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# Diagnosis and management of deep venous thrombosis

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## ABSTRACT

There is high incidence of venous thromboemoblism, comprising of deep vein thrombosis and pulmonary embolism, in hospitalized patients. The need for systemic thromborophylaxis is essential, especially in patient with inherited or acquired of postoperative deep vein thrombosis and pulmonary embolism. Similar animal experiments could end the present exclusive reliance on statistical analysis of data from large patient cohorts to evaluate prophylactic regimes. The reduction of need for such (usually retrospective) analyses could enable rationally-based clinical trials of prophylactic methods to be conducted more rapidly, and the success of such trials would lead to decreased incidences of DVT-related mortality and morbidity. Used in treatment prophylactic or therapeutic doses of anticoagulants, may present of surgery. General or regional anaesthesia may be considered depending on the type and degree of anticoagulation as judged by investigation. The dilemma regarding the type of anaesthesia can be solved if the anaesthesiologist is aware of the pharmacokinetics of drugs affecting haemostasis. The anaesthesiologist must keep abreast with latest developments of methods and drugs used in the prevention and management of venous thromboembolism and implications in the conduct of anaesthesia.

**Keywords:** Anaesthesia, Anaesthesia consideration, Deep vein thrombosis, Pulmonary embolism, Thromboembolism.

## INTRODUCTION

Venous thrombosis represents a spectrum of diseases that includes both deep venous thrombosis (DVT) and pulmonary embolism. Often, DVT is not suspected clinically leading to significant diagnostic delays. Venous thrombosis results in considerable, but potentially preventable, morbidity and mortality among hospitalized patients. Most of the hospitalized patients have a high risk of DVT, and hospitalization for acute medical-illness is known to be associated with about eight-fold increased risk of DVT1 Because of the high rate of missed diagnosis, the true incidence of DVT is unknown. There is a lack of adequate studies on the incidence of DVT. . Its sequelae often lead to mortality (via pulmonary embolism (PE) or chronic morbidity (post thrombotic syndrome), so prophylactic measures have long been considered priorities and are the foci of recent discussions and guidelines published on both sides of the Atlantic [1–4]. These and many similar papers rely on statistical analysis of data from large patient cohorts to evaluate prophylactic regimens. They mostly emphasize pharmacological anticoagulation (disabling of normal hemostatic function), with

mechanical methods such as intermittent pneumatic compression assigned a secondary or adjunctive role. For example, on the basis of a review of randomized trials since 1950, the 2011 American College of Physicians guideline recommended (i) assessment of medical (including stroke) patients for the risk of thromboembolism, (ii) pharmacological prophylaxis with heparin or related drug unless there is a serious risk of bleeding, and (iii) mechanical prophylaxis with graduated compression stockings in the event of a bleeding risk [4]. However, despite continual refinements of the pharmaceutical approach, DVT/PE-related mortality has shown only minimal reduction during recent decades, as reviewed in, for example, [5, 6]. The incidence of secondary (hospital-acquired) DVT in the USA more than tripled during the period 1989–2006, and there was a 2.5-fold increase in the number of admissions with a primary diagnosis of PE [7]. Several recent studies have cast doubt on the prophylactic value of anticoagulants [4, 6, 8]. A comprehensive review of trials indicated that heparin did not reduce overall mortality, though it decreased the incidence of PE [4,10], and a large trial showed that anticoagulant prophylaxis is associated with a risk of serious and potentially fatal bleeding and little benefit in terms of DVT/PE prophylaxis [8]. Indeed, it has been suspected for more than half a century that heparin does not prevent the initiation of DVT. In 1952, for instance, summarizing the results of a series of experiments in which intravenous fibrogenesis was induced in dogs, Samuels and Webster wrote "It appears, from these experiments, that fibrin may appear on the injured vessel walls even in cases where the blood is rendered incoagulable by heparin" [2, 3, 9]. Drug used warfarin (Coumadin) is usually started along with heparin.

- Warfarin is taken by mouth. It takes several days to fully work.
- Heparin is not stopped until the warfarin has been at the right dose for at least 2 days.
- You will most likely take warfarin for at least 3 months. Some people must take it longer, or even for the rest of their lives, depending on their risk for another clot.

Nevertheless, anticoagulant prophylaxis remains the standard of care for patients considered at risk for DVT and its sequelae. Coagulation is not the primary event in the generation of a venous thrombus, but rather a consequence of the morbid pathological process within one or more valve pockets that can lead to thrombogenesis [10, 11]. The incipient conflict in the recent literature could be resolved if this account of the etiology of DVT, the valve cusp hypoxia (VCH) thesis, were more widely appreciated [12, 13].

## ETIOLOGY

Rudolph Virchow in 1856 described the factors that predispose to DVT. Which and relevant even today Virchow triad comprises of 3 factors: Venous stasis, Damage to venous wall and Hypercoagulability.

### Patient –specific risk factors

These are either acquired or inherited hyper coagulable states associated with 4 high incidences of DVT and PE

### Inherited patient specific factors

- Factors V Leiden and Cambridge mutation (activated protein C resistance)
- Prothrombin gene mutation (20210A)
- Congenital deficiencies of antithrombin III. Protein C and Protein S.
- Dysfirbrogenaemia
- Hyperhomocysteinaemia
- An inherited abnormality may not be found in 40% to 60% of patients with idiopathic.

### Acquired patient- specific factors

- Previous DVT or family history of DVT
- Immobility, such as bed rest or sitting for long periods of time
- Recent surgery
- Above the age of 40
- Hormone therapy or oral contraceptives
- Pregnancy or post-partum
- Previous or current cancer
- Limb trauma and/or orthopedic procedures
- Coagulation abnormalities
- Obesity
- The overall risk of thrombosis in cancer patients is sevenfold as compared to non- cancer patient. Drugs used in cancer may directly contribute to thrombosis[14,15,16 ]

## Venous blood flow is influenced by two main factors

Vis a tergo resulting from the continuous entry of blood from the capillary beds into the venules and mechanical pumping resulting, for example, from upward pressure on the soles of the feet during walking and from contractions of the gastrocnemius and other skeletal muscles. When there is little or no mechanical pumping, vis a tergo dominates and the flow is continuous (laminar, streamline, nonpulsatile); when mechanical pumping takes place, the flow is discontinuous (intermittent, pulsatile). According to the VCH thesis [10, 11], DVT may follow when pathologically long periods (over 1.5–3.0 hours) of continuous venous blood flow result in severe hypoxemia in one or more valve pockets, leading in turn to injurious hypoxia of the valve cusp endothelium in the depths of the pocket(s) [11]. Should a burst of discontinuous flow, however brief, flush out the stagnant blood from such oxygen-starved pocket(s), the next refill of the pocket will automatically carry fresh, normally oxygenated blood from the vein lumen, containing living leukocytes and platelets. Such newly introduced cells may instantly marginate, settle on, and attack the lately unperfused, moribund endothelium. Living phagocytes are therefore likely to attach themselves to the dying parietalis endothelial layer lining the inner aspect of the valve cusp. Alternating protracted periods of such continuous (i.e., streamline) blood flow with restored normal (i.e., discontinuous) flow can progressively build up a burgeoning thrombus comprising accumulated dead blood cells and concomitantly generated fibrin.In more detail, the pathogenic process can be envisaged in terms of the following steps. (i)Normal venous blood flow is associated with a four-phase valve cycle, which was analyzed in detail by Lurie and colleagues [13, 14]. This cycle is strongly dependent on the pulsatility of flow, which in the lower limbs is ensured, for example, by the calf muscle pump and the upward pressure on the soles of the feet during walking. In simple terms, the valve cusp leaflets are forced apart (opening the valve) when the pressure caudad exceeds the pressure cephalad and are forced together again (closing the valve) when the converse holds. Under conditions when the calf muscle pump does not operate and there is no upward pressure on the soles of the feet, venous blood flow depends mostly on vis a tergo and becomes continuous (streamline), so the four-phase cycle ceases to operate. The valve cusp leaflets remain partly open, partly closed, their tips oscillating slightly in the streamline flow owing to the Venturi effect.(ii)Under these conditions, the blood within the valve pockets scarcely exchanges with the luminal blood in the vein. Instead, it circulates within the pocket, describing two vortices: a primary vortex near the mouth of the pocket, driven by the passing luminal blood and the Venturi effect on the cusp leaflet, and a slow secondary vortex in the depths of the pocket, driven by the primary vortex [15–17]. (iii)Respiring blood cells in this secondary vortex, and the endothelial cells in contact with it, progressively deplete the oxygen store of the blood trapped in such pockets. Theoretical calculations predict [11], and experimental measurements confirm [18], that the hypoxemia can become sufficiently severe after 1.5–3.0 hours to injure the endothelial cells; the PO2 registered in the cells deep in the pocket fell below the detection limit of the oxygen electrode (<0.14 kPa) after such a period [16,18]. (Since the blood flowing in the vein lumen remains oxygenated, this strongly suggests that the valve cusp leaflet is effectively impermeable to oxygen.)(iv)Although the endothelial cells in the depths of the valve pocket can maintain themselves temporarily by anaerobic metabolism [19,25], they are inevitably affected by this sustained and extreme hypoxia. In particular, the cells on the inner (parietalis) surface of the valve cusp leaflet are likely to become necrotic because—unlike the vein wall endothelial layer—they have no blood supply from vasa venarum [20,23]. In contrast, the endothelial cells on the circumferential wall of the valve pocket may survive because they receive a vasa venarum supply [20, 21] and hence are less susceptible to oxygen depletion of the blood in the pocket. Therefore, while they may become hypoxic, they need not become fatally anoxic. Endothelial cells subjected to nonfatal hypoxia undergo a constellation of phenotypic changes largely mediated by the early growth response-1 (egr-1) gene, which is activated via elk-1 under conditions of reduced oxygen tension [26, 28]. These phenotypic changes include signals that attract leukocytes and platelets and initiate local coagulation largely through the activation of tissue

factor [5,11,24,27,39]. If and when intermittent, discontinuous flow is restored, even transiently, the normal valve cycle [13, 14] resumes. The stagnant (hypoxemic) blood is evacuated from the valve pocket and replaced by fresh venous blood, containing living, active leukocytes and platelets. Phagocytes and platelets then marginate on and attack the necrotic parietalis endothelium of the lately hypoxic valve cusp leaflet, and the resulting accumulation of functioning-then-dying leukocytes (and platelets) is accompanied, or quickly succeeded, by fibrinogenesis[30].(vii)The next (and subsequent) sufficiently sustained episodes of continuous flow—once again rendering the valve pockets hypoxemic—may kill the blood cells that entered such valve pocket(s) during the previous discontinuous flow interludes. Continued alternation of continuous flow with brief discontinuous episodes may therefore result in the layered accumulation of generations of dead cells interspersed with dense extensions of fibrin, attached to the necrotic parietalis endothelium of the valve cusp leaflet.(viii)If and when this "protothrombus" grows sufficiently large to protrude from the mouth of the valve pocket into the vein lumen, it presents an abnormal surface on which the passing venous blood will coagulate, leading to further growth and generation of a frank and manifestly classically "layered" thrombus.(ix)Such a protruding, growing thrombus is subject to pressure from the flowing venous blood, and because it is "anchored" only to the necrotic (and hence fragile) parietalis endothelium, it is likely to embolize.[22, 29, 32, 33]

## Causes of Deep vein thrombosis

The causes of deep vein thrombosis (DVT) have been categorized under three main groups (referred to as Virchow's triad in medical terminology) and include:

- Vein injuries
- Faster blood clotting
- Decreased blood flow rate

## Vein injuries

Wherein the ability of the veins to pump the blood back to the heart is compromised can occur due to factors such as surgeries, injection of irritating substances into the vein, presence of underlying disorders such as Buerger's disease and preexisting clots [12, 40, 41]

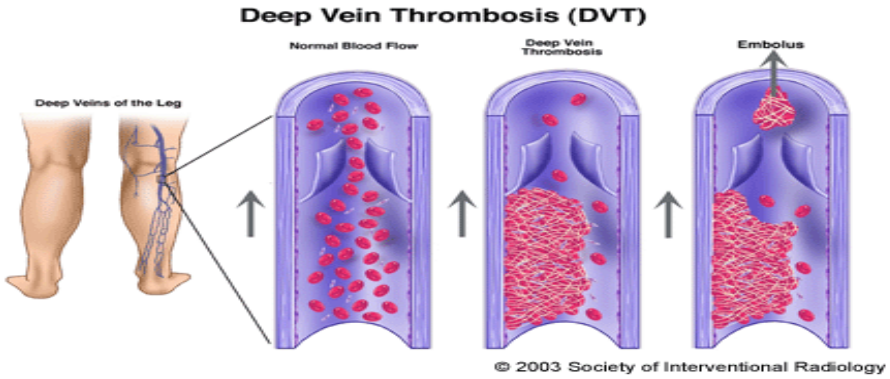
## Faster blood clotting

Decreased ability of the veins to pump the blood back can lead to pooling of the blood in the legs leading to the formation of clots. Deep vein thrombosis (DVT) can also be caused by other factors that enhance blood clotting. This includes various factors such as: presence of certain inherited disorders; cancer; administration of drugs such as oral contraceptives, estrogen; smoking; childbirth; surgery and dehydration (especially in older people).[42, 44]

## Decreased blood flow rate

Deep vein thrombosis (DVT) can occur as a result of decreased blood flow rate noted due to conditions such as:

- Prolonged bed rest.
- Decreased mobility of the legs due to injury or disease.
- Prolonged sitting – at work, while travel.



### Signs and symptoms

The difference between a **sign** and a **symptom** - the patient feels and describes a **symptom**, such as a pain, while **signs** can be detected by other people, including doctors and nurses, and may include a rash, redness or swelling [23,31].

As mentioned earlier, some people may have developed DVT and have no symptoms. If signs and symptoms do occur, they may include:

- Pain in the affected limb. In many patients, pain starts in the calf.
- Swelling in the affected limb
- The skin of the affected leg may feel warm
- The skin may go red, especially below the knee behind the leg. The skin may be discolored.
- The surface veins of the affected limb may become dilated
- Leg fatigue

In the majority of cases, only one leg is affected. However, on rare occasions both legs may have a DVT. If the clot becomes dislodged and finds it way to the lung, the following signs and symptoms may indicate

### 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.[34,43,44]

### Diagnosed

The doctor will ask patients questions about symptoms, their medical history, and carry out a physical examination. Diagnosing DVT from just signs and symptoms is usually not enough, and the doctor may recommend some tests [10, 20, 49].

### D-dimer test

D-dimer is a protein fragment which is present in blood after a blood clot is degraded by firbinolysis, if more than a certain amount is found in a blood test, it is likely that the patient has a blood clot in a vein [35].

### Ultrasound

This type of scan can detect clots in veins, and also determine bloodflow speed within a vein. If a doctor knows blood flow has slowed down, he/she may be able to locate a clot if there is one. A Doppler ultrasound (Doppler sonography) can tell how fast blood is flowing [36].

### Venogram

This diagnostic test may be used if the ultrasound scan and D-dimer tests are inconclusive. The doctor injects a dye into a vein in the patient's foot or groin. X-ray images can see the dye as it moves and will reveal the location of a blood clot, because the dye will not be able to flow around it - it will appear as a gap in the blood vessel [47, 50].

### Other imaging scans

Magnetic resonance imaging (MRI) or computerized tomography (CT) scans may reveal the presence of a clot. Often, such clots are revealed when these scans are ordered for other reasons [49].

## PREVENTION

DVT Prevention Strategies Lifestyle Changes The most common lifestyle risk factors for venous thromboembolism are the same problems that plague our Western society: obesity, inactivity, and cigarette smoking. Nevertheless, most inquiries about DVT prevention come from patients about to embark on longhaul air travel. Despite the drama of collapse and death from PE while in flight or after disembarking, the chance of this happening is only about 1 in 10,00,000 travelers [38,39].

Mechanical Measures For many patients at low risk of DVT, graduated elastic compression stockings will suffice. Vascular compression stockings usually lose their elasticity after about 3 months and should be replaced to maintain their effectiveness. Pneumatic compression boots are not practical unless the patient is hospitalized or homebound [40, 41].

### Pharmacological treatment

There are a variety of alternatives for treating a blood clot, depending on a number of factors, including its location in the body, the type of clot, and the patient's overall health. Listed below are some of the more common ones [37, 53].

| Treatment | Comments |
|---|---|
| **Compression stockings** | Insurance might not cover them, so be sure to check with your provider. |
| **Heparin** | Given intravenously at a hospital or by injection. Carries a higher risk of internal bleeding than low-molecular-weight heparin. |
| **Low-molecular-weight heparin** Dalteparin (*Fragmin*), enoxaparin (*Lovenox* and generic) | There's a risk of internal bleeding; Report any unusual bleeding or bruising to your doctor. |
| **Selective factor Xainhibitors** Fondaparinux (*Arixtra* and generic), rivaroxaban (*Xarelto*) | Both drugs reduce the risk of blood clots more than low-molecular-weight heparin, but may also increase risk of bleeding. Fondaparinux is given intravenously or by injection; Rivaroxaban is available as a pill. |
| **Surgery** | Done only in rare cases. |
| **Thrombolytics** Includes alteplase (*Activase*) | Used to treat life-threatening blood clots in the lungs. |
| **Warfarin** *Coumadin*, *Jantoven*, and generic | To reduce the risk of internal bleeding, don't start or stop any medications or dietary supplements without a doctor's approval. Eat a consistent diet and avoid eating unusually large amounts of food high in vitamin K, such as broccoli, collard greens, and kale. Report any unusual bleeding or bruising to a doctor. |

## Duration of Anticoagulation

Venous thromboembolism is a disease that may often recur, with a 5-year recurrence risk of up to 20–25%. Extended thromboprophylaxis is effective in preventing recurrence of VTE, but it is also associated with a substantially increased risk of major bleeding [48]. According to the ACCP guidelines anticoagulation should be stopped after 3 months in patients with a transient risk factor like surgery, trauma, immobilization, pregnancy, or female hormone intake (35, 37, 44–47).

## Choice of Prophylaxis General Surgery

## Hip Surgery

LMWH, oral anticoagulants, or adjusted-dose heparin is effective following hip surgery. Of these three approaches, LMWH is the most convenient because laboratory monitoring is not required. [37,46]

## Major Knee Surgery

Both LMWHs and intermittent pneumatic compression are effective in preventing venous thrombosis in patients undergoing major knee surgery. LMWH is more convenient and is the prophylactic method of choice. [49, 51, 52]

## Genitourinary Surgery, Neurosurgery, and Ocular Surgery

Intermittent pneumatic compression, with or without static graduated compression stockings, is effective and does not increase the risk of bleeding. [54, 55]

# CONCLUSION

Deep vein thrombosis followed by fatal pulmonary embolism is common in certain high-risk patient and after some high- risk surgical procedures. Because of high mortality prophylaxis against venous thrombolism has attained wide spread acceptance. These depend up on patient prophylactic or therapeutic dose of anticoagulants and general surgery.

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