THROMBOEMBOLISM

PATHOPHYSIOLOGY:

- PE occur when proximal portion of a DVT breaks off and lodges in precapillary pulmonary arteries
- Patients without prior heart of lung disease experience symptoms when *~20-30% of lung vasculature becomes occluded*
- DVT usually form in venous valves, where blood flow is slowest
    - 75-80% of hospitalized patients with PE have DVT
    - 40% of ambulatory ED patients with PE have concomitant DVT
- PE alters intrapulmonary blood flow
    - Obstructs blood flow, leading to segments of lung with high ventilation relative to perfusion --> ALVEOLAR DEAD SPACE
    - If a PE diverts a large volume of blood into areas of lung with a previously low VQ ratio, then hypoxaemia will result --> thus hypoxaemia in PE is UNPREDICTABLE.

RISK FACTORS FOR VENOUS THROMBOEMBOLISM:

- AGE:
    - Hyperbolic increase over age 50
- IMMOBILITY:
    - When over 48-72 hours.
    - Due to slow venous flow due to immobility
    - Major joint immobilization/splinting (highest risk to lowest as below):
        - Hip
        - Knee
        - Ankle
        - Shoulder
        - Elbow
    - *Travel >8 hours thought not to increase risk*
- SURGERY:
    - Causes venous stasis & activation of inflammation-coagulation axis
    - Particular risk in those requiring ETT/epidural/spinal within 4 weeks
    - HIGHEST RISK OPERATIONS:
        - Abdominal surgery (especially those removing cancers)
        - Joint replacements
        - Neurosurgery with resultant deficits
- THROMBOPHILIA:
    - *Malignancy related:*
        - Related to tumour burden and tumour type
        - Highest with adenocarcinomas
            - Ovarian, pancreatic, colon, prostate

- Haematologic:
    - Acute myeloblastic leukaemia
    - ALL
    - NHL
    - Polycyteameia
    - Multiple myeloma
- Use of EPO in all cancer patients raises risk of VTE
- METASTATIC DISEASE OF ANY ORIGIN IS HIGH RISK FACTOR

- *NON-MALIGNANCY RELATED:*
    - Pregnancy:
        - Triples risk from 1:10, 000 to 3:10, 000
        - Risk increases with each trimester, peaking one week post delivery (esp if delivery by LSCS)
    - Exogenous oestrogen administration
        - Risk increases with obesity and smoking
    - IBD
    - Nephrotic syndromes
        - *Due to diuresis of antithrombin protein*
        - Even in cases with no proteinuria and normal renal function have higher risk
    - Hereditary coagulopathies:
        - Factor V Leiden variants
        - Familial protein C deficiencies
    - OBESITY:
        - Dose dependent increase in risk (function of BMI)
    - Indwelling catheters (ie CVC etc)

CLINICAL FEATURES:

PULMONARY EMBOLISM:

- *HIGHLY VARIABLE PRESENTATIONS*

HALLMARK OF PE:

- Dyspnoea unexplained by auscultatory findings, ECG changes or obvious diagnosis on chest radiograph
- Second to SOB, chest pain with pleuritic features represents the second most common symptom of PE
    - HALF HAVE NO COMPLAINT OF PAIN
    - In theory, PE must CAUSE INFARCTION IN ORDER TO CAUSE PAIN

- Can cause PARADOXICAL EMBOLISM SYNDROME due to presence of PFO in 15% and elevated right heart pressures

- FACTORS AFFECTING PRESENTATION:
    - IF PREVIOUSLY HEALTHY:
        - One half have normal vital signs at diagnosis
    - PRIOR CARDIOPULMONARY DISEASE:
        - Worse dyspnoea than usual
    - COGNITIVE DYSFUNCTION
        - Approx 20% of missed PE in patients with baseline dementia
    - CLOT SIZE AND LOCATION:
        - Proximal clots cause VQ mismatch and SOB
        - Distal clots cause infarction with pain
    - GRADUAL LOADING OF PE
        - FEWER THAN HALF PATIENTS DESCRIBED SUDDEN ONSET OF SYMPTOMS
- PHYSICAL EXAMINATION:
    - Vitals suggest cardiopulmonary stress:
        - Tachycardia
        - Tachypnoeia
        - Hypoxia
        - Sometimes mild increase in temp
            - ~10% have fever >38C, BUT <2% have fever >39.2C
    - Most patients with PE have clear lungs
        - Pulmonary infarction can cause creps over affected lung segment

DEEP VENOUS THROMBOSIS:

- Acute signs and symptoms result from obstruction of venous blood flow and damage to valves
- Complaints of pain swelling or cramping
- 2cm discrepancy in measurement of leg diameter 10cm below tibial tubercle is predictive of DVT
- DON'T USE HOMANS SIGN - pain w/ dorsiflexion of ankle
- PHLEGMASIA ALBA DOLENS --> swollen, white, pale limb
- PHLEGMASIA CERULEA DOLENS --> dusky blue color
    - Both in proximal DVT
    - Both pose threat of limb loss --> THROMBOLYSIS OR THROMBECTOMY

DIAGNOSIS:

- Mean pulse oximetry LOWER
- Alveolar A-a gradient HIGHER
- PaCO2 usually low reflecting a 20-50% increase in ventilation to compensate for loss of lung efficiency secondary to increased dead space.

- CHEST X-RAY FINDINGS:
    - Cardiomegaly
    - Basilar atelectasis
    - Infiltrate
    - Pleural effusion
    - WESTERMARK SIGN (<5%):
        - Wedge-shaped area of lung oligaemia from complete lobar artery obstruction
    - HAMPTON HUMP: peripheral dome shaped opacification = infarction
    - Most importantly --> clear lungs and no APO
- ECG:
    - Sinus tachycardia.
    - Non-specific ST & T-wave changes.
    - When PE causes RV systolic pressure to exceed 40mmHg
        - TWI in V1-4
        - RBBB (complete or incomplete)
        - S1 Q3 T3

- DIAGNOSTIC TESTING:

Conundrum as false negative for PE can lead to death but false positives can lead to unnecessary anticoagulation and its attendant 1-2% risk of major haemorrhage

WELL'S CRITERIA

- Most robust scoring system for categorizing the pretest probability for both PE and DVT
    - Has a subjective component based on clinical gestalt and likelihood of an alternative diagnosis

Table 60-3 Wells Score for Pulmonary Embolism (PE)

Factor	Points*
Suspected deep venous thromboses	3
Alternative diagnosis less likely than PE	3
Heart rate >100 beats/min	1.5
Prior venous thromboembolism	1.5
Immobilization within prior 4 wk	1.5
Active malignancy	1
Hemoptysis	1

Risk score interpretation (probability of PE): >6 points: high risk (78.4%); 2–6 points: moderate risk (27.8%); <2 points: low risk (3.4%).

Alternatively; ≤ 4 = low risk & > 4 = non-low risk.

Table 60-4 Wells Score for Deep Venous Thrombosis	
Clinical Feature	**Points***
Active cancer (treatment within 6 mo, or palliation)	1
Paralysis, paresis, or immobilization of lower extremity	1
Bedridden for >3 d because of surgery (within 4 wk)	1
Localized tenderness along distribution of deep veins	1
Entire leg swollen	1
Unilateral calf swelling of >3 cm (below tibial tuberosity)	1
Unilateral pitting edema	1
Collateral superficial veins	1
Alternative diagnosis as likely as or more likely than deep venous thrombosis	−2

Risk score interpretation (probability of DVT): 3 points: high risk (75%); 1 or 2 points: moderate risk (17%); <1 point: low risk (3%).

D-DIMER:

- Works on the principle that clots contain fibrin which the body degrades naturally RELEASING D-DIMER
    - Remains elevated for at least 3 days after symptomatic VTE
    - HIGH SENSITIVITY (94-98%), LOW SPECIFICITY (50-60%)
- FALSE POSITIVE:
    - Age >70
    - Pregnancy
    - Active malignancy or mets
    - Surgical procedure within last week
    - Liver disease
    - RA
    - Infections
    - Trauma

- FALSE NEGATIVES:
    - Warfarin
    - Symptoms >5 days
    - Small clot burden
    - Isolated small pulmonary infarction
    - Isolated calf vein thrombosis

CT ANGIOGRAPHY:

- Identifies a clot as a filling defect
- SENSITIVITY AND SPECIFICITY HIGH (>90% on multi-detector scanners)
- RADIATION RISK --> increases lifetime risk of fatal cancer or leukaemia to 1 in 500 (higher in young women due to radiation to the breast)
- ANAPHYLACTOID RISK (IV CONTRAST)
- CONTRAST NEPHROPATHY:
    - Requiring dialysis is rare, ~ 25% relative increase in serum creatinine occurs in 5-10% of patients

V/Q SCANNING:

- Can identify a perfusion defect when ventilation is normal
- If ventilation portion shows homogeneous scintillation throughout the lung in the perfusion portion has nearly 100% sensitivity in ruling out PE

DECISION-MAKING TOOLS IN PE:

- Guides decision making in PE in terms of ordering tests:
    - CT SCANS may have high false positive rates in low risk populations
    - Thus when the pretest probability of PE is <2%, then the patient is more likely to be harmed than helped by a diagnostic test, even a D-dimer!

Table 60-7 Pulmonary Embolism Rule-Out Criteria (PERC Rule)
Age <50 y
Pulse oximetry >94% (breathing room air)
Heart rate <100 beats/min
No prior venous thromboembolism
No recent surgery or trauma (requiring hospitalization, intubation, or epidural anesthesia within prior 4 wk)
No hemoptysis
No estrogen use
No unilateral leg swelling

MNEMONIC.
- "HAD CLOTS"

DVT EVALUATION:

- Use Well's criteria:
    - if low prob score --> D dimer
        - if negative DVT ruled out,
        - if positive --> US and treat on basis of result
    - If high or moderate score --> US.
        - If positive then treat.
        - If negative, then do D dimer.
            - If negative then DVT unlikely.
            - If positive repeat US in one week

TREATMENT OF VTE:

- **Systematic heparinisation.**
    - LMWH shows slight benefit over UFH (benefit not large)
    - Time to therapeutic anticoagulation = inverse relationship w/ outcome
    - If severe renal insufficiency UFH is favoured

For PE, the benefit of empiric systemic anticoagulation for 24 hours exceeds the risks (bleeding or HITS) for any patient with a pretest probability of > 20%.

- REMOVE INDWELLING CATHETERS ASSOCIATED WITH DVT

- ***INDICATIONS FOR THROMBOLYSIS IN DVT:***
    - Severe DVT that causes PHLEGMASIA CERULEA DOLENS can lead to loss of a limb
    - Discuss CLOT-DIRECTED LYSIS should be discussed with interventional radiology or vascular surgeon
- SUPERFICIAL THROMBOPHLEBITIS:
    - Unless extensive, can be treatment with topical or systemic NSAIDS
    - If extensive, consider lower dose anticoagulation
- CALF VEIN OR SAPHENOUS VEIN THROMBOSIS:
    - PE incidence variable (0.3–8%). Repeat US in one week with no treatment. If there is a history of VTE, treat unless there are complications

INDICATION FOR FIBRINOLYSIS IN PE:

- PE classified into *THREE GROUPS:*
    - **MASSIVE:**
        - PE with SBP <90 for greater than 15 minutes or <100 in patient with a history of HT or a >40% reduction compared to baseline
    - **SUBMASSIVE:**
        - Normal or near normal BP but with evidence of cardiovascular stress:
            - Shock index (HR/SBP) >1
            - Oximetry <95%
            - Echo findings:
                - RV hypokinesis
                - RV dilation
                - RVSP >40mmHg
            - Troponins elevated
            - BNP >90
            - D dimer >8
    - *ALL OTHER CASES DEFINED AS LESS SEVERE*

- Patients with massive PE probably benefit
    - Benefit defined as survival and improved quality of life
- Fibrinolysis DOES NOT APPEAR TO reduce mortality in submassive PE
    - 40% of those with submassive PE have RV dysfunction and SOB at rest on most days
    - It is unknown whether fibrinolytics decrease morbidity

BEST EVIDENCE IS THAT FIBRINOLYSIS SHOULD ONLY BE USED IN CAREFULLY SELECTED PATIENTS (so long as there is no increased risk of bleeding):

- Cardiac arrest at any point
- Arterial hypotension and massive PE
- Respiratory failure despite oxygen administration and elevated WOB
- Right heart strain on echo

- CONTRAINDICATIONS:
    - Intracranial disease
    - Uncontrolled hypertension
    - Recent major surgery or trauma
    - Metastatic cancer
- IN CARDIOTHORACIC CENTRES:
    - Surgical embolectomy could be considered in young patients with large, proximal PE accompanied by hypotension
    - Mortality rate is approximately 30%, probably related to sicker subset of patients proceeding to this operation

PREGNANT WOMEN:

- *DO NOT USE WARFARIN IN PREGNANCY*
- Attempt to reduce radiation
- FIRST DIAGNOSTIC CHOICE IS ULTRASOUND !!
- VQ scanning associated with slightly higher risk of childhood cancer in affected offspring but carries lower risk of maternal breast cancer (lifetime risk ~13% higher)

DISPOSITION & FOLLOW-UP.

Most patients diagnosed with acute PE are admitted for further investigation (? underlying cause) and treatment.

Patients w/ severe PE require ICU admission.