DVT & PE – Prevention and Management

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Adapted from Lectures by Assoc. Prof. Ian Heslop.

Learning outcomes

Be able to:

- Relate the pathophysiology DVT and PE to the disease and risks of untreated thrombosis.
- Identify risk factors for DVT in different patient populations
- Apply preventative strategies to reduce risk of DVT and PE in different patient populations
- Justify recommendations for the treatment of DVT and PE

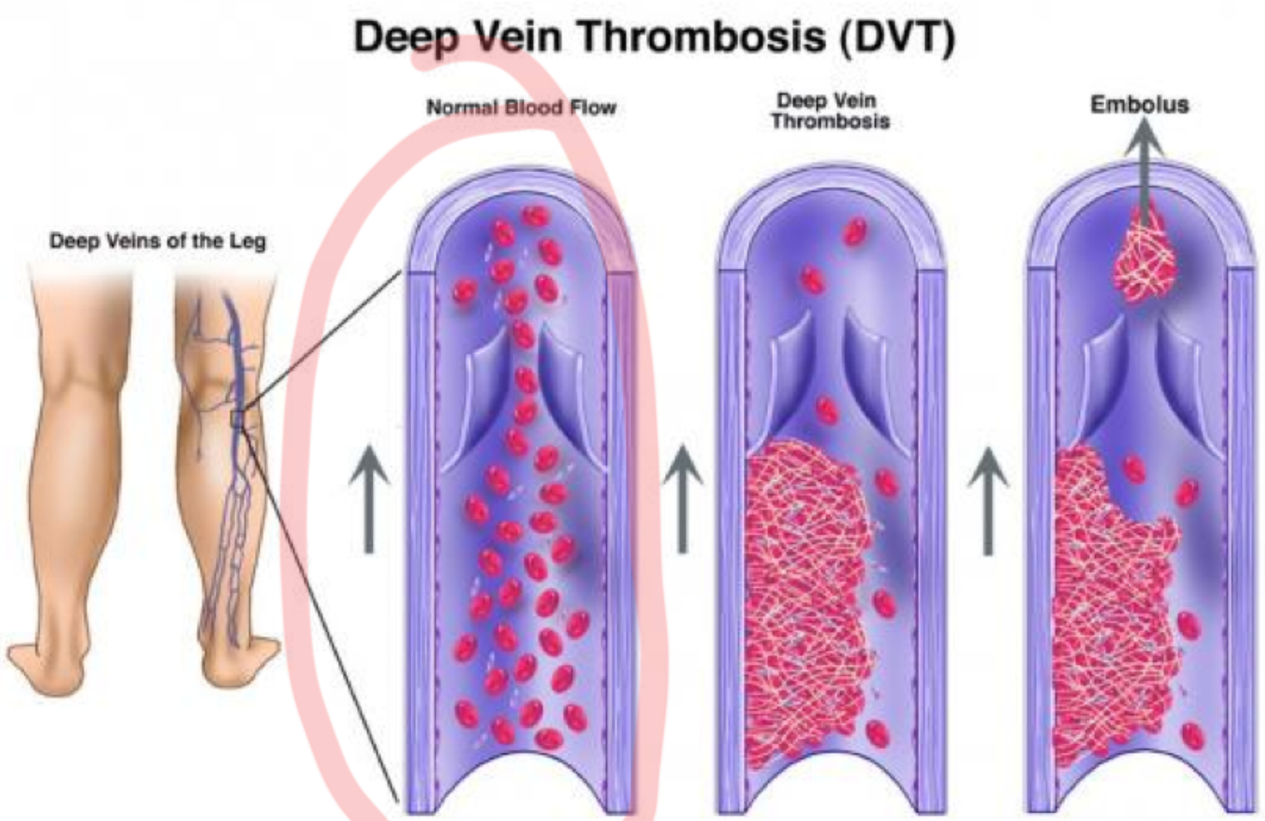
Deep Vein Thrombosis

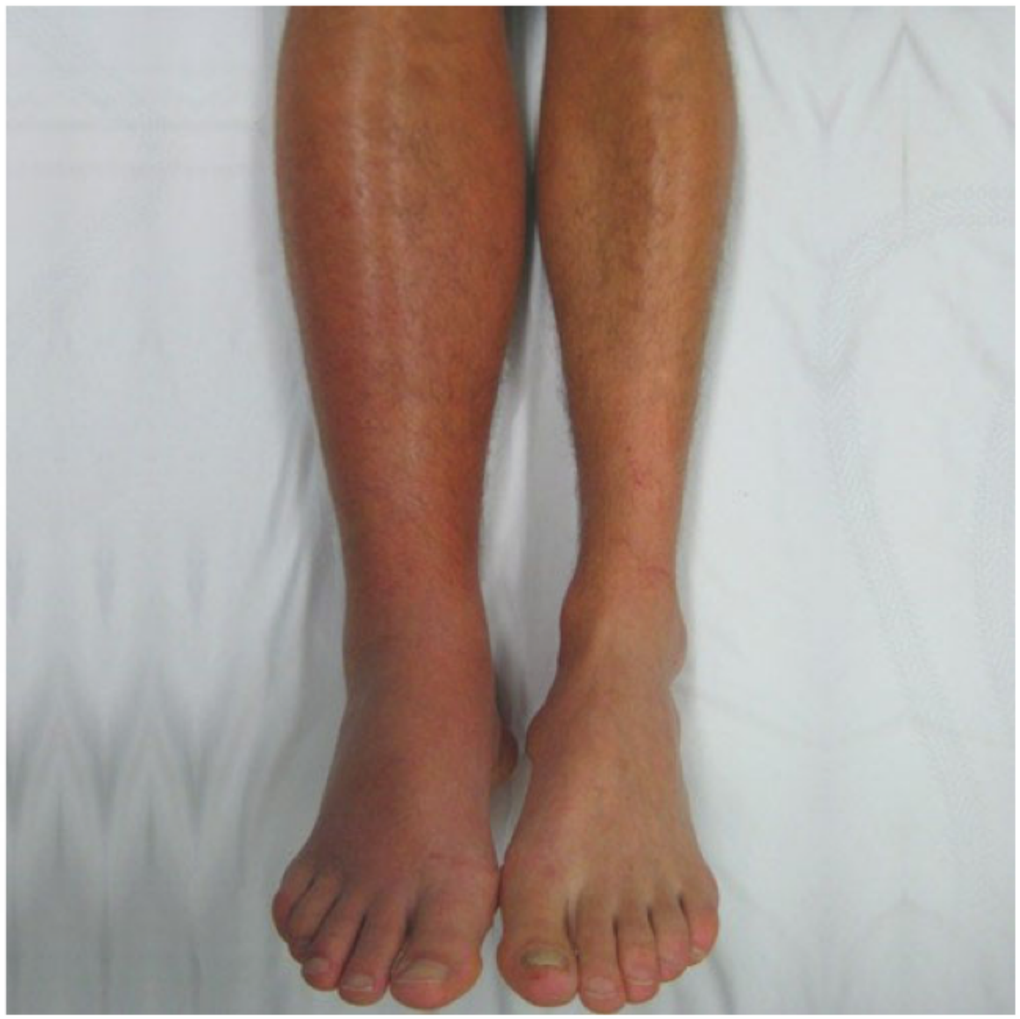
- In previous lectures we covered the
  - Coagulation system and
  - The main groups of drugs that can affect the coagulation system
    - Anti-platelets (week 2)
    - Anti-coagulants
    - Thrombolytics (Fibrinolytics)

- **In this lecture we will discuss the prevention and treatment of the two most common venous thromboembolic conditions:**
  - **Deep Vein Thrombosis and**
  - **Pulmonary Embolism**

https://youtu.be/0QEo9QAqA3k.

Deep vein thrombosis usually starts around the valvar cusp –stasis, turbulent blood flow etc

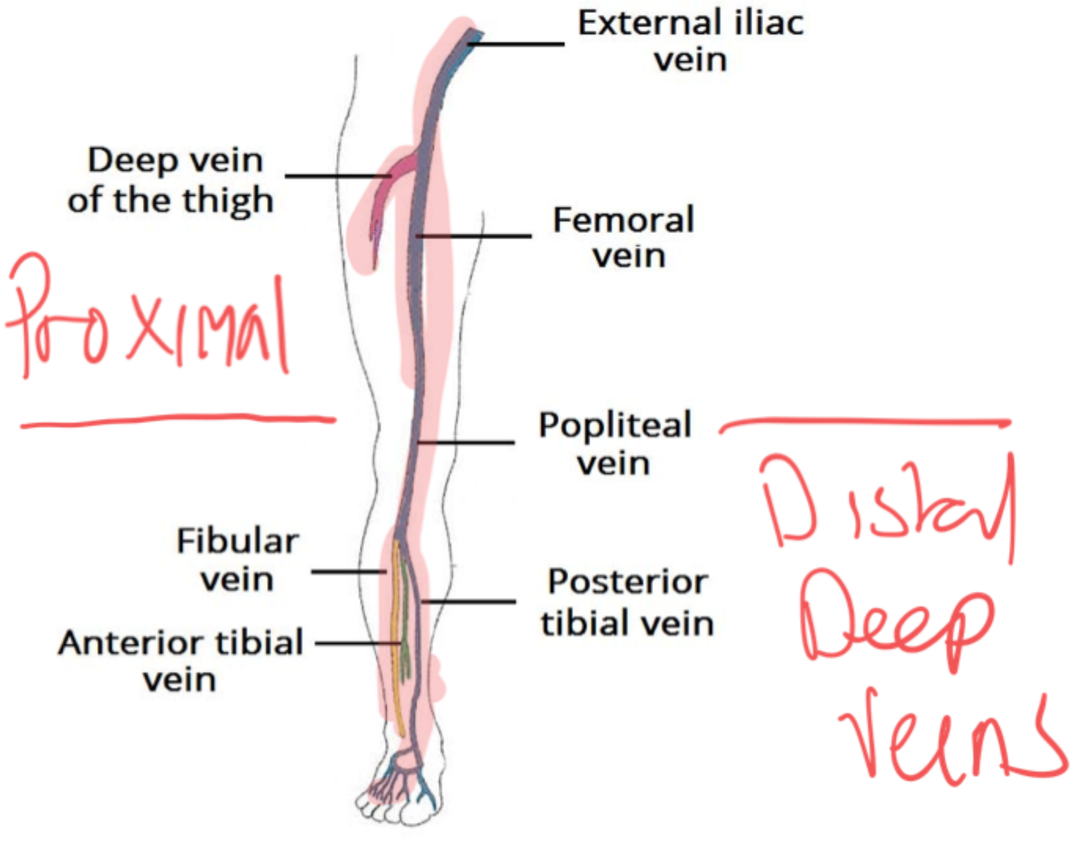




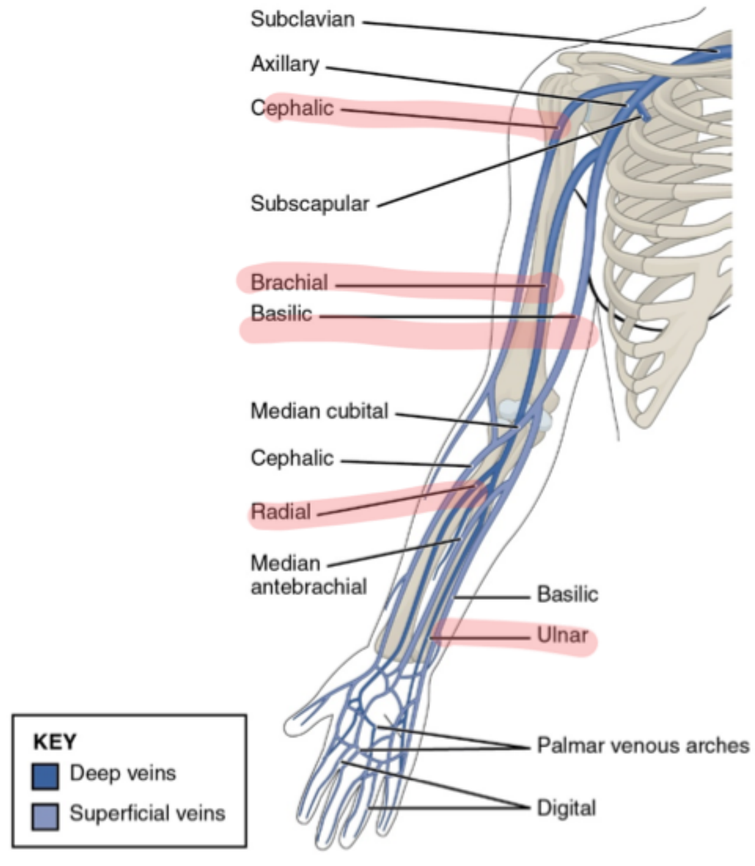
https://www.dicardiology.com/article/society-interventional-radiology-understand-long-term-risks-dvt.

What are the deep veins of the arm and leg we are talking about

Deep veins of the leg



Deep veins of the arm



https://teachmeobgyn.com/pregnancy/medical-disorders/haematological/venous-thromboembolism/

https://en.wikipedia.org/wiki/Basilic_vein.

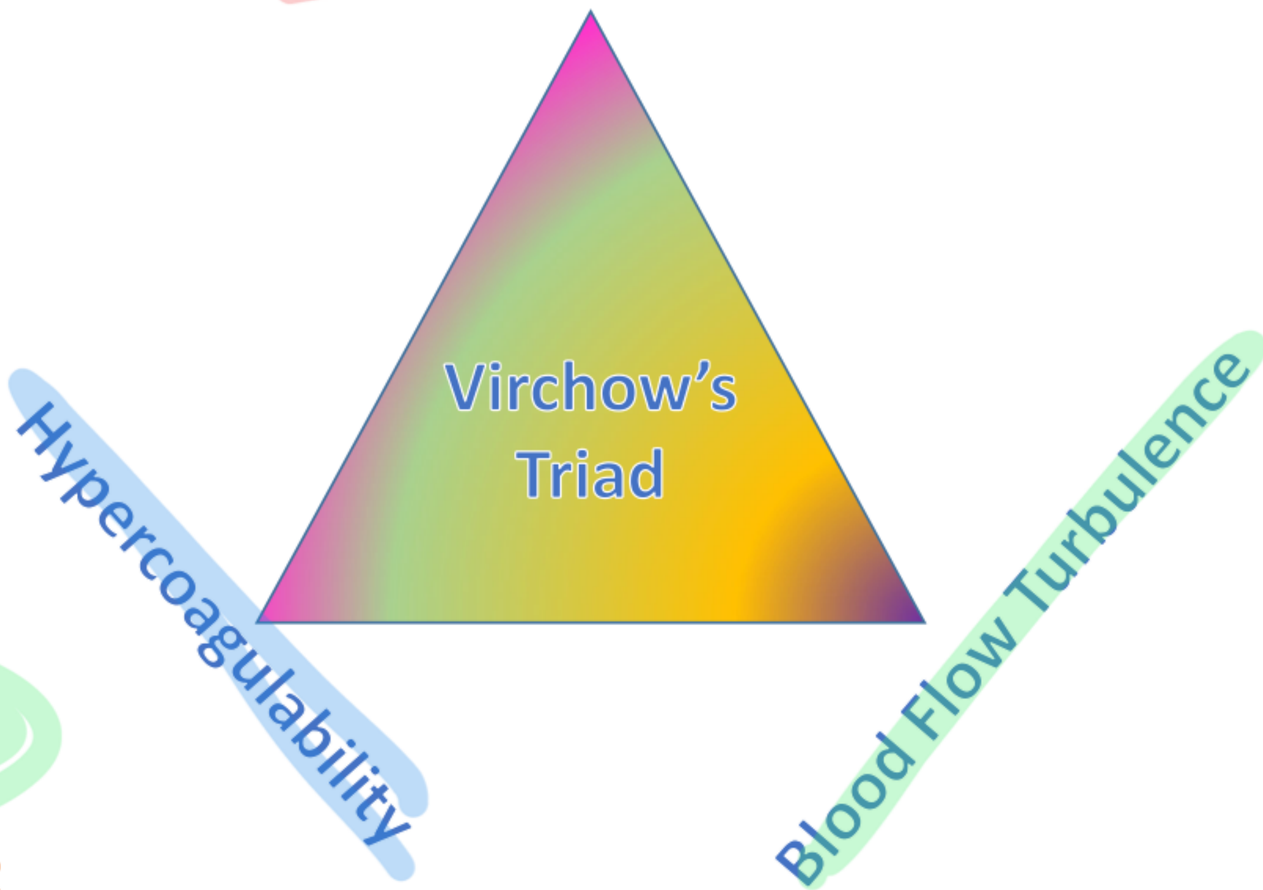
Virchow's Triad

- **Endothelial injury exposes collagen (as it does in arteries but not absolutely necessary as in artery clots)**
- **And if blood stasis or hypercoagulability is present:**
- **Causes platelet aggregation and triggers the coagulation system.**
  - This leads to thrombus formation, and a subsequent risk of emboli.
- **Most venous thrombi begin in the valve cusps of the deep calf veins** (usually due to a combination of the aforementioned risk factors).
- **Tissue thromboplastin is released, forming thrombin and fibrin, and trap red blood cells and propagate as a red or fibrin thrombus which is the predominant venous lesion.**

Forms a RED Clot

RBC + Fibrin + a little bit of Platelet

Main Physiological mechanisms involved in DVT



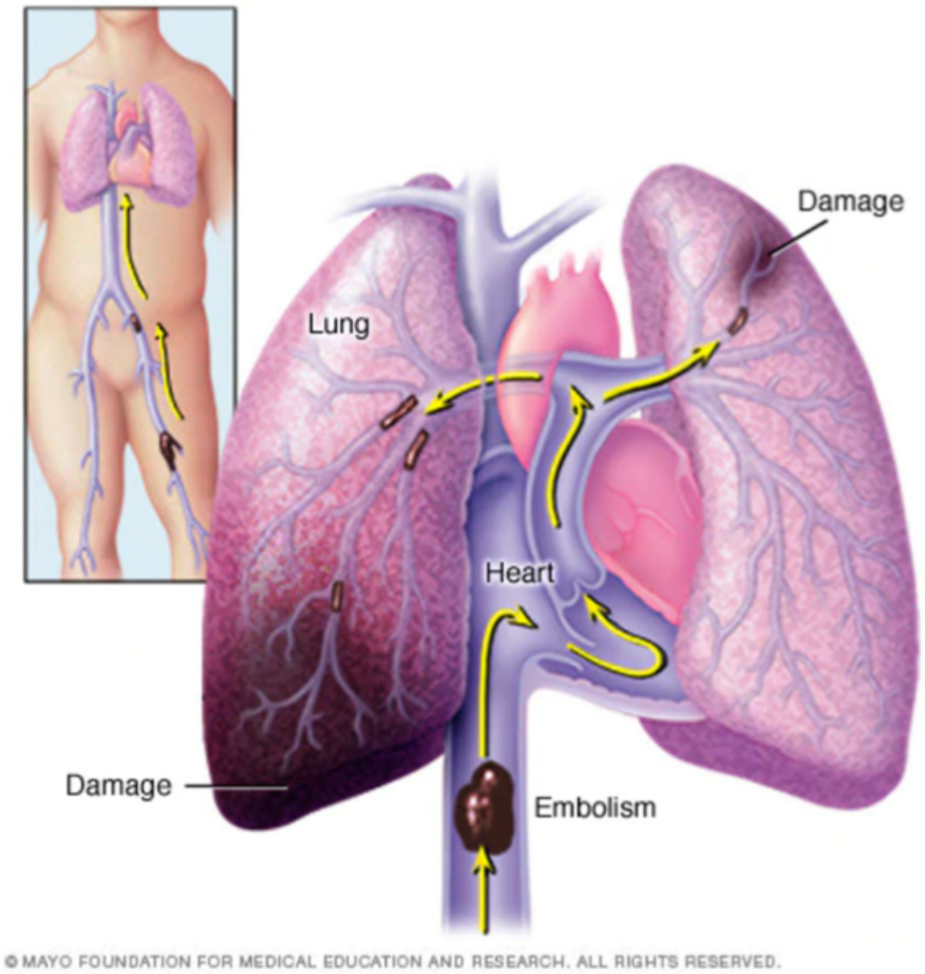
Risk factors for DVT

- **Possible factors that contribute to venous thrombosis include:**
  - **Injury to endothelium of the vein:**
    - Possibly due to in-dwelling catheters, injection of irritating substances, septic phlebitis ,etc.
  - **Hypercoagulability**
    - Associated with malignant tumors, blood dyscrasias, pregnancy, increased age, oral contraceptives, etc
  - **Stasis**
    - Associated with postoperative and postpartum states, varicose thrombophlebitis and the thrombophlebitis that may prolong the bed rest of chronic illnesses, heart failure, stroke and trauma
  - **Prolonged immobilisation of legs**
    - Traveling for long periods of time, (e.g. “Economy class syndrome”) is a risk factor for all people, and especially important in those with other risk factors.
- Increased age and pregnancy cause blood to favour clotting.
- Venous thrombi do NOT require initial damage unlike arterial thrombi; stasis and hypercoagulability is all that is needed to initiate platelet aggregation.

DVT symptoms

- **Symptoms:**
  - **DVT may be asymptomatic,**
  - **Or may manifest as a feeling of tenderness, pain, oedema, warmth, skin discolouration and prominent superficial veins over the affected area.**
  - At least 3 main veins drain the lower leg so thrombosis in one does not significantly obstruct venous return, so there may be no swelling, cyanosis of the skin or dilated superficial veins. Patients complain of soreness on standing and walking and is usually relieved by rest with the leg elevated. Examination shows deep tenderness .
  - Diagnosis confirmed with duplex ultrasound.

- **Prognosis:**
  - **DVT is usually benign but can cause lethal pulmonary emboli or chronic venous insufficiency.**



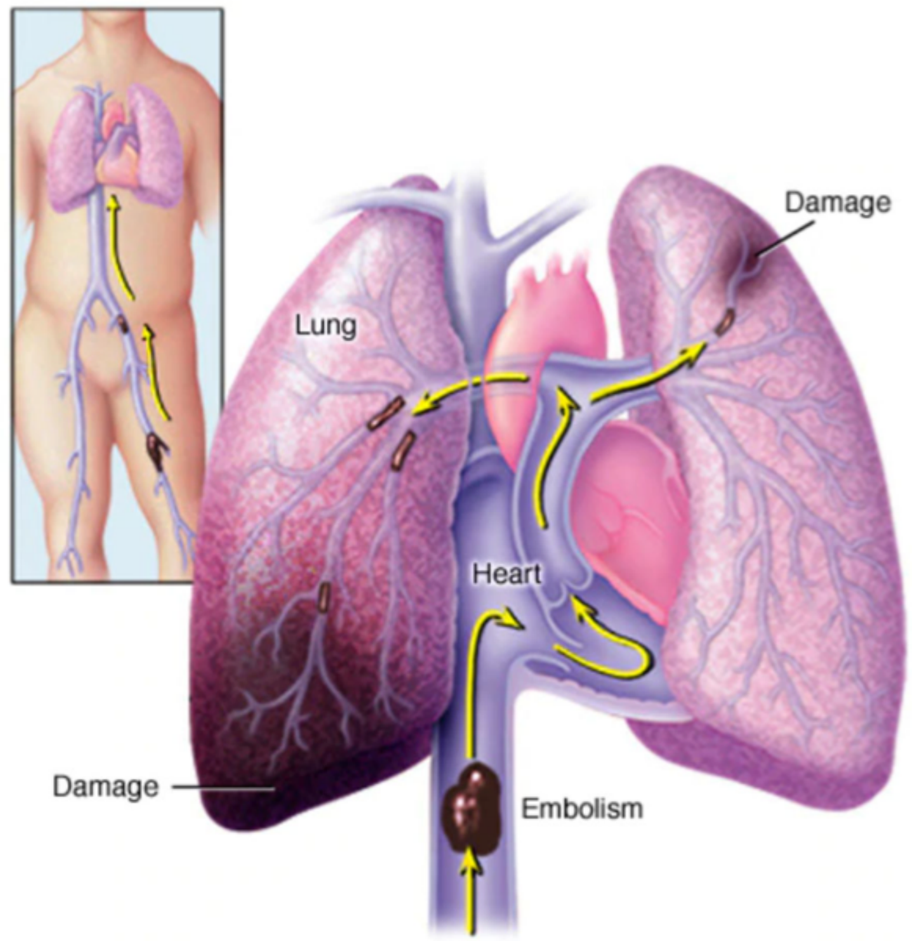
https://www.mayoclinic.org/diseases-conditions/pulmonary-embolism/symptoms-causes/syc-20354647#dialogId66791518

Pulmonary Embolism

- **Most common type of pulmonary embolus is a thrombus that has usually migrated from a leg or pelvic vein**

- **Once released into the venous circulation, thromboemboli are distributed to:**
  - **Both lungs – 65% of cases**
  - **Right lung – 25% of cases**
  - **Left lung – 10% of cases**

  - **Lower lobes are involved 4x more frequently than upper lobes**
  - **Most thromboemboli lodge in large or intermediate (elastic or muscular) pulmonary arteries and fewer reach the smaller arteries**



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Pulmonary Embolism

- **Acute PE is a dynamic process – thrombi begin to lyse (breakdown) immediately after reaching the lung**
  - Lysis is usually complete within several weeks in the absence of pre-existing cardiopulmonary disease
  - Even large thrombi may lyse significantly in a few days
  - **However, massive emboli may cause death within minutes if they block one of the major pulmonary vessels.**

- **Pathophysiology**
  - **PE may result in derangements in pulmonary haemodynamics, gas exchange and mechanics**
  - **Change in cardiopulmonary function varies with the size and number of emboli obstructing the pulmonary arteries and the patient's pre-embolic cardiopulmonary status (i.e. baseline pulmonary and cardiovascular functionality)**

Pulmonary Embolism

- **Resulting physiological changes include:**
  - **Pulmonary hypertension with right ventricular failure**
  - **Shock**
  - **Dyspnoea with tachypnea and hyperventilation**
  - **Arterial hypoxemia**
  - **Pulmonary infarction**

- **Symptoms**
  - **Clinical manifestations can be nonspecific and vary in intensity**
    - PE is notorious for being difficult to differentially diagnose from other pulmonary conditions.
  - **Small emboli may be asymptomatic**
  - **Manifestations usually develop abruptly in minutes and can last several days**

Pulmonary Embolism

- **Symptoms (cont)**
  - **Breathlessness, tachypnea**
  - **Anxiety and restlessness**
  - **Some patients may present with light-headedness, syncope, seizures and neurological deficit (reflects transient fall in cardiac output with secondary cerebral ischaemia)**
  - **Signs of a pulmonary infarct include cough, haemoptysis, pleuritic chest pain, fever, evidence of pleural fluid and possibly pleural friction rub.**

- **Diagnosis**
  - Chest x-ray, ECG, serum enzyme studies and lung perfusion scans may be used.

- **Prognosis**
  - **Mortality after the initial PE varies with the extent of the PE and the patient's pre-existing cardiopulmonary status**
    - **Likelihood that a patient with marked compromised cardiopulmonary function will die after significant PE is high (>25%)**
    - **Patient with normal cardiopulmonary function is unlikely to die unless the occlusion exceeds 50% of the pulmonary vascular bed**
    - **When the initial embolic event is fatal, death often occurs within 1-2hours**
  - **Likelihood of a recurrent embolus in an untreated patient is about 50% and as many as half of these recurrences will be fatal.**
  - **Anticoagulant therapy reduces the rate of recurrence to about 5%**

DVT Risk Factors

- **DVT is a common complication of hospital admission, and**
- **Simple prevention measures can greatly reduce an individuals' risk of suffering a DVT.**

- **Risk of developing DVT depends on:**
  - **Patient related factors (age, etc)**
  - **Features of predisposing medical condition or**
  - **The actual surgical procedure and it's aftercare**

- **Individual patient risk can be assessed using a stratification tool.**

Risk category	Medical	Surgical
High	• Stroke • Age > 70 years • Congestive heart failure • Shock • Cancer • Thrombophilia	• Orthopaedic surgery of pelvis, hip or lower limb • Major surgery, age > 60 years • Major surgery age 40-60 years with cancer or history of DVT or PE • thrombophilia
Moderate	• Immobilised patient with active disease	• Major surgery age 40-60 years • Minor surgery age > 60 years • Age 40-60 years and history of DVT/PE or oestrogen therapy
Low	• Minor medical illness	• Major surgery age <40 years • Minor surgery age < 60 years

DVT Prevention (general drugs used)

- **Low-dose heparin**
  - **Safe and effective**
  - **No monitoring of APTT required (for prevention regimens)**
  - **Cheaper than LMWHs but needs 2-3 (SC) injections per day**
  - **Less effective than LMWHs in some high risk situations (e.g. Orthopaedics)**

- **LMWHs** (e.g. Enoxaparin)

- **Factor Xa inhibitors**
  - **Apixaban and Rivaroxaban**
    - Oral anticoagulants for VTE prophylaxis after hip of knee replacement
    - More effective than Enoxaparin 40mg with similar risk of bleeding
  - **Fondaparinux**
    - More effective than LMWHs in reducing VTE in orthopaedics

- **Direct Thrombin Inhibitors**
  - **Dabigatran**
    - **Oral prophylaxis for VTE prophylaxis after elective total hip or knee replacement**
    - **Similar efficacy and bleeding rates to Enoxaparin**
- **Other measures**
  - **Compression stockings**
    - **May prevent asymptomatic DVT in general surgery and when immobile, but have not been shown to prevent pulmonary embolism**
    - **May cause superficial thrombophlebitis in varicose veins**
    - **May cause ischaemic complications in patients with peripheral vascular disease or diabetic neuropathy**
  - **Hydration**
  - **Calf exercises/regular leg movement**

DVT Prevention - surgical prophylaxis

Assessment made against risk factors for developing VTE and PE and also risk of bleeding

Pharmacological treatment examples

- Total hip replacement: LMWH or fondaparinux or rivaroxaban or dabigatran or apixaban for 28-35 days
- Total knee replacement: LMWH or fondaparinux or rivaroxaban or dabigatran or apixaban for 10-14 days
- Hip fracture: LMWH or fondaparinux for 28-35 days
- Major surgery: LMWH, UFH for up to 1 week or fully mobilized
- Neurosurgery: UFH or LMWH – caution as high risk of bleeding
- Trauma: consider LMWH when risk of bleeding is low
- Cancer patients: LMWH or UFH [NB4] depending on bleeding risk; continue for at least 7 to 10 days postoperatively
- Consider 28 days of LMWH in patients having major abdominal or pelvic surgery for cancer

DVT Prevention -non-surgical prophylaxis

Recommended Prophylactic regimes

- For patients with ischaemic stroke with immobility.
  - Depending on degree of immobility LVWH or UFH until medical condition is stable
- For patients with other conditions that predispose patient to VTE
  - LMWH or UFH [NB2]; continue until resolution of acute medical illness, mobilisation or hospital discharge

DVT Prevention (surgical prophylaxis)

- **Long Distance Air travel:**
  - Increased risk of DVT associated with long distance air travel due to blood stasis.
  - Advisable that passengers traveling by air >5hours
    - Drink a lot of fluids – but avoid excessive alcohol
    - Dehydration may cause low blood volume and inadequate blood clearance from the legs
    - Perform calf contractions each hour for a number of minutes
  - Moderate risk passengers should also use knee length graduated compression stockings (at least 20mmHg pressure at the ankle)
  - High risk passengers should have LMWH immediately before departure

Treatment of DVT and PE without haemodynamic compromise

- **Objectives of <u>treating</u> an established venous thromboembolism is to prevent:**
  - **Thrombus extension/enlargement**
  - **Pulmonary Embolism (PE)**
  - **Post-thrombotic syndrome**
  - **Recurrent venous thromboembolism**
- Less evidence to guide treatment of distal DVT compared for proximal DVT and PE
  - Treat distal DVT in same way as proximal DVT and PE
- Adequate anticoagulant therapy reduces death associated with PE

Pregnancy: LMWH – no safety data for others. Avoid warfarin – foetal harm

Cancer associated VTE: LMWH – no safety data for others. Avoid warfarin – higher incidence of reoccurrence

- Oral factor Xa inhibitors
  - Apixaban 10mg orally, BD for days then decrease to 5mg BD

    <u>Or</u>
  - Rivaroxaban 15mg orally BD for 21 days then reduce to 20mg once daily

<u>OR</u>

- Direct thrombin Inhibitor
  - Parenteral anticoagulant (heparin/LMWH) for 5 days then start dabigatran

<u>Or</u>

- Vitamin K inhibitor
  - Parenteral anticoagulant (heparin/LMWH) + Warfarin then cease heparin once INR in range
  - Target INR 2-3

PE + Shock and hypotension

- Thrombolytic therapy + anticoagulant therapy
  - Alteplase bolus + infusion or tenecteplase bolus

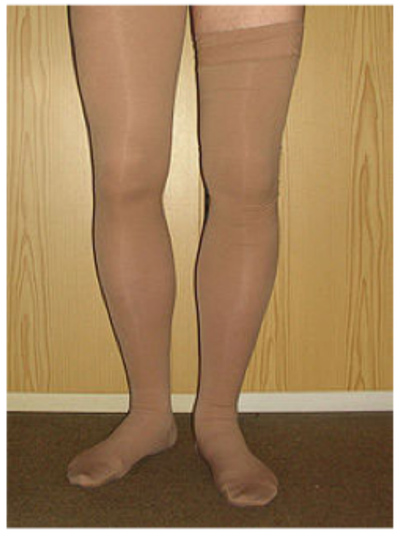
- Or
- Unfractionated heparin

THEN

- Low Molecular Weight Heparin
  - Dalteparin or enoxaparin

Duration of treatment

- Proximal DVT or PE and major provoking factor no longer present: 3 months
- Isolated distal DVT and major provoking factor no longer present: 6 weeks



- Unprovoked proximal or distal DVT or PE : 3 months
- Compression stockings
- Graduated compression stockings should be used in all cases (should provide 30-40mmHg pressure at the ankle and extend to the knee). Should be worn for up to 18 months and indefinitely if post-thrombotic syndrome is present

Summary

- The formation of a DVT usually involves three factors (Virchow's Triad) – Damage to the vessel wall, hypercoagulability and turbulent blood flow.
- DVT in form in the deep veins of the arm and leg. They are capable of throwing off a emboli which can lodge in the lungs causing a pulmonary embolism.
- Aside from injury and hypercoagulability, stasis and prolonged immobilization of the legs are associated with a higher risk of DVT.
- Drug classes used to prevent and treat DVT include low dose heparin and LMWH's, Factor Xa inhibitors and direct thrombin inhibitors.
- Mechanical measures include compression stockings, hydration and calf and leg exercises.
- Where a pulmonary embolism causes haemodynamic compromise, thrombolytic therapy is used to rapidly dissolve the clot followed by treatment with an anticoagulant for 6-12 weeks.