

DEEP VENOUS THROMBOSIS

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Introduction

Venous thromboembolism (VTE)

A condition in which a blood clot (thrombus) forms in a vein, which in some cases then breaks free and enters the circulation as an embolus, finally lodging in and completely obstructing a blood vessel, e.g., in lungs causing a PE

The most common type of venous thromboembolism is **deep vein thrombosis**, which occurs in veins deep within the muscles of the leg, arm and pelvis.

A **superficial venous thrombosis** (also called **phlebitis** or **superficial thrombophlebitis**) is a blood clot that develops in a vein close to the surface of the skin. These types of blood clots do not usually travel to the lungs unless they move from the superficial system into the deep venous system first.

Definition

- **Deep vein thrombosis is the formation of a blood clot in one of the deep veins of the body, usually in the leg**

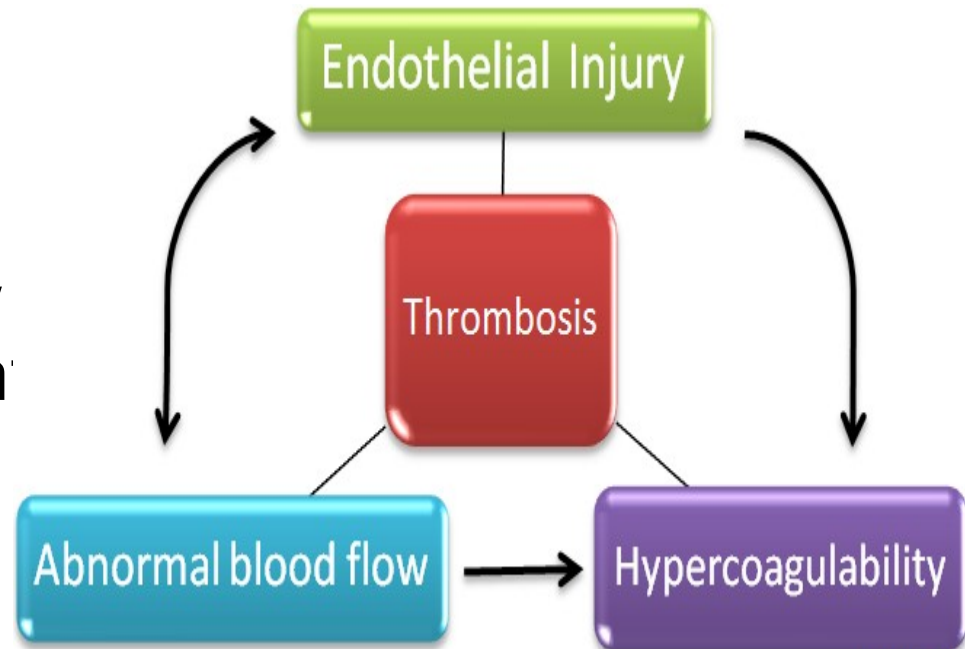
ETIOLOGY

- DVT usually originates in the lower extremity venous level ,starting at the calf vein level and progressing proximally to involve popliteal ,femoral ,or iliac system. .80-90 % pulmonary emboli originates here .

Virchow triad

More than 100 years ago, Virchow describes the three broad categories of factors that are thought to contribute to thrombosis

- venous stasis,
- endothelial damage,
- hypercoagulable state



Venous stasis

- prolonged bed rest (4 days or more)
- A cast on the leg
- Limb paralysis from stroke or spinal cord injury
- extended travel in a vehicle

Hypercoagulability

- Surgery and trauma (responsible for up to 40% of all thromboembolic disease) injury which damages veins, or surgery can slow down the flow of blood, thus raising the chances of blood clots. General anesthetics can dilate the veins, which makes it more likely that blood pools and clots form.
- Malignancy...some types are associated with a higher risk of DVT, as are some cancer therapies.
- Increased estrogen (due to a fall in protein 'S) Increased estrogen occurs during all stages of pregnancy—the first three months postpartum, after elective abortion, and during treatment with oral contraceptive pills

Inherited disorders of coagulation

- deficiencies of protein 'S,
- ' protein 'C,' and
- antithrombin III.

Acquired disorders of coagulation

- nephrotic syndrome results in urinary loss of antithrombin III,
- Antiphospholipid antibodies accelerate coagulation and include the lupus anticoagulant and anticardiolipin antibodies.

- Inflammatory processes, such as
- systemic lupus erythematosus (SLE),
 - sickle cell disease, and
 - inflammatory bowel disease (IBD),
- also predispose to thrombosis, causing hypercoagulability

Endothelial Injury

- Trauma,
- surgery, and
- invasive procedure may disrupt venous integrity
- Iatrogenic causes of venous thrombosis are increasing due to the widespread use of central venous catheters, particularly subclavian and internal jugular lines. These lines are an important cause of upper extremity DVT, particularly in children.

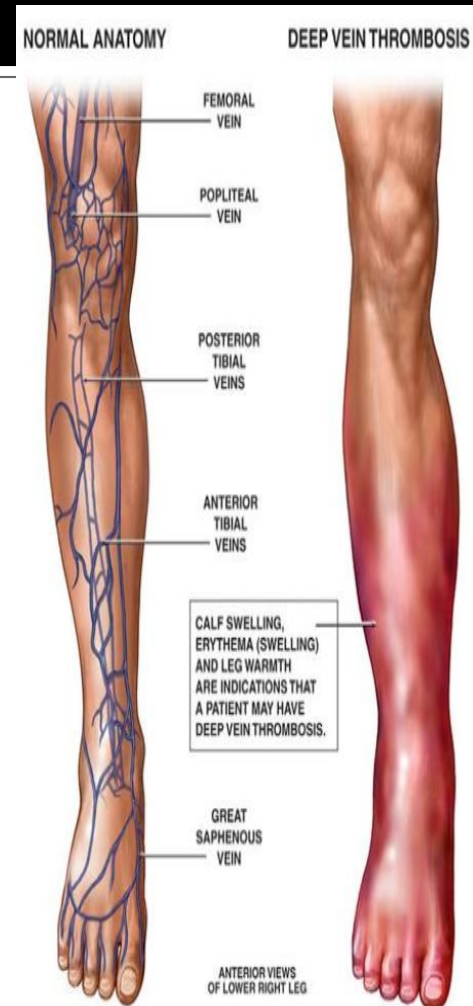
Clinical Pathophysiology

- The beginning of venous thrombosis is thought to be caused by tissue factor, which leads to conversion of prothrombin to thrombin, followed by fibrin deposition. The fibrin appears to attach to the endothelial lining, a surface that normally acts to prevent clotting.
- When a clot forms, the coagulation cascade promotes clot growth proximally. Thrombus can extend from the superficial veins into the deep system from which it can embolize to the lungs.

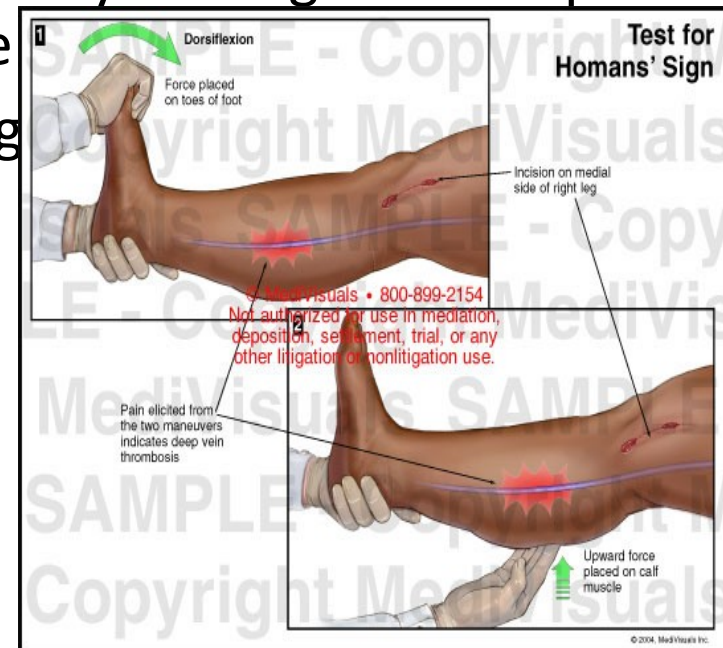
- Opposing the coagulation cascade is the endogenous fibrinolytic system. After the clot organizes or dissolves, most veins will recanalize in several weeks. Residual clots retract.
- But in presence of risk factors this clot propagates proximally and may lodge an emboli to lung
- Residual clots and venous hypertension due to narrowing of lumen may destroy valves, leading to the postphlebitic syndrome, which develops within 5-10 years,
- Edema , sclerosis, and ulceration characterize this syndrome, which develops in 40-80% of patients with DVT.

Presentation And Clinical Examination

- In the majority of cases, only one leg is affected. However, on rare occasions both legs may have a DVT.
- Calf pain or tenderness, or both
- The skin of the affected leg may feel warm
- Swelling below knee in distal deep vein thrombosis and up to groin in proximal deep vein thrombosis
- Superficial venous dilatation
- The skin may go red, especially below the knee behind the leg. The skin may be discolored.
- Cyanosis can occur with severe obstruction
- Leg fatigue



- Palpate distal pulses and evaluate capillary refill to assess limb perfusion.
- Move and palpate all joints to detect acute arthritis or other joint pathology.
- Homans' sign: pain in the posterior calf or knee with forced dorsiflexion of the foot while the knee is fully extended. This is not a commonly used test and should not be done. This test is less used today because it can potentially dislodge the deep vein thrombosis (DVT) and travel to the
- exam for signs suggestive of underlying predisposing factors



Signs of pulmonary embolism:

- Breathlessness - this may develop slowly, or come on suddenly
- Chest pain, pain is usually more severe during inhalation, eating, coughing, stooping or bending over. During exertion the pain will get worse, and will not go away when the patient rests.
- Coughing may produce bloody or bloodstained sputum
- Wheezing
- Lightheadedness, and sometimes even fainting (collapse)
- Unexplained anxiety
- Accelerated heartbeat

Wells Clinical Prediction Guide

- The Wells clinical prediction guide incorporates risk factors, clinical signs, and the presence or absence of alternative diagnoses. A high score is 3 or more, a moderate score 1–2 and a low score 0.

Wells Clinical Prediction Guide (1997)

Clinical Parameter:	Score
■ Active Cancer (treatment ongoing/ or within 6mths/ or palliative)	1
■ Paralysis or recent plaster immobilisation	1
■ Recently bed-ridden for >3days, or major surgery <4wks	1
■ Localised tenderness along distribution of deep veins	1
■ Entire leg swelling	1
■ Calf swelling >3cm compared to asymptomatic leg	1
■ Pitting oedema (> in sx leg)	1
■ Collateral superficial veins (non-varicose)	1
■ Alternative diagnosis (as likely or > that of DVT)	-2

■ Total of Above Score

High probability: Score 3 or more

Moderate probability: Score = 1 or 2

Low probability: Score 0

Diagnostic Studies

- Clinical examination alone is able to confirm only 20-30% of cases of DVT
- Two important investigations are
 - A) Blood Tests i.e d-dimers and INR
 - B) Imaging Studies

Blood Tests

- the D-dimer
- INR.
- Currently D-dimer assays have predictive value for DVT, and the
- INR is useful for guiding the management of patients with known DVT who are on warfarin (Coumadin)

D-dimer

- D-dimer is a specific degradation product of cross-linked fibrin. Because concurrent production and breakdown of clot characterize thrombosis, patients with thromboembolic disease have elevated levels of D-dimer
- three major approaches for measuring D-dimer
 - ELISA
 - latex agglutination
 - blood agglutination test

- False-positive D-dimers occur in patients with
- recent (within 10 days) surgery or trauma.
 - recent myocardial infarction or stroke, acute infection
 - disseminated intravascular coagulation,
 - pregnancy or recent delivery,
 - active collagen vascular disease, or metastatic cancer

Imaging Studies

- Invasive
 - venography,
 - radiolabeled fibrinogen and.
- noninvasive
 - ultrasound,
 - plethysmography,
 - MRI techniques

venography

- gold standard" modality for the diagnosis of DVT
- Advantages
- Venography is also useful if the patient has a high clinical probability of thrombosis and a negative ultrasound,
- it is also valuable in symptomatic patients with a history of prior thrombosis in whom the ultrasound is non-diagnostic.



side effects

- phlebitis
- anaphylaxis

Nuclear Medicine Studies

- Because the radioactive isotope incorporates into a growing thrombus, this test can distinguish new clot from an old clot

Plethysmography

- Mercury-filled strain gauges used to continuously measure circumference of the extremity to determine circulatory capacity, e.g. at mid calf. It is a non-invasive method used to detect venous thrombosis in these areas of the body.

Ultrasonography

- color-flow Duplex scanning is the imaging test of choice for patients with suspected DVT
- inexpensive,
- noninvasive,
- widely available
- Ultrasound can also distinguish other causes of leg swelling, such as tumor, popliteal cyst, abscess, aneurysm, or hematoma.

clinical limitations

- expensive
- reader dependent
- Duplex scans are less likely to detect non-occluding thrombi.
- During the second half of pregnancy, ultrasound becomes less specific, because the gravid uterus compresses the inferior vena cava, thereby changing Doppler flow in the lower extremities

Magnetic Resonance Imaging

- It detects leg, pelvis, and pulmonary thrombi and is 97% sensitive and 95% specific for DVT.
- It distinguishes a mature from an immature clot.
- MRI is safe in all stages of pregnancy.

DIFFERENTIAL DIAGNOSIS

- Cellulitis
- Thrombophlebitis
- Arthritis
- Asymmetric peripheral edema secondary to CHF, liver disease, renal failure, or nephrotic syndrome
- lymphangitis
- Extrinsic compression of iliac vein secondary to tumor, hematoma, or abscess
- Hematoma
- Lymphedema
- Ruptured Baker cyst
- Stress fractures or other bony lesions
- Superficial thrombophlebitis
- Varicose veins

Management Guidelines

- Using the pretest probability score calculated from the Wells Clinical Prediction rule, patients are stratified into 3 risk groups—high, moderate, or low.
- The results from duplex ultrasound are incorporated as well:
- If the patient is high or moderate risk and the duplex ultrasound study is positive, treat for DVT.

- If the duplex study is negative and the patient is low risk, DVT has been ruled out.
- If the patient is high risk but the ultrasound study was negative, the patient still has a significant probability of DVT
- If the patient is low risk but the ultrasound study is positive, some authors recommend a second confirmatory study such as a venogram before treating for DVT

Objectives of Treatment

The primary objectives of the treatment of DVT are to

- prevent pulmonary embolism,
- reduce morbidity, and
- prevent or minimize the risk of developing the postphlebitic syndrome.

Treatment Options

- Anticoagulation
- Thrombolytic therapy for DVT
- Surgery for DVT
- Filters for DVT
- Compression stockings

Anticoagulation

Two types

- 1) Heparin**
- 2) Warfarin**

Heparin

- **Mechanism of action**

Heparin binds to the enzyme inhibitor antithrombin III (AT), causing a conformational change that results in its activation which then inactivates thrombin

- After an initial bolus of 80 U/kg, a constant maintenance infusion of 18 U/kg is initiated. The aPTT(all clotting factors except seven and thirteen) is checked 6 hours after the bolus and adjusted accordingly. .it is said that text references refer to a therapeutic aPTT target of 1.5- 2.0 times the mean of the reference range
- The aPTT is repeated every 6 hours until 2 successive aPTTs are therapeutic. Thereafter, the aPTT is monitored every 24 hours as well as the hematocrit and platelet count.

- Heparin induced thrombocytopenia(HIT)

Heparin occurs naturally in the human body, but the development of HIT antibodies suggests heparin sulfate act as a hapten, and thus targeted by the immune system, their development usually takes about five days. These antibodies form a complex with heparin in the bloodstream. The tail of the antibody then binds to a protein on the surface of the platelet. This results in platelet activation ,which initiate the formation of blood clots and the consumption of platelets; the platelet count falls as a result, leading to thrombocytopenia. Three agents are used to provide anticoagulation in patients with strongly suspected or proven HIT: danaparoid(LMW heparin), lepirudin, and argatroban.(direct thrombin inhibitor)

At the present time, 3 LMWH preparations,

- Enoxaparin,
- Dalteparin, and
- Ardeparin

warfarin

- Interferes with hepatic synthesis of vitamin K-dependent coagulation factors i.e *factors* II, VII, IX and X (and proteins C, S, and Z)
- Dose must be individualized and adjusted to maintain INR between 2-3
- 2-10 mg/d PO

- for the first three days of "warfarinization", the levels of protein C and protein S (proteins of anticoagulation) drop faster than pro-coagulation proteins such as factor II, VII, IX and X. Therefore bridging anticoagulant therapies (such as enoxaparin) are often used to reverse this temporary hypercoagulable state
- caution in active tuberculosis or diabetes; patients with protein C or S deficiency are at risk of developing skin necrosis

Duration of anticoagulation in patients with deep vein thrombosis

- Transient cause and no other risk factors: 3 months
- Idiopathic: 3-6 months
- Ongoing risk for example, malignancy: 6 -12 months
- Recurrent pulmonary embolism or deep vein thrombosis: 6-12 months
- Patients with high risk of recurrent thrombosis exceeding risk of anticoagulation: indefinite duration (subject to review)

Thrombolytic therapy

A mechanical thrombectomy device can remove venous clots, but it is recommended only as an option when the following conditions apply: "iliofemoral DVT, symptoms for < 7 days (criterion used in the single randomized trial), good functional status, life expectancy of ≥ 1 year, and both resources and expertise are available

Thrombolytic therapy does not prevent

- clot propagation,
- rethrombosis, or
- subsequent embolization.
- Heparin therapy and oral anticoagulant therapy always must follow a course of thrombolysis.

Surgery for DVT

Open surgical thrombectomy has a very limited role in the management of acute DVT. The limitations to the procedure are obvious, and the results are ambiguous at best. For this reason, open surgical thrombectomy for DVT is reserved as a last resort for those patients with threatened limb loss secondary to extensive DVT

Indications

- when anticoagulant therapy is ineffective
- unsafe,
- contraindicated.



- These pulmonary emboli removed at autopsy look like casts of the deep veins of the leg where they originated.

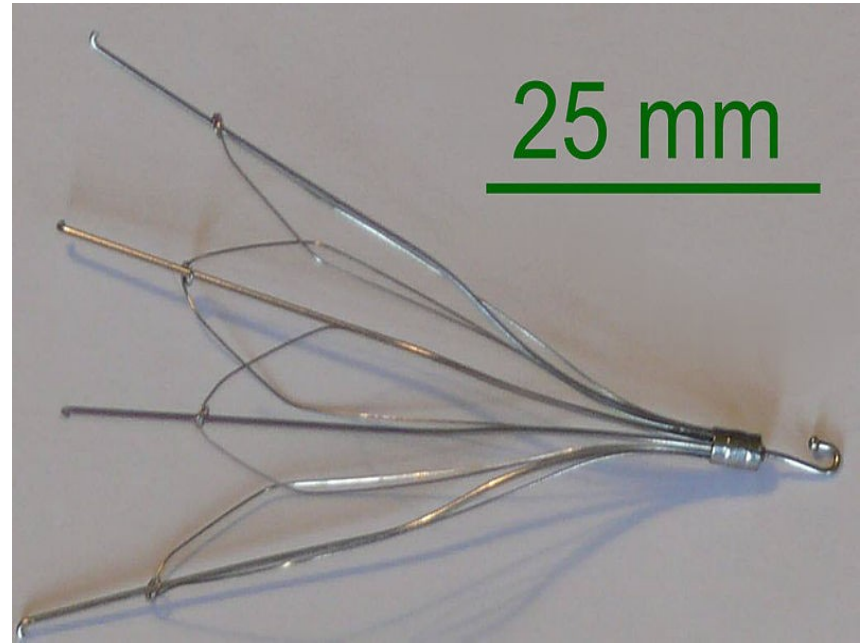




This patient underwent a thrombectomy. The thrombus has been laid over the approximate location in the leg veins where it developed.

Filters for DVT

- this tiny umbrella-like device is inserted into the vein to catch blood clots and stop them moving up into the lungs, while allowing blood flow to continue. It is inserted in the vena cava



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- **Indications for insertion of an inferior vena cava filter**
 - Pulmonary embolism with contraindication to anticoagulation
 - Recurrent pulmonary embolism despite adequate anticoagulation
 - Deep vein thrombosis with contraindication to anticoagulation
 - Deep vein thrombosis in patients with pre-existing pulmonary hypertension
 - Free floating thrombus in proximal vein
 - Failure of existing filter device
 - Post pulmonary embolectomy

Compression stockings (routinely recommended)



Complications

- Acute pulmonary embolism
- Postthrombotic Syndrome
- Blood clot in the kidney, called renal vein thrombosis
- Blood clot in the heart, leading to heart attack
- Blood clot in the brain, leading to stroke
- Chronic venous insufficiency

Prognosis:

- All patients with proximal vein DVT are at long-term risk of developing chronic venous insufficiency.
- About 20% of untreated proximal (above the calf) DVTs progress to pulmonary emboli, and 10-20% of these are fatal. With aggressive anticoagulant therapy, the mortality is decreased 5- to 10-fold.
- DVT confined to the calf virtually never causes clinically significant emboli and thus does not require anticoagulation

Patient Education:

- Advise women taking estrogen of the risks and common symptoms of thromboembolic disease.
- Discourage prolonged immobility, particularly on plane rides and long car trips
- Advise patient at risk to use compression stockings

PROPHYLAXIS

- Identify any patient who is at risk.
- Prevent dehydration.
- During operation avoid prolonged calf compression.
- Passive leg exercises should be encouraged whilst patient on bed.
- Foot of bed should be elevated to increase venous return.
- Early mobilization should be rule for all surgical patients.



Thanks