
Deep Venous Thrombosis

Venous thrombosis involving the deep veins is a major US health problem that affects over 2.5 million people annually. The most serious complication of a deep venous thrombosis (DVT) is pulmonary embolism (PE), which is associated with 50,000 to 200,000 deaths each year. DVT and PE are often silent and difficult to detect by clinical examination; however, DVT rarely occurs in the absence of risk factors. This article reviews normal venous anatomy and discusses the etiology of DVT, its clinical manifestations, and diagnosis. Then it reviews treatment of DVT, highlighting the nurse's role. A discussion of DVT prophylaxis based on patient risk follows. Key words: *anticoagulation, deep venous thrombosis, DVT prophylaxis, low-dose heparin, low-molecular-weight heparin, nursing measures, unfractionated heparin, Virchow's triad, warfarin*

Anne M. Aquila, APRN
Vascular Program Coordinator
Hospital of Saint Raphael
New Haven, Connecticut

Venous thrombosis involving the deep veins is a major health problem in the United States today, affecting more than 2.5 million people each year. The most serious complication of a deep venous thrombosis (DVT) is pulmonary embolism (PE), which is associated with 50,000 to 200,000 deaths annually.¹ It is impossible to determine the true mortality rate because of difficulty in diagnosing PE with certainty in the absence of an autopsy; moreover, many patients who die of a PE have concomitant medical conditions that may have contributed to their death.

Both DVT and PE are often silent and difficult to detect by clinical examination. It is important to keep in mind that clinical examination includes attention to patient history, not just physical examination because DVT rarely occurs in the absence of risk factors. Several groups of patients at high risk for developing venous thromboembolic disease have been identified.² These include patients undergoing various types of surgery—general, orthopaedic, gynecologic-obstetric, urolo-

gic, and neurosurgical. Of these groups, orthopaedic patients appear to be especially prone to thrombosis, particularly patients with hip fracture/hip replacement and knee reconstruction. Patients with various medical diseases, usually chronic, also are at risk for thrombotic events. With many high-risk groups identified, it is reasonable then to consider ways to prevent embolic phenomena. Preventive measures are not only cost-effective, but also less risky and better tolerated by the patient than specific treatment modalities.

This article begins by reviewing normal venous anatomy. A discussion of the etiology of DVT, its clinical manifestations, and diagnosis follows. The treatment of DVT is then reviewed, highlighting the nurse's role. A discussion of DVT prophylaxis based on patient risk concludes the presentation.

VENOUS ANATOMY

The primary function of the systemic veins is to provide for the return of blood to the right side of the heart. The veins, however, do not function simply as passive conduits for the flow of blood. Instead, venous hemodynamics are complicated by the presence of low pressure within the system (as compared with the arteries),

J Cardiovasc Nurs 2001;15(4):25–44
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vein collapsibility, flow variation with respiration, the effect of gravity, and even retrograde pulse transmission from right heart contraction.³

Microscopic anatomy

In comparison to arteries, veins are thinner walled and less muscular. The layers of the veins, namely the intima, media, and adventitia, are identifiable microscopically. The innermost layer—the intima—consists of a confluent layer of endothelial cells that is in contact with the blood flowing within the lumen of the vein. These cells are metabolically active and produce prostacyclin, plasmin, and endothelium-derived relaxing factor, which are important inhibitors of intravascular coagulation.⁴ Alterations in this endothelial lining may play a role in the development of thrombus. In the larger veins, a subendothelial layer of supportive tissue can be identified within the intimal layer.

A primary difference between arteries and veins is found in the composition of the media, which is generally thicker in arteries and accounts for the artery's firm and minimally distensible properties. The adventitia is a thin layer of loose connective tissue surrounding the vein.

Macroscopic anatomy

Unlike the arteries, veins possess valves along their entire length. Each valve consists of two very thin-walled cusps that originate at opposite sides of the vein wall and oppose in the midline. Ordinarily, valves allow for the unidirectional flow of blood back to the heart. Blood is able to flow in a proximal direction through the valve between the valve cusps. Reverse flow is prevented by the apposition of the two cusps when pressure above the valve is greater than below.

The location of the venous valves is variable. Generally speaking, valves are more numerous and more closely located

in the smaller, more distal veins. Few valves are located in the femoral veins; the vena cava and common iliac veins are valveless.^{5,6}

Gross anatomy

Lower extremity veins can be conceptually separated into three separate but interconnected systems that work together to provide total outflow for the extremity: the deep venous system, the superficial venous system, and the perforating or communicating system. The deep veins of the legs lie beneath the deep fascia within the leg musculature and are well supported by surrounding tissue. They provide 90% to 95% of venous outflow from the leg. Deep veins above the knee are the iliac and femoral. Deep veins below the knee are the popliteal, peroneal, anterior tibial, and posterior tibial.

Superficial veins run in the subcutaneous tissue and are relatively poorly supported. The principal superficial veins of the lower extremity are the greater and lesser saphenous. The proximal ends of these veins empty directly into the deep venous system at the popliteal and femoral levels.

There are between four and six major communicating veins that traverse the deep fascia of the legs and form a communication between the superficial and deep venous circulation. They are located at the area just superior to the medial malleolus, the medial calf, and the medial lower thigh.^{5,6} Each of these communicating veins has venous valves that normally direct flow from the superficial veins to the deep veins and prevent reflux in the opposite direction.

Venous physiology

Venous physiology is in many respects more complex than arterial physiology. Venous compliance and normal venous hemodynamics influence physiology in the venous system.

Compliance

Veins are collapsible tubes, so transmural pressure (ie, the difference between the intraluminal forces acting to expand the vein and the external pressures acting to compress the vein) determines their shape and thus their volume. Because veins can stretch and distend, they can increase their intraluminal volume with only minimal elevation in the venous pressure. This ability to accommodate large shifts in volume with only minimal changes in venous pressure is known as compliance.⁵

Normal venous hemodynamics

Venous hemodynamics differs greatly from the hemodynamics of the arterial circulation. In the arterial circulation dynamic pressure exerted by the contraction of the left ventricle is the dominant force providing a mean arterial pressure between 90 and 100 mm Hg. On the venous side, dynamic forces have been greatly dis-

sipated by the passage of blood through the high-resistance arteriolar capillary bed at the level of the right atrium. With standing, hydrostatic pressure (ie, the pressure created by the weight of the column of blood) greatly exceeds the dynamic pressure and acts to impede venous return. The driving force to overcome gravity when one is in the standing position is provided by the musculovenous pump or "calf muscle pump" (Fig 1).

When leg muscles contract, they raise pressure in and around all the structures within the deep fascia. As this pressure within the deep veins rises above that in the superficial veins, blood moves into the larger veins in the deep system and toward the heart; the valves in the perforating system close, preventing blood reflux into the superficial system. With muscle relaxation, pressure within the deep venous system falls below that in the superficial system and blood passes from the superficial to the deep system via the perfora-

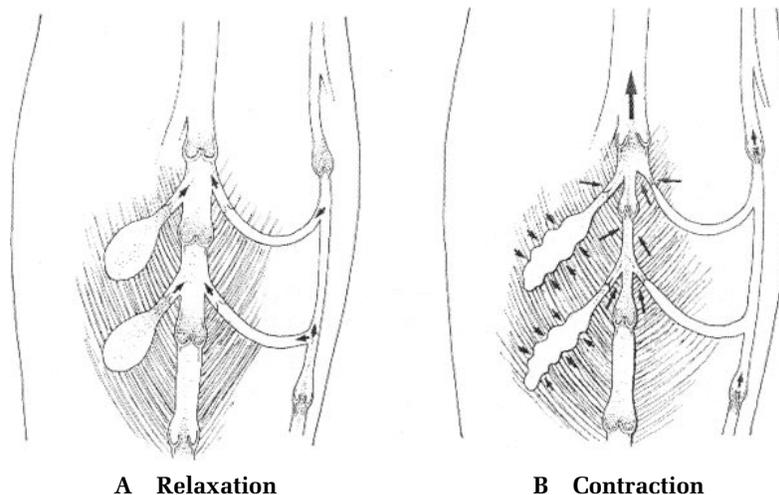


Fig 1. (A) Veins within the calf muscle pump during relaxation. Note the filling of the deep veins from the perforating veins and lower leg with proper deep venous valve closure in the standing position. (B) Veins within the calf muscle pump during muscle contraction with ejection of blood toward the heart. Note the proper closure of the valves of the communicating veins in a nondiseased venous system. *Source:* Reprinted with permission from Hahn TL, Dalsing MC, Chronic venous disease, in *Vascular Nursing*, 3rd ed. V Fahey, ed., p. 366, © 1999, WB Saunders Company.

tors. Pressures in excess of 200 mm Hg can be generated when the calf muscles contract, which is more than enough to provide energy for venous return. With the recumbent position, the pressure exerted by gravity is eliminated and venous flow becomes relatively phasic in nature; it is to a great extent driven by changes in abdominal and thoracic pressure induced by respiration.^{5,6}

ETIOLOGY OF DVT

Understanding of the pathophysiology of DVT and PE dates back to 1856 when Rudolph Virchow, a German pathologist, first recognized the association between the two entities. Virchow's triad of (1) venous stasis, (2) vessel wall injury, and (3) hypercoagulability—more appropriately called the prothrombotic state—is generally accepted as including the main precipitating factors in the generation of venous thrombi⁷ (see the box titled, "Risk Factors Associated with Deep Venous Thrombosis").

Venous stasis

Blood flow is normally reduced around venous valves.^{1,6} Immobility, which results when one is subjected to a period of bed rest, serves to further alter blood flow by influencing the functioning of the musculovenous pump. With prolonged bed rest, there is loss of the regular repetitive muscular contraction in the legs, which impairs the peristaltic propulsion of venous blood flow. This alteration promotes venous stasis. While some controversy about the role of stasis in the development of DVT exists, in the surgical patient venous stasis is perhaps the most treatable of the causative factors.¹ Stasis may develop when surgical procedures exceed 30 minutes in duration or when general anesthesia causes venodilation and venous stasis. Other condi-

Risk Factors Associated with Deep Venous Thrombosis

- I. Venous stasis
 - Heart disease
 - Congestive heart failure
 - Myocardial infarction
 - Cardiomyopathy
 - Constrictive pericarditis
 - Dehydration
 - Immobility (bed rest >72 hours, long travel)
 - Paralysis
 - Incompetent venous valves
 - Obesity (>20% ideal body weight)
 - Pregnancy
 - Surgery lasting more than 45 minutes
 - Age >40 years
- II. Vessel wall injury
 - Trauma
 - Fracture
 - Extensive burns
 - Infection
 - Venipuncture
 - Intravenous infusion of irritant solutions
 - Previous history of deep venous thrombosis
 - History of previous major surgery
- III. Hypercoagulability
 - Alterations in hemostatic mechanisms
 - Protein C resistance or deficiency
 - Antithrombin III deficiency or resistance
 - Protein S deficiency
 - Factor V R506Q (Leiden) mutation
 - Polycythemia vera
 - Anemias
 - Trauma/surgery
 - Malignancy
 - Oral contraceptive use
 - Systemic infection

tions that promote venous stasis include heart disease (congestive heart failure, myocardial infarction, cardiomyopathy), obesity, dehydration, pregnancy, malignancy and a debilitated state, and stroke.⁸

Vessel wall injury

It has been suggested that venodilation that occurs under general anesthesia can disrupt the endothelial or innermost lining of the vein, exposing the thrombogenic subendothelial surface.¹ Thus, a vessel that should normally not allow clot to form may become obstructed by platelets and fibrin that accumulate at the site of injury. The box titled, "Risk Factors Associated with Deep Venous Thrombosis" lists other factors that may promote vessel wall injury.

Hypercoagulability (prothrombotic state)

Hypercoagulability exists when coagulation overrides fibrinolysis. The coagulation cascade mediates intravenous thrombus formation by two basic pathways: the intrinsic system and the extrinsic system. Both systems lead to thrombin formation and the development of a fibrin clot. The fibrinolytic system is associated with the coagulation cascade and acts to prevent clot propagation and allows for clot dissolution as healing takes place.

Although preoperative coagulation tests cannot identify patients who will develop DVT, there are several inherited disorders that clearly predispose patients to its development. The most important inhibitor of activated factor X is antithrombin III. A deficiency in it as well as other factors (see the box titled "Risk Factors Associated with Deep Venous Thrombosis") may render an individual more likely to clot. Other unexplained prothrombotic states are associated with trauma, major surgical procedures in proportion to the length of operation, obesity, advanced age, and sepsis.¹ In addition to an increase in coagulability of the blood after trauma or operation, systemic plasma fibrinolytic activity is reduced for as long as 10 days. This is known to be a significant factor in the development of DVT.¹

The association of DVT and malignancy has been clarified recently with the de-

monstration that some tumors release tissue factor into the circulation. Tissue factor appears to be derived from not only neoplastic cells but also regional infiltration of activated macrophages around the tumors.^{1,9} This thrombogenic effect of malignant cells is of more concern in patients receiving chemotherapy, another factor associated with an increased incidence of thromboembolic disease.

PATHOPHYSIOLOGY OF DVT

Most venous thrombi originate behind valve pockets¹⁰ (Fig 2) as the vein wall is slightly dilated behind each of the venous valve leaflets. While this dilated area allows for prompt valve closure, flow is slower or stagnant in these small areas. It is not known whether previous damage to the endothelium of the vein is necessary

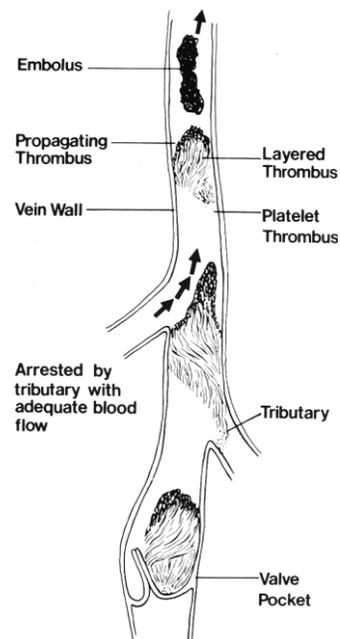


Fig 2. Development of deep vein thrombosis and pulmonary embolism. *Source:* Reprinted from VA Fahey, Life-threatening pulmonary embolism, *Critical Care Nursing Quarterly*, Vol. 8, No. 2, p. 82, © 1985, Aspen Publishers, Inc.

for thrombus formation, however, stagnant hypoxemia is capable of causing endothelial injury and stasis retains all the procoagulant factors locally, leading to successive regional activation of the coagulation cascade and further platelet and fibrin deposition.^{1,11}

Once a thrombus forms, it enlarges and may extend proximally and distally, thereby occluding the vessel lumen. Various scenarios may occur. If the thrombus fails to obstruct the entire lumen, it is enveloped by endothelium (recanalization) and the coagulation or thrombogenic process ceases.¹² Even though clot formation was interrupted and the vessel reopened, the venous valves may still be destroyed by the inflammatory reaction that accompanies the original thrombotic process. This individual may go on to develop a chronic venous disorder such as post-phlebotic syndrome. In fact, 29% to 79% of patients with DVT will develop this problem.¹³ The thrombus also may develop a floating "tail" that is highly susceptible to becoming dislodged and traveling proximally into the pulmonary arterial circulation, resulting in a PE. It is now generally accepted that 90% of all clinically significant PEs can be traced to a lower extremity DVT.^{8,14}

CLINICAL MANIFESTATIONS

DVT generally occurs in the lower extremity (Fig 3), but also may occur in the upper extremities, although with a lower frequency. Upper-extremity DVT is usually associated with an identifiable predisposing condition such as a cervical rib or muscular band that causes venous compression or following deep venous instrumentation.¹⁵ The more frequent use of central venous catheters for prolonged venous access, hyperalimentation, and dialysis access and hemodynamic monitoring has led to an increase in catheter-related central venous thrombosis.^{15,16}

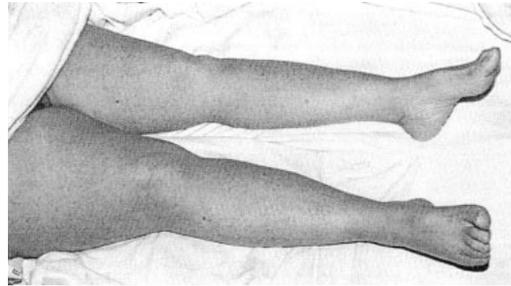


Fig 3. Classic symptom of deep vein thrombosis. Note the unilateral right leg swelling, especially at thigh and calf. *Source:* Reprinted with permission from Walsh ME, Rice KL, Venous thrombosis and pulmonary embolism, in *Vascular Nursing*, 3rd ed., V Fahey, ed., p. 347, © 1999, WB Saunders Company.

The physical findings in DVT are determined by location of the venous obstruction, the size of the thrombus, whether the vein lumen is partially or totally obstructed, and the adequacy of the collateral circulation. Thus, physical findings may be absent if the vein lumen is partially obstructed or if collateral channels allow for flow around an obstruction.

The patient may exhibit unilateral edema, which results from congestion of venous, lymphatic, and capillary beds distal to the thrombotic occlusion. An increase in the diameter of one calf, ankle, or thigh in relation to the other or pitting edema in only one leg also may be observed. Homan's sign, which is defined as pain in the calf on forced dorsiflexion of the foot, is not a sensitive or specific test for DVT.¹⁷ A more accurate finding is pain that occurs when palpating the calf or along a vein.¹⁸ Less common manifestations include prominent superficial veins and a palpable cord. When a palpable cord is found it helps to differentiate a superficial phlebitis from a DVT by virtue of its subcutaneous location. The inflammatory response of the superficial venous system also may cause

the affected extremity to be erythematous and warm to the touch.

Obstruction of the large veins (eg, the iliofemoral veins) may take on the form of phlegmasia alba dolens (white leg) or phlegmasia cerulea dolens (blue leg). Phlegmasia alba dolens is the term used to describe the white or milky leg caused by iliofemoral vein thrombosis with associated arterial spasm. It is usually observed in postpartum women. In this patient pulses may be weak or absent, and the leg is cold. Swelling occurs in later stages. Phlegmasia cerulea dolens is commonly seen in advanced stages of some cancers. Here there is almost total occlusion of venous outflow, with increased pressure contributing to arterial inflow obstruction. It can lead to gangrene if left untreated. Patients typically experience a sudden onset of pain, massive edema, and cyanosis of the extremity. The patient may be hypotensive due to interstitial fluid extravasation and hemoconcentration may occur, which further influences thrombosis.¹⁹

Approximately 50% of patients with a DVT will be asymptomatic. Thus a suspected diagnosis needs to be confirmed by objective means.

DIAGNOSTIC EVALUATION

Venography

While clinical evaluation of the patient with DVT is important, it is unreliable. Historically, venography was considered the "gold standard" for providing an accurate diagnosis of DVT. The test consists of the injection of contrast medium into a vein in the foot. A tourniquet on the lower leg promotes filling of the deep venous system. Typically a positive study results when the contrast media fail to fill the deep system, with passage of contrast medium into the superficial system or demonstration of discrete filling defects. Disadvantages of the

test include patient discomfort from the injection, expense, and potential reaction to the contrast medium.¹

Duplex study

The term *duplex study* refers to the determination of venous flow by a combination of Doppler analysis and B-mode (brightness mode) ultrasound. Color-enhanced Doppler imaging has added to the speed and accuracy of the measurements. Advantages of the test include its ability to be performed at the bedside, its noninvasive and nonthrombogenic nature, and its sensitivity and specificity, which are comparable to those of venography. It is the most appropriate initial screening test for clinically suspected DVT; if negative, it will safely exclude the diagnosis of DVT in the area studied.^{1,20}

The Doppler probe can be used alone at the bedside to detect DVT with a high degree of accuracy if the examiner is skilled and experienced. Doppler tracks sound waves created by blood moving through the vessel. It can detect the lack of flow, the effect of compression on venous flow, and changes in flow velocity. A negative Doppler study is reassuring, but a positive or equivocal test should be confirmed by adding B-mode ultrasound or by contrast venography. The test is less sensitive to calf vein thrombi but can be used in patients who are wearing a plaster cast. B-mode ultrasonography allows visualization of venous valvular movement, accelerated blood flow in the presence of thrombus, and even imaging of the thrombus itself, depending on its age. Fresh thrombi are not echogenic but can be identified when pressure of the probe fails to compress the walls of the vein, as would normally be expected. The size of the vein also can be demonstrated, and an affected vessel can be compared with a normal vessel in the same individual.

TREATMENT OF DVT

In a patient with DVT, the goals of therapy are to (1) minimize the risk of pulmonary embolism, (2) limit further thrombosis, and (3) facilitate the resolution of existing thrombi and avoid the post-phlebotic syndrome. Traditionally, bed rest was recommended for about 5 days following the acute event. This time period allowed the thrombus to stabilize and adhere to the vein wall, thus decreasing the risk of embolization. Progressive ambulation then was started. Today there is variability among practitioners as to the amount of prescribed bed rest. This variability is due in part to the shift in treatment of DVT to the outpatient setting using low-molecular-weight heparin (LMWH).

Leg elevation is recommended when the patient is lying down. The affected extremity should be elevated at least 10° to 20° above the level of the heart to promote venous return and decrease venous congestion.²¹ After the acute event resolves, graduated compression stockings should be used to promote venous return and decrease residual swelling, thereby reducing the risk of post-phlebotic syndrome. For proper fit, the nurse should measure the largest calf and ankle circumference and the length from the bottom of the heel to the bend of the knee. Stockings are designed so that the greatest pressure is exerted at the ankle, with pressure decreasing proximally. Compression stockings are discussed further under nonpharmacologic (mechanical) prophylaxis for DVT.

Mild analgesics such as acetaminophen may be ordered to decrease pain associated with venous distention. Local moist heat also may be applied to the affected extremity at prescribed intervals to decrease pain and inflammation. Leg elevation also may serve to relieve pain and discomfort.

Anticoagulation remains the first-line treatment for patients with distal and proximal DVT. Therapy should start with an agent that has immediate anticoagulant effect, and it should be given at an adequate dosage. Failure to reach the prescribed intensity of anticoagulation in the first 24 hours of treatment increases the risk of recurrent venous thromboembolism 15 times.²²

Anticoagulation therapy: A historical perspective

Heparin has been the standard initial therapy for DVT since the 1940s. For many years, evidence of the efficacy of heparin in patients with DVT was based on experimental studies in animals and uncontrolled clinical experience. Not until 1992 did a randomized, double-blind trial²³ demonstrate that patients with DVT do require initial treatment with full-dose heparin.

Historically, admission to the hospital was deemed necessary for patients with DVT, so treatment with dose-adjusted standard (unfractionated) heparin (UH) could commence. In the 1980s these patients were typically hospitalized for 7 to 14 days before being discharged on oral anticoagulant therapy.²⁴ In the 1990s, it was determined that the duration of heparin therapy could be safely shortened to 5 days if oral anticoagulant therapy commenced at the same time as heparin therapy.^{25,26} The advent of LMWH preparations made it possible to commence heparin therapy in an outpatient setting. The use of LMWHs can serve to eliminate or drastically reduce hospital length of stay for individuals with DVT.^{27,28}

Comparing UH and LMWH

Heparin is a glycosaminoglycan extracted from a variety of animal tissues such as porcine intestine mucosa and bovine lung

tissue. Heparin acts as an anticoagulant by binding to plasma antithrombin III, the body's naturally occurring anticoagulant. This interaction brings about a conformational change in antithrombin III that greatly increases its ability to inactivate coagulation enzymes, including thrombin and factor Xa.²⁹ Preparations of UH consist of a heterogeneous mixture of polysaccharide chains ranging in molecular weight from about 3,000 to 30,000. Preparations of LMWH are derived from UH by either enzymatic or chemical depolymerization to yield fragments that are one third the size of UH, with a mean molecular weight of about 4,000 to 6,000.²⁹ The anticoagulant activity of both UH and LMWH resides in a unique pentasaccharide sequence that is randomly distributed along the heparin chains and binds with high affinity to antithrombin III.

The principal difference between UH and LMWH is in the inhibitory effect on factor Xa and thrombin. Because of differences in their chemical composition, UH has equivalent inhibitory activity against both thrombin and factor Xa, whereas LMWH preferentially inactivates factor Xa.

LMWH preparations have several advantages over UH. Unlike UH, LMWH can inactivate platelet-bound factor Xa and can resist inhibition by platelet factor 4, which is released during clotting.²⁹ LMWHs have a longer plasma half-life and a more predictable anticoagulant response to weight-adjusted doses than UH. These properties allow LMWHs to be given once or twice a day and without laboratory monitoring.²⁹

Outpatient therapy with LMWH

Prior to the initiation of therapy, baseline laboratory parameters of activated partial thromboplastin time (APTT), prothrombin time (PT) as an international normalized ratio (PT/INR), and platelet count or complete blood cell count must

be obtained. Not all patients are candidates for outpatient therapy due to preexisting conditions, age, or anticipated poor compliance; thus careful screening of patients is necessary. LMWH is dosed based on patient weight; it may be given subcutaneously every day or twice a day, depending on the LMWH preparation being used. Oral anticoagulation with warfarin (Coumadin) is begun concomitantly. The PT/INR is typically drawn on day 3 of warfarin therapy and adjusted if needed to maintain an INR of 2.0 to 3.0. The INR is monitored daily until stable and therapeutic (INR of 2.0 to 3.0 for two consecutive days). Typically therapy with LMWH is continued for 5 days and the INR is between 2.0 and 3.0. Oral anticoagulation therapy is continued for 3 to 6 months unless patient status requires a longer duration of therapy.^{27,28} Care outside the hospital increases pressure on community facilities to provide proper anticoagulant therapy. Patients may be taught self-injection of LMWH at home or require assistance to administer the medication. Additional teaching may be needed including patient understanding of what DVT is, an understanding of self-care activities such as limb monitoring and medications, and follow-up care including blood drawing and signs and symptoms to report to the health care provider.

Inpatient therapy with intravenous UH

While treatment of DVT with LMWH has proved safe and effective,^{27,28} it will take time for institutions and practitioners to transition from one treatment method to another. Thus, intravenous (IV) UH may be used. If inpatient therapy with IVUH is chosen, baseline laboratory parameters of APTT, PT/INR, and platelet count or complete blood cell count are obtained. The goal of therapy is to maintain the APTT ratio between 1.5 and 2.5 times the control.

Traditionally, the patient was given a bolus dose of 5,000 units of heparin followed by a continuous heparin infusion of 1,000 to 1,500 units/hour. Of primary importance is using adequate doses of heparin (at least a 5,000-unit bolus) followed by an intravenous infusion of 30,000 units/day. Adjusting heparin doses in response to APTT values also is important, especially in patients receiving subtherapeutic doses of heparin. Some patients may have persistently subtherapeutic APTT values despite receiving high therapeutic doses of heparin. Heparin levels may assist in the treatment of these patients.²⁹

Since appropriate dosage adjustments of intravenous heparin therapy can be problematic, studies^{30,31} have reviewed the use of dose-adjusted nomograms. They have demonstrated that by dosing heparin based on weight, a therapeutic APTT is more likely to be achieved in the first 24 hours.

When APTT is therapeutic, it is initially obtained daily. Continuous heparin infusion continues for 3 to 4 days. Oral anticoagulation with warfarin is started within the first 24 hours of heparin dosing and when the APTT is within the prescribed therapeutic range.

Heparin side effects or complications and nursing considerations

Bleeding is the major complication of anticoagulant therapy, and there is a strong relationship between the intensity of anticoagulant therapy and the risk of bleeding. Any heparin preparation has the potential to induce bleeding by inhibiting blood coagulation, impairing platelet function, and increasing capillary permeability. Based on data reviewed at the fifth American College of Chest Physicians (ACCP) conference,³² the risk of bleeding associated with IVUH in patients with acute venous thromboembolism is less than 3%. There is some evidence to suggest that this bleeding risk increases with heparin dosage and age

greater than 70 years. Thus, when administering heparin therapy, the nurse must be attuned to major bleeding such as intracranial or retroperitoneal as well as minor bleeding that might take the form of easy bruising, blood in the urine or stool, epistaxis, or hematemesis. Patients need to be aware of the bleeding risk and know the importance of reporting any bleeding noted. Serious bleeding associated with IVUH therapy may require administration of protamine sulfate, a strongly basic protein that binds and neutralizes heparin. Each milligram of protamine neutralizes approximately 100 units of heparin. Protamine may cause hypotension and should be given slowly over 10 minutes.²⁹ LMWH is not associated with increased major bleeding compared with standard heparin in acute venous thromboembolism.³²

Heparin-induced thrombocytopenia (HIT) is a well-recognized complication of heparin therapy. It is caused by antibodies, predominantly immunoglobulin G (IgG), that activate platelets, leading to thrombocytopenia. HIT may occur in an early benign, reversible nonimmune form where the platelet count recovers despite heparin therapy.²⁹

Late thrombocytopenia is IgG mediated. It is associated with a substantial risk of thrombotic complications and will usually persist unless heparin therapy is discontinued. The frequency of this form of HIT is uncertain due to its patient population definition, definition of thrombocytopenia, dose and duration of heparin therapy, and the heparin preparation used. In the previously unexposed patient, platelet count begins to fall 5 to 10 days after starting therapy, although overt thrombocytopenia may not be reached for a few more days.²⁹ Monitoring of platelets is recommended at intervals, often beginning day 3 of therapy and then every other day while the patient is receiving heparin. In the previously exposed patient, platelet count may begin to fall within 24 hours. Thrombosis attri-

butable to HIT occurs in about 1% of patients who receive intravenous therapeutic heparin for more than 5 days. Venous thrombosis is more common than arterial thrombosis. Once heparin is discontinued, platelet counts will be within the normal range for 90% of individuals within 1 week. The optimal management of HIT is uncertain. A consensus is emerging that agents that rapidly control thrombin generation (danaparoid, hirudin, and argatroban) are likely to be effective for the treatment of HIT.²⁹ The incidence of thrombocytopenia is reduced with LMWH, perhaps due to reduced binding to platelets.²⁹

Osteoporosis is usually seen only with long-term UH therapy as it is thought to cause direct resorption of bone. The reduction in osteoporosis demonstrated with LMWH is possibly due to reduced binding to osteoblasts that results in less activation of osteoclasts and an associated reduction in bone loss.²⁹

Anticoagulation with warfarin

Warfarin prevents thrombosis by inhibiting the synthesis of functionally active vitamin K–dependent clotting factors II, VII, IX, and X.³³ These vitamin K–dependent clotting factors vary considerably in their half-lives (II, 60 to 120 hours; VII, 5 to 6 hours; IX, 17 to 40 hours; X, 20 to 48 hours). Due to this variability in clearing the vitamin K–dependent clotting factors from the body, warfarin is not fully effective in inhibiting the clotting process for 3 to 4 days.

Progress has been made in the control of oral anticoagulant therapy because the importance of reporting PT results as an INR is now recognized. A recommendation of an INR of 2.0 to 3.0 is made for treatment of venous thrombosis and PE as well as for prophylaxis of venous thrombosis in high-risk surgery.³³

Dosing with warfarin is usually begun simultaneously with the initiation of

IVUH or subcutaneous LMWH. Dosing is very individualized and is based on the PT/INR. Studies have compared 5-mg and 10-mg loading doses in the initiation of warfarin therapy. A 5-mg loading dose has been shown to produce less excessive anticoagulation than a 10-mg loading dose.³⁴ As warfarin is not fully effective in inhibiting the clotting process for 3 to 4 days, overlapping with IVUH or LMWH is recommended with heparin stopped once the INR has reached 2.0 to 3.0.

Oral anticoagulation is generally continued for 3 to 6 months to prevent recurrent thrombosis in patients with proximal vein thrombosis and symptomatic calf vein thrombosis. For patients with recurrent venous thrombosis, antithrombin III deficiency, protein C deficiency, protein S deficiency, and malignant neoplasms, anticoagulation may be maintained indefinitely.

Special consideration must be given to the effects of dietary vitamin K on warfarin levels. Patients are instructed to maintain a consistent diet and avoid eating large quantities of foods high in vitamin K such as dark green leafy vegetables. Many drugs also interact with warfarin and may potentiate or inhibit its effect. A detailed list of the patient's medications should be reviewed prior to dosing warfarin.

Warfarin side effects and nursing considerations

As previously noted, bleeding is a risk of anticoagulant therapy. The major determinants of oral anticoagulant-induced bleeding are the intensity of the anticoagulant effect, patient-specific characteristics, and the duration of therapy. There is good evidence to suggest that lower-intensity oral anticoagulant therapy aiming for an INR of 2.5 (range 2.0 to 3.0) is associated with a lower risk of bleeding than therapy targeted at a higher intensity.³³

A nonhemorrhagic side effect of warfarin is skin necrosis. This uncommon

complication is usually observed on the third to eighth day of therapy. It results when thrombi form in the small vessels and adipose tissue. This tissue becomes necrotic and sloughs, promoting infection. Sites affected by this process include the breasts, thighs, buttocks, and legs.³⁵ Studies point to a correlation between protein C deficiency³⁶ and, to a lesser extent, protein S deficiency and skin necrosis. Treatment includes cessation of the drug, resumption of heparin therapy or increased dosage, and comfort measures. Surgical debridement, topical antibacterial ointments, and skin grafting may be necessary with more extensive tissue damage.³⁷ For patients who may require long-life anticoagulant therapy, warfarin may be restarted at a low dose, with heparin given concomitantly and gradually increased over several weeks. This approach should avoid an abrupt fall in protein C levels before there is a reduction in the levels of factors II, IX, and X.^{35,36}

Thrombolytic therapy

Thrombolytic agents affect the coagulation cascade by acting directly or indirectly on plasminogen, effecting its conversion to plasmin and promoting fibrinolysis. Streptokinase (SK) and tissue plasminogen activator (tPA) are the agents currently approved for clinical use in venous thromboembolic disease. The application and duration of thrombolytic therapy in the treatment of DVT and PE remain variable. In the treatment of DVT, it appears that early use of a thrombolytic such as SK can decrease subsequent pain, swelling, and loss of venous valves and may reduce the incidence of post-phlebotic syndrome.³⁸ Work is still needed as to the optimum dose and duration of thrombolytic therapy for DVT and PE. In DVT, SK is approved for 48 to 72 hours of intravenous therapy. All thrombolytic agents act systemically, thus bleeding is a risk.

Operative thrombectomy

Direct surgical removal of a thrombus from the deep veins of the leg by way of the common femoral vein has been facilitated by the use of embolectomy catheters for the extraction of clot. Surgery is usually reserved for those patients with phlegmasia cerulea dolens who are at risk of limb loss or who demonstrate extensive iliofemoral vein thrombosis and impending venous gangrene.¹

Inferior vena caval interruption

Adequate anticoagulation is usually effective in managing DVT. However, in select circumstances (see the box titled "Indications for Vena Caval Filter Placement"), vena caval interruption is performed. The most popular method of inferior vena caval interruption is placement of a filter.¹ This six-legged device can be inserted through the internal jugular vein or femoral vein and advanced into place in the inferior vena cava using fluoroscopic guidance. The long-term patency rate of the filter is 98%. Complications of filter placement include recurrent emboli, venous insufficiency, air embolism, and improper placement or migration of the device.^{1,38}

PREVENTION OF DVT

The goal of prophylaxis in patients with risk factors for DVT is to prevent both its occurrence and its consequences, mainly pulmonary emboli and post-phlebotic syndrome. Patients with DVT often have no symptoms, and therefore its detection is likely to be delayed. Of the patients who will eventually die of PE, two thirds survive less than 30 minutes after the event—not long enough for most forms of treatment to be effective.² Preventing DVT in patients at risk is clearly preferable to treating the condition after it appears, a view that is supported by cost-effectiveness analysis.²

Indications for Vena Caval Filter Placement

- Recurrent thromboembolism despite adequate anticoagulation
- Confirmed deep venous thrombosis or thromboembolism with a contraindication to anticoagulation therapy
- Complication of anticoagulation requiring discontinuation of therapy
- Recurrent pulmonary embolism with associated pulmonary hypertension and cor pulmonale
- Propagating or free-floating thrombus
- Immediately following pulmonary embolectomy
- Prophylaxis in high-risk patients
 - Propagating or free-floating thrombus
 - Occlusion of more than 50% of the pulmonary vascular bed and patient unable to tolerate additional embolism
 - Patient with extension/propagation of iliofemoral thrombus despite anticoagulation

A number of clinical risk factors for DVT have been identified. Based on these risk factors, patients can be classified as at risk for the development of calf vein or proximal vein thrombosis as well as clinical or fatal PE (Table 1). Prophylactic measures can then be instituted that are tailored to meet each patient's risk (Table 2). The primary prophylactic methods have been clinically evaluated and are directed at one or more elements of Virchow's triad. They include nonpharmacologic (mechanical) and pharmacologic modalities.

Mechanical modalities and nursing considerations

Early ambulation

Early ambulation is accepted as increasing venous flow and reducing venous stasis even though it has not been subjected to rigorous clinical trials. It is important to get patients up and moving as soon as possible, however, many patients develop thrombi during surgery and immediately postoperatively before activity and progressive ambulation can be instituted. One study³⁹ demonstrated that approxi-

mately 50% of deep vein thrombi were detected on the first postoperative day and 30% on the second, suggesting that a large percentage develop in the operating room. So while early ambulation should be encouraged in all patients, it should be relied on as the sole method for DVT prevention in only those patients under age 40 with no additional risk factors who underwent procedures less than 30 minutes in duration.²

Graduated compression stockings

Simple elastic stockings or support hose, the forerunners of the graduated compression stocking, have been shown to be entirely without value. This fact, combined with common misconceptions about the various mechanical prophylactic options, has caused confusion about the prophylactic use of all stockings. The only kind of stocking that has been shown to be effective is the graduated compression stocking, which achieves highest compression at the ankle, with gradually decreasing pressure continuing up the leg.³⁹⁻⁴¹ Compression pressure applied from the standard hospital graduated compression stocking is: ankle, 20 to 30 mm Hg; midcalf, 14 to

Table 1. Classification of level of risk

	% Calf vein thrombosis	% Proximal vein thrombosis	% Clinical PE	% Fatal PE
Low				
Uncomplicated minor surgery in patients < 40 years with no clinical risk factors	2	0.4	0.2	0.002
Moderate				
Any surgery (major or minor) in patients 40–60 years with no additional risk factors; major surgery in patients <40 years with no additional risk factors; minor surgery in patients with risk factors	10–20	2–4	1–2	0.1–0.4
High				
Major surgery in patients >60 years without additional risk factors; major surgery in patients 40–60 years with additional risk factors; patients with myocardial infarction and medical patients with risk factors	20–40	4–8	2–4	0.4–1.0
Highest				
Major surgery in patients >40 years plus prior venous thromboembolism or malignant disease or hyper-coagulable state; patients with elective major lower extremity orthopaedic surgery, hip fracture, stroke, multiple trauma, or spinal cord injury	40–80	10–20	4–10	1–5

PE, pulmonary embolus.

Source: Adapted with permission from GP Clagett, FA Anderson, W Geerts, et al, "Prevention of Venous Thromboembolism," *Chest*, Vol. 114, pp. 531S–560S, © 1998.

21 mm Hg; and midhigh, 8 to 13 mm Hg. Stockings prevent DVT by augmenting the velocity of venous return from the legs, thereby reducing venous stasis.^{2,40–42}

Typically stockings are applied before surgery and are worn until the patient is

fully ambulatory. Despite the availability of different lengths, knee-high stockings are more effective in the prevention of DVT, less expensive, and easier to apply. As Table 2 illustrates, stockings can be used alone in low-risk patients or be com-

Table 2. Patient risk category and regimens to prevent venous thromboembolism

Method	Description	Patient risk
Graduated compression stockings*	Applied before surgery and worn until fully ambulatory	Low/moderate
Intermittent pneumatic compression*	Begun immediately before surgery and continued until fully ambulatory	Low/moderate
Venous foot pump*	Applied before surgery and worn until fully ambulatory	High/orthopaedic surgery
Low-dose unfractionated heparin (LDUH)	5,000 units given subcutaneously every 8–12 hours, starting 1–2 hours before surgery	Moderate/high
Low-molecular-weight heparin (LMWH)	Various doses depending on preparation and class	Moderate/high/highest
Mini-dose warfarin	1 mg/day begun 10–14 days before surgery; goal: INR of 1.5 after surgery	Highest
Pre- and postoperative two-step warfarin	1–2.5 mg/day 5–14 days before surgery aiming for 2- to 3-second increase in prothrombin time during surgery; 2.5–5 mg/day aiming for prothrombin time ratio of 1.3–1.5 (INR 2:3) in the post-operative period	Highest
Moderate-dose warfarin	5 mg the day of or the day after surgery; adjust dose for prothrombin time ratio 1.3–1.5 (INR 2:3) by day 5	Highest

INR, international normalized ratio.

*May be combined with LDUH or LMWH in highest risk patients.

Source: Adapted with permission from GP Clagett, FA Anderson, W Geerts, et al, "Prevention of Venous Thromboembolism," *Chest*, Vol. 114, pp. 531S–560S, © 1998.

bined with other modalities in moderate- or high-risk patients.² Stockings need to fit properly and be applied correctly. If too tight, they may exert a tourniquet effect, thereby promoting venous stasis, the very problem trying to be prevented. A tight stocking also can cause redness and promote skin breakdown. If too loose, the stocking will not provide adequate compression.

Due to their design, compression stockings may be difficult to apply for those with

decreased strength or manual dexterity. To apply a graduated compression stocking, it is helpful to first turn it inside out as far as the heel. Then, placing thumbs inside the foot part, slip the stocking on until the heel is properly aligned.⁴² The fabric then can be gathered up and eased over the ankle and up the leg. Some stockings are equipped with devices that make application easier. Stockings should be removed at least once a day to inspect the legs and feet for redness and skin breakdown. Stockings are avail-

able in several ready-made sizes, but also can be custom-made.

Intermittent (external) pneumatic compression

Intermittent (external) pneumatic compression (IPC) is a noninvasive method of preventing DVT. Two inflatable sleeves applied to the patient's lower leg replicate the pumping action of the musculovenous pump. Available devices provide single-chamber (uniform) or sequential (segmental) compression and consist of the sleeves that are connected via air tubes to a pump (compression unit). With single-chamber compression, a uniform pressure in alternating equal cycles is applied to the limb. Sequential compression provides a wave-like or milking action as the graded pressure changes sequentially cephalad along the leg. The pattern of intermittent compression reduces venous pooling and increases the velocity of venous flow, thereby decreasing stasis. IPC also increases blood fibrinolytic activity as its gentle squeeze stimulates the release of tissue plasminogen activator from the endothelial layer of the vein wall.^{2,8,39,41,43} IPC is well suited for patients who cannot tolerate anticoagulant therapy because of bleeding risk. These include neurosurgical patients and those undergoing urologic and prostate surgery. IPC also may be combined with pharmacologic modalities in the very-high-risk patient (Table 2) and also may show benefit when combined with LMWH or low-dose UH (LDUH) in other patient groups.² The devices should not be used in individuals with evidence of lower extremity ischemia related to peripheral artery disease or those with an acute DVT. Sleeves should be applied correctly, and their application should be checked periodically. One study⁴⁴ described proper application of IPC devices in only 78% of patients in an intensive care unit and in 48% of patients on routine

nursing units. Proper positioning of the sleeves should be assessed, and the sleeves should be removed at specified intervals daily to inspect the skin for redness or breakdown.

Venous foot pump

Venous foot pumps were developed to mimic the natural effects of walking and weight-bearing on the circulation in the feet and legs and provide an alternative to the traditional thigh or calf compression device.⁴⁵ The foot device consists of inflation pads and rigid sole feet covers that wrap around the arch of the foot and connect via hoses to a compression unit or pump. When the foot pads inflate there is compression, stretching, and flattening of the entire plantar plexus located in the dorsum of the foot. The compression of the venous plantar plexus enhances venous blood flow, thereby decreasing the risk of DVT. Foot pumps have been used as a primary method of prophylaxis in orthopaedic procedures and may be combined with pharmacologic modalities as well.⁴⁶⁻⁴⁸ The foot pads should be checked for proper placement and proper inflation at predetermined intervals. The skin also should be checked for irritation. The device is contraindicated in patients with conditions where an increase of fluid to the heart may be detrimental (ie, congestive heart failure) or in the setting of an acute DVT.

Pharmacologic modalities and nursing considerations

Low-dose unfractionated heparin

LDUH is usually given in a dose of 5,000 units subcutaneously 1 to 2 hours preoperatively, and then 5,000 units every 8 to 12 hours until the patient is discharged.^{2,8} Dosing does not require anticoagulant monitoring due to its minimal effect on the APTT. Heparin dosed as discussed is effective in preventing not only

calf vein thrombosis, but also proximal vein thrombosis and major PE.² It can be used alone in moderate-risk patients or in combination with mechanical modalities for those at very high risk (Table 2). The risk of serious bleeding with LDUH prophylaxis is less than 2%.³²

Contraindications for LDUH include any previous reaction to heparin such as thrombocytopenia or urticaria, major trauma, intracranial lesions, spinal lesions, or eye surgery. It is important to note that

wound hematomas increase with LDUH as well as LMWH; this can be an important problem resulting in wound infection, dehiscence, and infection of a prosthetic device placed at the time of surgery.⁴⁹

Low-molecular-weight heparin

Like LDUH, the LMWH agents are generally given subcutaneously before surgery and then once or twice daily until the patient is discharged. Dosing regimens for

Nursing Measures To Prevent Deep Venous Thrombosis

- Identify risk factors present in the patient that predispose him or her to deep venous thrombosis; reevaluate patient status frequently.
- Implement ordered prophylactic regimen.
 - Nonpharmacologic (mechanical)
 - a. Graduated compression stockings
 - b. Intermittent (external) pneumatic compression
 - c. Venous foot pump
 - Pharmacologic
 - a. Subcutaneous low-dose unfractionated heparin
 - b. Subcutaneous low-molecular-weight heparin
 - c. Oral anticoagulants
- Document patient tolerance to ordered prophylactic regimen(s).
- Assess all extremities on a regular basis.
 - Pain/tenderness
 - Unilateral edema
 - Erythema
 - Warmth
- Encourage early ambulation and the performance of active leg exercises every hour while patient is awake.
- Perform passive range of motion exercises every shift if patient is immobile.
- Monitor for low-grade fever to detect thrombophlebitis.
- Encourage fluid intake to avoid dehydration; maintain accurate intake and output.
- Use stool softeners to avoid straining, which increases venous pressure.
- Avoid use of knee gatch.
- Patient education
 - What deep venous thrombosis is and why it develops
 - Risk factor awareness; highlight any risk factors patient possesses such as orthopaedic surgery, older age, a long general surgery operation, malignancy
 - Signs and symptoms (if deep venous thrombosis occurred, review with the patient his or her own signs/symptoms if present)
 - Methods to prevent deep venous thrombosis
 - a. Perform regular activity such as walking, cycling, and swimming to promote venous return.
 - b. Avoid prolonged sitting/standing.
 - c. Elevate legs with prolonged sitting.
 - d. Avoid constrictive garments: garters, girdles, tight-fitting stockings.

prophylaxis are specific for each LMWH preparation and also vary with patient risk category and type of surgery or injury.² In all patients having spinal or epidural catheters for regional analgesia, LMWH should be used with caution.²

Oral anticoagulants

Warfarin may be started the day of or day after surgery at a dose of 5 mg. The dose is adjusted thereafter, aiming for an INR of 2.0 to 3.0 by day 5.^{2,49} This type of dosing is referred to as adjusted-dose perioperative warfarin. Dosing according to this method may not prevent the formation of small venous thrombi that form soon after surgery. However, it is effective for inhibiting the extension of these thrombi and may prevent clinically significant PE. Warfarin also may be dosed via a pre- and postoperative two-step method or via a mini-dose method. Parameters for the INR are followed with either dosing method. Warfarin is most commonly reserved for high-risk patients such as those undergo-

ing total knee or hip replacement. The box titled "Nursing Measures To Prevent Deep Venous Thrombosis" summarizes nursing management measures.

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PE remains the most common preventable cause of death in hospitalized patients. It is most often a complication of venous thrombosis that originates in the deep veins of the legs. Patients present with a variety of risk factors that predispose them to DVT and subsequent PE. The presence of one or more of these risk factors enables appropriate prophylactic regimens to be instituted.

The nurse plays a key role in preventing DVT by educating the patient regarding his or her prophylactic regimen as well as monitoring patient adherence and tolerance to that regimen. Being aware of patients at risk and knowledgeable regarding the signs and symptoms of DVT will allow for prompt identification, management, and education of the patient should DVT occur.

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