Deep Vein Thrombosis: Symptoms and Treatment

Deep vein thrombosis is the development of single or multiple blood clots within the deep veins of the extremities or pelvis, usually accompanied by inflammation of the vessel wall.

Thrombosis of the deep veins occurs most often in the calf but may also occur in the thigh or pelvis. It may be primary or an extension of more peripheral disease.

Most cases in pregnancy are confined to the deep veins of the lower extremity, Proximal vein thrombosis are iliac or femoral vein, Calf vein thrombosis is distal vein thrombosis

Etiology:

- Three generic factors promote clotting

a) Hypercoagulable states

- Cancer
- Nephrotic syndrome
- Sepsis
- Inflammatory conditions such as ulcerative colitis
- Increased estrogen-like in pregnancy and use of oral contraceptives
- Antiphospholipid syndrome
- Protein deficiencies
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    - Protein S
    - Protein C
    - Antithrombin III
- Newer hypercoagulable states
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    - Factor V
    - Leiden
    - Prothrombin gene mutations

b) Stasis

- Prolonged bed rest
- Immobility from a cast
- Long plane or train ride
- Neurologic disorders with paralysis
- Congestive heart failure
- Obesity

c) Vascular damage

- Trauma

- Surgery
- Central lines especially in the case of upper extremity thrombophlebitis

d) Multifactorial issues

- Advancing age
- Prior thromboembolism

Risk factors:

- Advanced age (Usually over 40 years)
- Obesity
- Cancer
- Pregnancy
- Oral contraceptive use (oral contraceptives and replacement estrogens)
- Hyperlipidemia
- Diabetes mellitus
- Hemoconcentration following transfusion for severe anemia
- Certain hypercoagulable states (protein C and S deficiencies, hyperhomocysteinemia)
- Recently, the factor V Leiden mutation has been implicated as a potentially important cause.

The puerperium has been known as the time when severe thrombophlebitis conditions and pulmonary embolism occur, probably as a result of the once-prevalent recommendation of prolonged bedrest following parturition.

The risk of recurrence in a subsequent pregnancy is substantial

Pathogenesis:

A constant balance exists between intravascular clot-promoting and clot-dissolving forces. When the former overpowers the latter, clot results.

Endothelial injury can expose collagen, causing platelet aggregation and tissue thromboplastin release that, when stasis or hypercoagulability is present, trigger the coagulation mechanism.

Tissue thromboplastin is released, forming thrombin and fibrin that trap RBCs and propagate proximally as a red or fibrin thrombus, which is the predominant morphologic venous lesion (the white or platelet thrombus is the principal component of most arterial lesions).

When a small blood vessel is transected or damaged, the injury initiates a series of events that lead to the formation of a clot (hemostasis).

The initial event is constriction of the vessel and formation of a temporary hemostatic plug of platelets that is triggered when platelets bind to collagen and aggregate. This is followed by the conversion of the plug into the definitive clot. The loose aggregation of platelets in the temporary plug is bound together and converted into the definitive clot by fibrin.

The clotting mechanism responsible for the formation of fibrin involves a cascade of reactions in

which inactive enzymes are activated, and the activated enzymes, in turn, activate other inactive enzymes.

The fundamental reaction in the clotting of blood is a conversion of the soluble plasma protein fibrinogen to insoluble fibrin. The conversion of fibrinogen to fibrin is catalyzed by thrombin

Clinical presentation:

The signs and symptoms of deep venous thrombosis involving the lower extremity vary greatly, depending in large measure upon the degree of occlusion and the intensity of the inflammatory response.

The patient may complain of a dull ache or frank pain in the leg or calf.

- There may be tenderness or spasm in the calf muscle.
- Leg swelling-Greater than 1 cm difference is usually significant.
- Leg warmth and redness.
- Palpable cord.
- **Phlegmasia cerulea dolens-**Cold, tender, swollen and blue leg (secondary arterial insufficiency). In **phlegmasia alba dolens-**Cold, tender and white leg (secondary arterial insufficiency)
- Dorsiflexion of the foot may elicit pain in the calf (Homans' sign). Although a positive Homans' sign is specific, the test is not very sensitive (about 25%).
- Slight elevation of the temperature and pulse is frequently noted.
- If the clot is in the femoral vein or in the pelvis, swelling of the extremity may be more severe.

Classical puerperal thrombophlebitis involving the lower extremity, sometimes called phlegmasia alba dolens or milk leg, is abrupt in onset, with severe pain and edema of the leg and thigh.

- Occasionally, reflex arterial spasm causes a pale, cool extremity with diminished pulsations.
- More likely, there may be an appreciable volume of clot yet little reaction in the form of pain, heat, or swelling.
- Chronic venous insufficiency may develop as a long-term consequence.

Diagnosis:

Compression ultrasonography or impedance plethysmography usually provides a definite diagnosis.

Real-time ultrasonography, used along with duplex and color Doppler ultrasound, is currently the procedure of choice to detect proximal deep vein thrombosis

Both are noninvasive and are sensitive and specific.

If these tests are not diagnostic, contrast venography is the gold standard and should be performed.

Although venography or phlebography remains the standard for confirmation of deep venous thrombosis, noninvasive methods have largely replaced this test to confirm the clinical diagnosis

In pregnant women, thrombosis associated with pulmonary embolism frequently originates in the iliac veins.

Treatment of deep vein thrombosis

1. Medical treatment

Once the diagnosis of a significant deep vein thrombosis extending into the veins proximal to the calf has been made, anticoagulants should be started immediately.

Traditionally, intravenous unfractionated heparin has been the first-line therapy. subcutaneous low molecular weight heparin has gained acceptance.

Coagulation studies, including international normalized ratio (INR) and partial thromboplastin time (PTT), should be done before anticoagulant therapy is started; these tests provide a basis for interpreting the degree of anticoagulation achieved with unfractionated heparin.

When using unfractionated heparin, the **PTT** should be kept to 2-3 times the control value.

The more predictable bioavailability, clearance, and activity of low molecular weight heparins obviate the need for laboratory monitoring except in unusual circumstances.

Intravenous protamine sulfate can be used in emergencies to counteract the effects of heparin.

Heparin should be continued at least 3-5 days after the disappearance of all signs and symptoms and effective long-term therapy has been established.

Oral anticoagulants such as dicumarol and warfarin are contraindicated in pregnant patients but are often started at the same time as heparin in other patients. Started shortly after heparin has been administered. Not before heparin because of the theoretic risk for inducing a transient hypercoagulable state

The therapeutic effect of these agents is measured by the **INR**. Whereas heparin prolongs the clotting time almost immediately, the oral anticoagulants do not exert their full effect for 48-72 hours.

Heparin is usually started for its immediate short-term effect and then replaced with oral anticoagulants for long-term treatment.

Once-daily low molecular weight heparin can be used long-term in patients for whom bleeding is a particular risk or laboratory monitoring is problematic

If using warfarin, the INR should be determined daily until equilibrium levels of 2.0-3.0 are attained. Emergency reversal can be achieved with 2 units of fresh frozen plasma.

Anticoagulation is usually continued empirically for 3 months. Possible complications of therapy,

including hematuria, hemoptysis, hematemesis, melena, and easy bruisability.

Patients should also be given a list of over-the-counter medications to avoid, including nonsteroidal anti-inflammatory drugs, aspirin, and antibiotics, which may affect their anticoagulation.

Medication:

- **In uncomplicated DVT:**LMWH [enoxaparin (Lovenox) 1 mg/kg/dose twice a day SC; dalteparin (Fragmin)]. No laboratory monitoring is required.
- **In complicated DVT:** Heparin (unfractionated) 80 units/kg IV bolus followed by continuous infusion starting at 18 units/kg/hr.
- Tinzaparin: 175 IU/kg SQ QD
- Adjust dosage based on **activated partial thromboplastin time (aPTT)**