Pulmonary Embolism

Background

Pulmonary embolism (PE) is an obstruction of part of the pulmonary arterial tree. Embolus usually travelled from a distant site via the venous system but occasionally may be sourced from the left side of the heart if there is a left to right shunt.

Emboli Types

- Thrombotic – By far the commonest cause, most often secondary to DVT
- Air - CVC
- Amniotic fluid – long labour, CS. Massive PE→CVS collapse, ARDS, DIC.
- Fat – long bone fracture. Usually at 12-24hrs. Cardiorespiratory + neurological signs. ARDS, petechiae upper thorax & arms. High mortality.
- Bone fragments/marrow
- Bone cement – orthopaedic surgery
- Mycotic
- Foreign particles – talc & needle fragments (usually IVDU), shrapnel

Clinical Classification/Stratification

Massive PE (5%) – Haemodynamic compromise: Cardiac arrest, shock or sustained ↓BP present.
Submassive PE - No hypotension but either RV dysfn (on ECG, Echo, CT, BNP) or myocardial necrosis (↑Trp) which may indicate poorer prognosis & may benefit from more aggressive Rx.
Nonmassive PE - Haemodynamically stable, no RV dysfn nor myocardial necrosis.

Epidemiology

Annual incidence: ~0.25% (USA). However post-surgery incidence is ~1%.
Commonly missed cause of morbidity/death found at post-mortem.

Pathophysiology

Thromboembolism from: increased blood coagulability, stasis, or blood vessel abnormalities (Virchow's Triad). Some patients with dyspnoea or RVF have severe pulm HT due to silent recurrent PE (chronic thromboembolic pulmonary hypertension). Some may be due to vasculitis.

Risk Factors

Major:

- Surgery: Major abdominal/pelvic surgery or hip/knee replacement. Postop intensive care
- Obstetrics: Late pregnancy, puerperium, Caesarean section
- Lower limb/Pelvic problems: Trauma, fracture , varicose veins (only if prev VV surgery or superficial thrombophlebitis)
- Malignancy: Abdominal/pelvic, advanced/metastatic.
- Reduced mobility: Hospitalisation, institutional care, spinal cord injury.
- Previous proven VTE, IVDU

Minor:

- Cardiovascular: CHD, CCF, HT, superficial venous thrombosis, indwelling CVC
- Oestrogens: Pregnancy, OCP, HRT
- Haematological: Thrombotic disorders (e.g. AT III, Prot C, Prot S deficiencies; Factor V Leiden mutation, antiphospholipid Ab), myeloproliferative disorders, polycythaemia
- Renal: Nephrotic syndrome, chronic dialysis, paroxysmal nocturnal haemoglobinuria
- Miscellaneous: Smoking, COPD, neurological disability, occult malignancy, long distance sedentary travel, DM, obesity, other chronic diseases (IBD, Bechet's disease).

Presentation

History – Dyspnoea (85%), pleuritic CP (75%), apprehension (60%), cough (50%), haemoptysis (30%), sweats (25%), syncope (15%), non-pleuritic CP (15%).

Examination - May be normal. ↑RR (90%>16, 65%>20) & ↑HR (45%>100) common, pleural rub, low grade ↑T (45%), signs of DVT (33%), signs of RV strain (raised JVP, RV heave, gallop rhythm, AF, loud P2, pulm regurg murmur). In massive PE: ↓BP, cyanosis, signs of shock or impaired consciousness, cardiac arrest (classically PEA).

Pre-Test Probability

Scoring systems for a pre-test clinical probability can be used to determine initial risk which can then be refined with screening tests (e.g. D-Dimer) and definitive investigations (e.g. CTPA)

*Simplified Wells Score (**AD PITCH**):*

Criterion	Score
Alternative Dx less likely than PE	3.0
Signs/symptoms of **D**VT	3.0
Previous VTE	1.5
Immobilization (>3days) or surgery in the previous 4 wks	1.5
Tachycardia>100/min	1.5
Cancer in last 6/12	1.0
Haemoptysis	1.0

Probability (PE %) – **Low**<2.0 (1.3%), **Mod** 2-6 (16.2%), **High**>6 (40.6%)

A potential problem with this score is the subjective 1st criterion.

Revised & Simplified Geneva Scores:

Criterion		Revised	Simplified
Age >65y		1	1
Prev DVT or PE		3	1
Surgery <4wks		2	1
Active malignancy		2	1
Unilateral lower limb pain		3	1
Pain on leg palpation & unilateral oedema		4	1
Haemoptysis		2	1
HR	75-94	3	1
	≥95	5	1

Rev - **Low** ≤3 (8%), **Mod** 4-10 (28%), **High** ≥11 (74%)
Simp - **Low** <2 (8%), **Mod** 2-4 (29%), **High** 5-7 (64%)

PERC PE Rule-out Criteria (***HAD CLOTS***)

- **H**ormone - exogenous oestrogen
- **A**ge≥50
- **D**VT/PE history
- **C**oughing blood
- **L**eg swelling (or clinical signs of DVT)
- **O**$_2$ sats in air <95%
- **T**achycardia (HR≥100)
- **S**urgery or trauma <28d

If none of these met (and low risk by Wells) then <2% risk of PE.

Differential Diagnosis

Include: ACS, aortic dissection, tamponade, pneumonia, pneumothorax, sepsis, endocarditis.

Investigations

Bloods: (usual baseline for alt Dx – FBC, UEC, β-hCG, coags)

- **D-Dimer** – May be ↑ if post-op, pregnant, infection, RA, Ca, trauma, etc. Used if pre-test prob is **Low** as sens ~95% but spec low. Accuracy assay-dependent. ELISA is best.
- **ABG** – Used in orig Geneva score. Can't rule in/out PE. Commonly:↓PO_2, ↓PCO_2 & ↑A-a grad.
- **Cardiac Troponins** – may indicate alternative Dx or RV strain in submassive PE subset.
- (**BNP** – may be raised in PE, but not sensitive nor specific. May help risk strat with trop.)

ECG: Abnormal in 40-70%: non-specific ST-T wave changes, sinus tachycardia, P pulm, AF/flutter, RAD, RBBB, RVH/strain (R +ve in V_1), $S_IQ_{III}T_{III}$, ↓T in right chest & inferior leads

Imaging

- **CXR** – No diagnostic changes. May be subtly abnormal (~80%), normal or show alt Dx. Needed for interpretation of V/Q scan. In PE may show: ↑CTR, atelectasis, small pleural effusion, ↑hemidiaphragm, Westermark sign (prominent PA, early cut-off of vascular markings), Hampton's hump (homogeneous pulm infarction wedge in lung periphery).
- **Echo** – Poor diagnostic tool for PE (except in large proximal PE [TOE/TTE]) but good for RV dysfunction (dilatation, hypokinesis, TR, pulm art HT) and so mortality prediction.
- **CT Pulmonary Angiography** – 1st line unless **CI:** RF/contrast allergy. Can combine with **CT venography** of lower limbs to ↑sens. May provide alt Dx.
- **V/Q Scan** (Xe or Tc) – Not useful if prior lung disease. Results: *Normal* (no perfusion defects→high neg pred value), *low* (matched defects), *intermediate* (1 mod-large mismatched seg), *high* (≥2 large mismatched segs).
- **Doppler USS of legs** – 50%-80% PEs have lower extremity DVT. Calf DVT rarely assoc with PE. Proximal DVT sens 60% & spec ~95%. First line if pregnant or DVT signs.
- **Pulm Angiography** – Gold std. High sens/spec. Mort 1%. Cx 1-5%. **CI:** RF/contrast allergy.
- **MRPA** – improving sens/spec & non-invasive/contrast-free, but costly & limited expertise

Management

Initial

- Oxygen 100%
- ECG/Oximetry monitoring, order CXR
- Obtain IV access, take bloods and give analgesia PRN
- Stratify based on haemodynamic state, RV dysfn (Echo, CTPA) & myocardial necrosis (Trop, BNP)

Massive PE

- If cardiac arrest: CPR & thrombolysis (r-tPA 50mg bolus +/- rpt in 15mins if no ROSC)
- UFH and thrombolysis or embolectomy
- Consider fluid bolus ≤500ml may help BP, consider inotropes (adrenaline or NA)

Sub-Massive PE

- Anticoagulate (UFH if likely to thrombolyse, else LMWH or fondaparinux)
- Consider thrombolysis if deteriorating, or mod to severe RV dysfn/myocardial necrosis

Thrombolysis Review:

- No trials comparing regimens or comparison to surgery
- Cx: ICH/fatal haemorrhage in <2%. Major bleeding episode up top 10%
- Contraindications – None in cardiac arrest. Otherwise low risk PE and standard CI (see below):

General Thrombolysis CI

- *Absolute*
  - ICH risk: PHx ICH, ischaemic CVA>3h and ≤3m, Brain AVM or Ca, ?SAH, sig. HI/facial inj<3w
  - Bleeding risk: Active bleeding/diathesis, suspect aortic dissection
- *Relative*
  - ICH risk: Hx sev HT or SBP>180±DBP>110, ischaemic CVA>3m, dementia, other intracranial dz
  - Bleeding risk – oral anticoagulant, CPR>10min, major trauma/surgery <3w, int bleeding<4w, active PUD, non-compressible vascular punctures, pregnancy (except in PE)

Sometimes pericarditis, endocarditis, advanced liver disease and diabetic retuinopathy are listed too.

- Doses:
  - **r-tPA/alteplase** 10mg IV bolus & then 90mg infused over 2hrs
  - 2 x **reteplase** 10units IV boluses 30mins apart.
  - **SK** 250,000units IV over 30min & then 100,000units/hr for 24hrs
  - Withhold heparin until after thrombolytic infusion (unlike in AMI).

?Non-massive PE

Assess clinical PTP (Wells): If low and all PERC neg then PE excluded (<2%).
If PERC pos or Wells mod risk→rapid ELISA D-Dimer & if neg then PE excluded (<2%).
Otherwise Image: **ECHO** if shock/signs of RV dysfunction/strain, **CTPA ± CT venography** or if CT CI: **V/Q** or **USS** can be done.
If Echo positive → Treat as PE ±?thrombolysis as ↓prognosis
If CTPA Result Positive (%=PIOPED$_{II}$ probabilities of PE)
- If PTP low (58%) → need further Ix, Else (92-96%) → Treat as PE

If CTPA Result Negative
- If PTP low, mod → PE excluded (4%, 11%) Else (40%)→ need further Ix

If V/Q scan probability High→Treat as PE, N or (Low & low PTP)→PE excluded (5%) Else USS
If USS positive → Treat as PE
Anticoagulation:

- **LMWH** e.g. **Enoxaparin**: 1mg/kg SC bd or 1.5mg/kg od (max dose 100mg bd)
- **UFH**: 80units/kg IV bolus & infusion started at 18units/kg/hr (aim APTT 60-80s)
- **Fondaparinux**: 5-10mg od based on wt. Avoid if unstable or severe renal insufficiency
- **Warfarin** (not pregnancy). For 1st case: 3-6mo if surgical PE, or 6-12mo (non-surgical). Start 5mg PO od while on heparin as init ↑clotting. Aim INR 2-3. ?Life-long if 2nd case.

Emergency management of PE in pregnancy

Resus, elevate R side, get O&G team. Echo if shocked.
If massive-Mx options: UFH, thrombolysis (if life-threatening) or thoracotomy/embolectomy
Otherwise assign pre-test probability.
D-dimer if in 1st/2nd trimester and low risk (preg ↑PE risk 5x, so perhaps never low risk).
If D-dimer negative PE excluded (as D-dimer normally ↑ in pregnancy).
Otherwise bilateral leg Doppler USS (note only ~10% will be abnormal).
If positive for DVT, assume PE → give heparin. LMWH preferred as less SE. Warfarin **CI**.
If negative → shielded CXR & get informed consent for minimised CTPA or low-dose V/Q (can skip ventilation scan if perfusion scan normal) and empty bladder promptly after contrast.

- Helical CTPA has lower foetal radiation dose than V/Q (both well below recommended dose limits and the risks of inappropriate anticoagulation or missed PE are far higher), & can exclude DDx, but has higher maternal breast exposure & ?slight ↑breast Ca risk.
- Currently perfusion scan recommended as less breast radiation unless abnormal CXR. Debatable as CTPA in 1st/2nd trimester has ↑accuracy & ↓foetal dose. Need to discuss risks with patient and scan protocol with radiologist first.
- If CTPA, the baby needs TFTs in 1st week as risk of contrast-induced hypothyroidism.

Complications

- RHF ± LVF, pulmonary hypertension
- Complications of anticoagulation: 3% major bleeding @ 3mo and mortality of 0.3%
- Recurrence <10%

Prognosis

- Mortality: overall 7-11%. <5% if non-massive. 30% if shock, 70% if cardiac arrest.
- Chronic thromboembolic pulmonary HT may be 2° to recurrent small emboli, or a different disease entity from acute PE. If untreated, usually fatal <3 years of Dx.

Prevention

- In hospital – mobilise, maintain hydration, TEDS, SC heparin (LMWH, UFH).