board for Actelion Pharmaceuticals, the manufacturers of bosentan, and on the TRAX PMS Advisory Board. He has received payment from pharmaceutical companies for organising educational seminars.

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Suspected pulmonary embolism

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In June 2003 the British Thoracic Society (BTS) published 'Guidelines for the management of suspected acute pulmonary embolism'.[1] Its title acknowledges the clinical experience that pulmonary embolism (PE) is not easy to diagnose. A frequent thought sequence, particularly of junior physicians, is:

1 Unrecognised PE can be fatal.
2 Common symptoms in PE are chest pain, *and/or* dyspnoea *and/or* haemoptysis.
3 Therefore any patient with the above symptom(s) may have PE.
4 If there is any doubt, it is negligent not to investigate for PE.

This fear of missing PE may account for physicians being better at excluding PE (wrong in only 10% of cases) than in diagnosing it (wrong in 30% of cases) on clinical grounds.[2] In all major studies of suspected PE, it is excluded in 65–85% of cases. Unfortunately, these studies rarely discuss the nature of the true non-PE diagnosis and whether this could have been ascertained earlier; this could be a fruitful and revealing local audit project.[3]

Symptoms in pulmonary embolism and other acute chest illnesses

The commonest alternative diagnoses are shown in Table 1. The table demonstrates how assessing presenting symptom(s) in the light of chest anatomy can focus thinking towards the probable diagnosis. PE is a disease of the pulmonary circulation, hence indirectly affecting the lung parenchyma, whereas symptoms such as cough and haemoptysis may instead arise from the airways. Junior doctors often assume that non-cardiac chest pain might be due to PE, unaware that the lung has no pain fibres. PE can cause chest pain only if there are peripheral parenchymal changes spreading outside the lung to the (very sensitive) parietal pleura. Where chest radiograph (CXR) shows normal lung parenchyma, acute pleuritic chest pain most likely arises from the parietal pleura (perhaps with an effusion) or chest wall, making PE unlikely.

Dyspnoea, tachypnoea and hypoxia are

Key Points

Symptoms compatible with pulmonary embolism (PE) are not by themselves sufficient justification for organising special imaging tests

The correct diagnosis can often be reached by careful consideration of (a) clinical information (b) knowledge of chest anatomy, and (c) a good quality departmental chest X-ray

A combination of low clinical probability plus low/negative D-dimer makes further imaging and anticoagulation unnecessary

Computed tomographic pulmonary angiography should now be considered the principal imaging test for PE

Suspected massive PE justifies (a) immediate advice from a consultant physician (b) emergency echocardiogram, and (c) consideration of early thrombolysis

Decisions about duration of anticoagulation should be made by three (not 6) months, both in PE and deep vein thrombosis

KEY WORDS: anticoagulation, clinical probability, computed tomographic pulmonary angiography, D-dimer, massive, thrombolysis.

common in PE, and indeed in conjunction with a normal CXR suggest that this is the probable diagnosis. (It remains unclear how sudden loss of lung perfusion with preserved ventilation produces hypoxia.) It has long been known that a patient with a respiratory rate below 20 per minute is unlikely to have PE, especially if normoxic.

Although cough may be described by patients with PE, it is rarely a prominent symptom. Fever is common in PE, but such patients never volunteer this so PE is unlikely in a patient with febrile symptoms. Similarly, a patient with an acute chest illness associated with anorexia will have a chest infection, and wheeze is far more likely to be due to acute airways disease.

To clarify the correct diagnosis, it is essential to have a good quality departmental postero-anterior (PA) erect CXR, but depressingly this is often not achieved or rigorously inspected. Obvious pneumonia is the most frequent oversight[3] and, to a lesser extent, even pleural effusions and lung cancer.

Computed tomographic pulmonary angiography

If a patient with suspected PE has a concurrent, clinically apparent deep vein thrombosis (DVT), leg ultrasound is

Table 1. Pulmonary embolism or another diagnosis? Clinical clues.

	Chest wall	Heart	Pleura	Parenchyma	Airways
Pain	If tenderness where pain, ***musculo-skeletal*** cause	Unless massive PE, central pain may be ***pericarditis*** or ***cardiac ischaemia***	Common is ***viral pleurisy***, often with shoulder pain and/or CXR pleural reaction	Only if acute disease (visible on CXR) spreading across to parietal pleura	N/A
Haemoptysis	N/A	N/A	N/A	Due to haemorrhage in PE, CXR usually abnormal	Common is ***acute bronchitis***, perhaps ***lung cancer***
Dyspnoea	If saturation on air >98%, consider ***hyperventilation***	***LVF*** should be obvious clinically and on CXR	Only if large ***effusion*** or ***pneumothorax*** (obvious on CXR)	If febrile symptoms, CXR changes will be due to ***pneumonia***	***COPD*** and ***asthma*** should be obvious; peak flow will be low

Conditions ***commonly*** (bold, italic underlined) and ***occasionally*** (bold, italic) misdiagnosed as acute PE.
If respiratory rate <20 per min ***and*** normal saturation on air ***and*** normal CXR, PE is very unlikely.
COPD = chronic obstructive pulmonary disease; CXR = chest X-ray; LVF = left ventricular failure; N/A = not applicable; PE = pulmonary embolism.

Table 2. Imaging in pulmonary embolism.

	Peripheral	Segmental	Main (central)	Comment
Clinical picture	*Pulmonary haemorrhage*: • tachypnoea >20 per min • haemoptysis and/or • pleural pain	*Isolated dyspnoea*: • unexplained hypoxia • unremarkable CXR • unremarkable ECG	*Sudden collapse*: • hypotension • raised JVP • RV gallop	• these may overlap • may progress with time
Isotope scanning	• variable accuracy	• variable accuracy	• diagnostic	• 30–70% non-diagnostic • need clinical probability • perfusion alone is enough
Conventional pulmonary angiography	• variable interpretation	• 90% accurate	• diagnostic	• gold(ish) standard • complications are rare • rarely done nowadays
CTPA	• unreliable; but most also have segmental clot	• 90% accurate	• diagnostic, often with cardiac changes	• may show another cause • does not image periphery
Echocardiography	• unhelpful	• helpful if >30% obstruction	• diagnostic	• may show another cause • shows acute right heart strain • RV clot occasionally seen

CTPA = computed tomographic pulmonary angiography; CXR = chest X-ray; JVP = jugular venous pressure; RV = right ventricular.

usually diagnostic – hence rendering lung imaging unnecessary.

Several imaging modalities can confirm PE (Table 2), but computed tomographic pulmonary angiography (CTPA) is increasingly accepted as the central diagnostic tool. Typical appearances are shown in Fig 1. The equipment is available in all UK acute hospitals, many with multislice scanners which, as well as being rapid, are good at showing subsegmental thrombus.[4] Evidence continues to accumulate that it is safe to withhold anticoagulation where good quality standard CTPA shows no clot;[5,6] by three months only 0.8% had new documented PE (six studies, 1,559 patients). In PE-negative cases, CTPA frequently shows:

- the true explanation for the acute respiratory illness, often obvious in retrospect
- an important unexpected finding which requires action
- other abnormalities which may be clinically unimportant.

Dispersal of thrombus is slow even with heparin, so clot remains detectable after several days or even weeks.[7] Reduction in clot burden is due to a combination of plasminogen activation and fragmentation into smaller clots that travel distally, factors that reduce accuracy of imaging modalities. In any case, it is desirable to make an early diagnosis in order to limit duration of heparin and hospital stay – hence the recommendation that CTPA is 'ideally' performed within 24 hours,[1] and it would seem unwise to delay longer than four days.

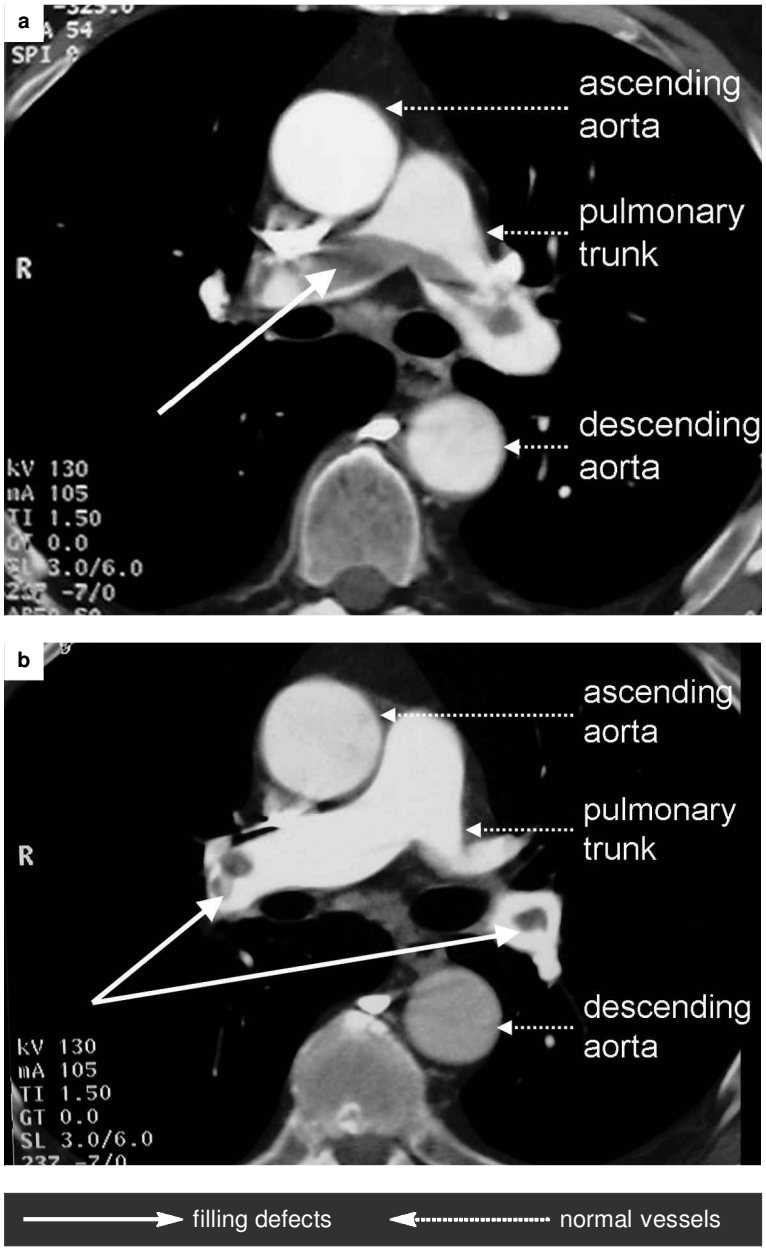

Fig 1. Computed tomographic pulmonary angiographic appearances of pulmonary embolism: (a) central major clot; **(b)** bilateral segmental clot.

Isotope scanning

Because of the pressure on CT scanning departments, and because PE is found in only a minority of suspected cases, many hospitals prefer isotope scanning. The disadvantage of this procedure is that many such scans are non-diagnostic, particularly in those with:

- abnormal CXR
- chronic symptomatic cardiac or lung disease, and/or
- previous PE.

In fact, this approach may merely delay CTPA. Moreover, 30% of acute hospitals do not have nuclear medicine on-site.

Excluding pulmonary embolism without special imaging

Because of pressure on radiology departments, there is great interest in studies showing that it is safe to withhold special imaging and anticoagulation in those with *both* low clinical probability *and* low/negative (depending upon the test) D-dimer. As mentioned above, only 10% of those with low clinical 3probability are eventually shown to have PE. There is a similar error rate for low/ negative D-dimer. Because these appear to be independent variables, in combination they effectively exclude PE.[8] The major practical problem is that, although D-dimer tests should be used only when PE is a reasonable possibility, junior doctors frequently arrange them for any patient in whom PE is just conceivable, interpreting a positive result as strengthening this

suspicion. It has therefore been proposed that D-dimer tests should be accessible only to clinicians with at least six months' post-registration experience of acute general medicine.[9]

Validated methods of assessing clinical probability involve giving a weighted score to a number of parameters, using clinical information and basic investigations. However, they are complex and not as user-friendly as the method proposed by the BTS, which performed equally well in a recent multicentre study of 643 patients (35% with PE).[10] The BTS method requires there to be a reasonable possibility of PE; by assessing both (a) presence of a major risk factor, and (b) absence of a reasonable alternative diagnosis, clinical probability is **high** with *both* (a) *and* (b), **intermediate** with *either*, and **low** with *neither*.

Figure 2 summarises how the above considerations can be applied in clinical practice.[1]

Special situations

Chronic cardiopulmonary disease and current inpatients

Assessing the likelihood of PE is particularly difficult in both chronic cardiopulmonary disease and current inpatients (particularly postoperative and intensive care):

- clinical probability is often already at least intermediate
- D-dimer is likely to be high/positive anyway, and
- abnormalities in basic investigations may be largely due to underlying disease.

Assessment and decisions are best made by an senior physician and the threshold for CTPA is likely to be lower.

Pregnancy

This also applies to suspected PE in pregnancy. A useful strategy is to perform leg ultrasound, starting with the left leg (where 90% of proximal DVTs occur in pregnancy), and proceed to CTPA if this is negative.[11] Isotope lung scanning is an inferior alternative, not only because it may be non-diagnostic but also because the radiation dose to the uterus is substantially higher than with CTPA (even though the latter gives a higher whole-body dose). PE is unusual during the first trimester.

Massive pulmonary embolus

Advice from a senior is also recommended in the situation of massive PE where urgent action is required. When a patient has a cardiac arrest in hospital in circumstances strongly suggesting massive PE, a bolus of thrombolytic given during attempted resuscitation is justified;[12] if successful, the diagnosis can be confirmed later.

Before such a crisis arises, massive PE can be inferred by the combination of circulatory collapse, marked hypoxia, engorgement of neck veins and (usually) right ventricular gallop, in which case echocardiography or CTPA (Table 2) should be arranged urgently prior to thrombolysis.

Duration of warfarin

This article is primarily about diagnosis, but there is widespread confusion and variation in practice concerning duration of anticoagulation. There is now good evidence that warfarin merely delays recurrence when continued beyond three months.[1,13] Therefore, irrespective of whether the initial event was DVT and/or PE at three (not six) months, the following action is recommended:

1 If due to a temporary risk factor (eg postoperative, orthopaedic, long-haul flight), warfarin is stopped.
2 For idiopathic PE, anticoagulation can usually be discontinued, only to be restarted in the event of a proven recurrence.

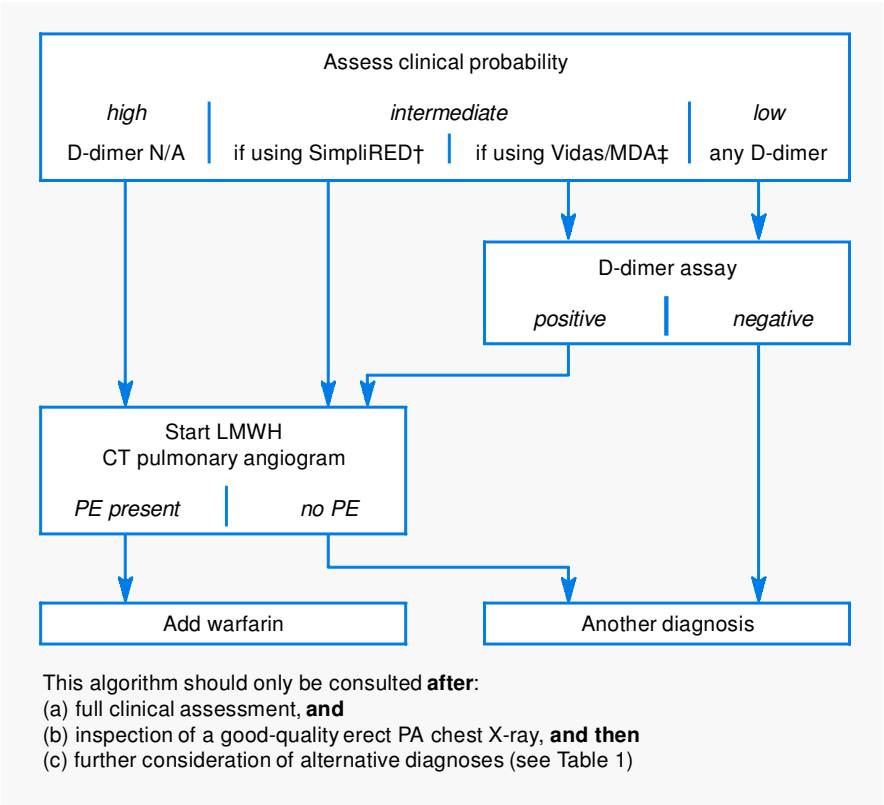

Fig 2. Algorithm for investigation of suspected non-massive pulmonary embolism (PE) (CT = computed tomography; LMWH = low molecular weight heparin; N/A = not applicable; PA = postero-anterior).
†VIDAS/MDA useful for both *low* and *intermediate* clinical probability.
‡SimpliRED only useful for *low* clinical probability, but better specificity.

3 In patients with sudden and severe idiopathic PE or persistent major risk factors such as malignancy many clinicians would prefer prolonged anticoagulation. This would be discontinued only should the patient have limited life expectancy *or* be unable to comply with treatment *or* develop major bleeding.

Conflicts of interest:

None.

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