become the method of choice for imaging the pulmonary vasculature in patients with suspected PE.

It is important to appreciate that, although there are risk scores and various D-dimer assays available, clinical suspicion of VTE may still need to be followed up when these results are negative. In this situation it is best to discuss the case further with respiratory physicians and radiologists.

Management

Initial resuscitation

- Oxygen 100%.
- Obtain IV access, monitor closely, start baseline investigations.
- Give analgesia if necessary (eg, morphine).
- Assess circulation: suspect massive PE if systolic BP is <90 mm Hg or there is a fall of 40 mm Hg, for 15 minutes, not due to other causes.

Anticoagulation therapy[4]

- Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed PE, with the following exceptions:
  - For patients with severe renal impairment or established chronic kidney disease (estimated glomerular filtration rate (eGFR) <30 ml/min/1.73 m²) offer unfractionated heparin (UFH) with dose adjustments based on the activated partial thromboplastin time (aPTT) or LMWH with dose adjustments based on an anti-Xa assay.
  - For patients with an increased risk of bleeding, consider UFH.
  - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy.

- Start the LMWH, fondaparinux or UFH as soon as possible and continue it for at least five days or until the international normalised ratio (INR) is 2 or above for at least 24 hours, whichever is longer.
- Offer LMWH to patients with active cancer and confirmed PE, and continue the LMWH for six months. At six months, assess the risks and benefits of continuing anticoagulation.
- Offer a vitamin K antagonist (VKA) to patients with confirmed PE within 24 hours of diagnosis and continue the VKA for three months. At three months, assess the risks and benefits of continuing VKA treatment.
- Offer a VKA beyond three months to patients with an unprovoked PE, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding.
- **Rivaroxaban[7]**:
  - Rivaroxaban is recommended by NICE as an option for treating PE and preventing recurrent DVT and PE in adults.
The duration of treatment recommended depends on bleeding risk and other clinical criteria. Short-term treatment (at least three months) is recommended for people with transient risk factors such as recent surgery and trauma. Longer treatment is recommended for people with permanent risk factors, or idiopathic (unprovoked) DVT or PE.

Provide patients who are having anticoagulation treatment with an anticoagulant information booklet and an anticoagulant alert card and advise them to carry the anticoagulant alert card at all times.

Other treatments

- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic instability. Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic stability.
- Offer temporary inferior vena caval filters to patients with PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment.
- Consider inferior vena caval filters for patients with recurrent PE despite adequate anticoagulation treatment only after considering alternative treatments such as increasing target INR to 3-4 for long-term high-intensity oral anticoagulant therapy, or switching treatment to LMWH.
- Ensure that a strategy exists for removing the inferior vena caval filter at the earliest possible opportunity.

Surgical embolectomy has been performed for high-risk PE, and also for selected patients with intermediate- or high-risk PE, particularly if thrombolysis is contra-indicated or has failed. Surgical embolectomy has also been successfully performed in patients with right heart thrombi straddling the interatrial septum through a patent foramen ovale.

Pregnancy

PE is the leading cause of pregnancy-related maternal death in developed countries. The risk of PE is higher in the postpartum period, particularly after a caesarean section. Pregnancy does not alter the clinical features of PE but, as pregnant women often complain of breathlessness, this symptom should be interpreted with caution.

Complications and prognosis

- If left untreated, the prognosis for PE is poor. Even when treated, some patients develop chronic thromboembolic pulmonary hypertension, which is caused by obstruction of the pulmonary arteries due to PE. This puts excessive pressure on the heart, which can cause heart failure.
- In the International Cooperative Pulmonary Embolism Registry, the all-cause mortality rate at three months associated with acute PE was 17%. PE was considered to be the cause of death in 45% of patients.
- Important prognostic factors associated with death from PE were age older than 70 years, cancer, congestive heart failure, COPD, systolic arterial hypotension, tachypnoea, and right ventricular hypokinesis on echocardiography.
- The mortality rate is lower in those who are haemodynamically stable and higher in those who present in cardiorespiratory arrest.
- Some patients with dyspnoea or right heart failure have severe pulmonary hypertension due to silent recurrent PE (chronic thromboembolic pulmonary hypertension). This condition is probably a distinct disease entity, different from acute PE.

Prevention

See the separate Prevention of Venous Thromboembolism article.

Further reading & references

4. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing; NICE Clinical Guideline (June 2012, updated Nov 2015)
7. Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism; NICE Technology Appraisal Guidance, June 2013

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<th>Peer Reviewer:</th>
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<tr>
<td>Dr Colin Tidy</td>
<td>Dr John Cox</td>
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