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Focusing on lower extremity

DVT

By MaryAnn D'Alesandro, DNP, RN, CNOR, BC

HOSPITAL-ACQUIRED deep vein thrombosis (DVT) and subsequent pulmonary embolism (PE), collectively known as venous thromboembolism (VTE), are highly preventable inpatient complications. "Prevention is key" is a time-honored saying. The key to prevention of hospital-acquired VTE is to rely on evidence-based practices, such as efficient screening, early detection and interventions, and patient education. This article focuses on the etiology, assessment, diagnosis, and prevention of lower extremity DVT, the leading cause of PE.

Scoping out the problem

According to the CDC, as many as 900,000 people (1 to 2 per 1,000)

could be affected by VTE each year in the United States.¹ An estimated 60,000 to 100,000 Americans die of VTE.² In addition:

- 10% to 30% of patients will die within 1 month of VTE diagnosis.
- Sudden death is the first sign in about 25% of people who have a PE.
- Among people who've had a DVT, 50% will have long-term complications (postthrombotic syndrome) such as extremity pain, venous dilation, edema, pigmentation, and venous ulcers.
- Over 90% of acute PEs occur due to lower extremity DVT that results in an embolism.³
- About 33% of people with VTE will have a recurrence within 10 years.

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- Approximately 5% to 8% of the U.S. population has one of several genetic risk factors, also known as inherited thrombophilias, that increase the risk of thrombosis.¹

Understanding the pathophysiology

Three categories of risk factors for VTE are often called Virchow's triad: alterations in blood flow (venous stasis), vascular endothelial injury, and hypercoagulability.⁴ (See *Risk factors associated with venous thrombosis.*)

Normal venous blood flow depends on the action of muscles in the extremities and the functional adequacy of venous valves, which allow unidirectional blood flow.⁵ *Venous stasis* occurs when the venous valves are dysfunctional or extremity muscles are inactive. Acquired risk factors for venous stasis include prolonged immobility, heart failure, and spinal cord injury resulting in paralysis.

Vascular endothelial injury may be caused by direct or indirect trauma to the veins.⁶ Direct injury

can be caused by surgery, indwelling venous catheters, multiple trauma, and burn injuries. Examples of indirect injury include diabetes and sepsis.⁶ Vascular endothelial injury stimulates platelet activation and initiates the coagulation cascade, which predisposes the patient to thrombus formation.^{5,7} (See *Understanding hemostasis.*)

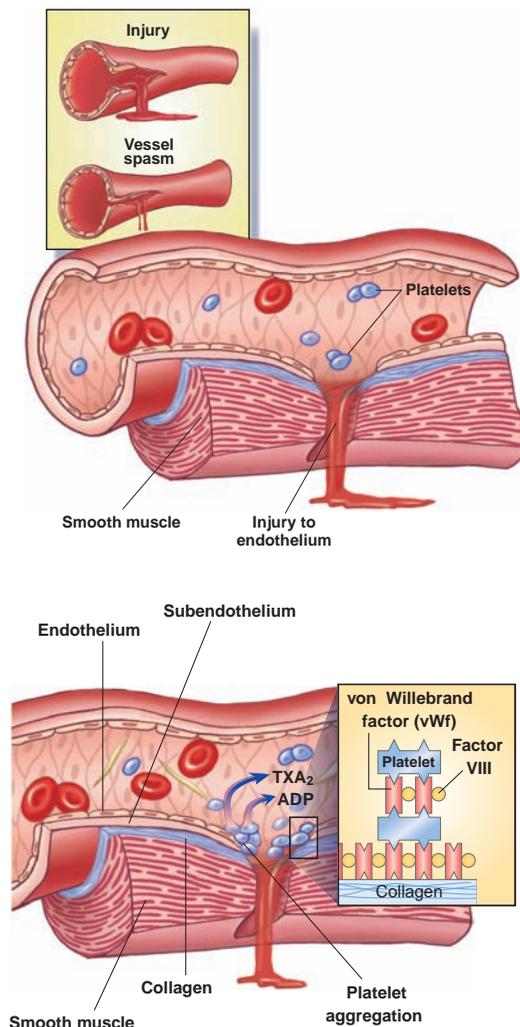
Hypercoagulability describes a predisposition to thrombus formation. Also called hypercoagulation state or thrombophilia, it can either

Understanding hemostasis

Hemostasis is the process of blood clot formation at the site of vessel injury and is divided into five stages: (1) vessel spasm, (2) formation of the platelet plug, (3) development of a blood clot as a result of the coagulation process, (4) clot retraction, and (5) clot dissolution. The process involves the interaction of substrates, enzymes, protein cofactors, and calcium ions that circulate in the blood or are released from platelets and cells in the vessel wall.

1. Vessel spasm. Injury to a blood vessel causes vascular smooth muscle in the vessel wall to contract (*inset*). This instantaneously reduces the flow of blood from the vessel rupture. Both local nervous reflexes and local humoral factors such as thromboxane A₂ (TXA₂), which is released from platelets, contribute to the vasoconstriction.

2. Formation of the platelet plug. Seconds after vessel injury, von Willebrand factor released from the endothelium binds to platelet receptors, causing adhesion of the platelets to the exposed collagen fibers (*inset*). As the platelets adhere to the collagen fibers on the damaged vessel wall, they become activated and release adenosine diphosphate (ADP) and TXA₂. The ADP and TXA₂ attract additional platelets, leading to platelet aggregation.



Source: Porth CM. *Essentials of Pathophysiology: Concepts of Altered Health States*. 3rd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2011:266-267.

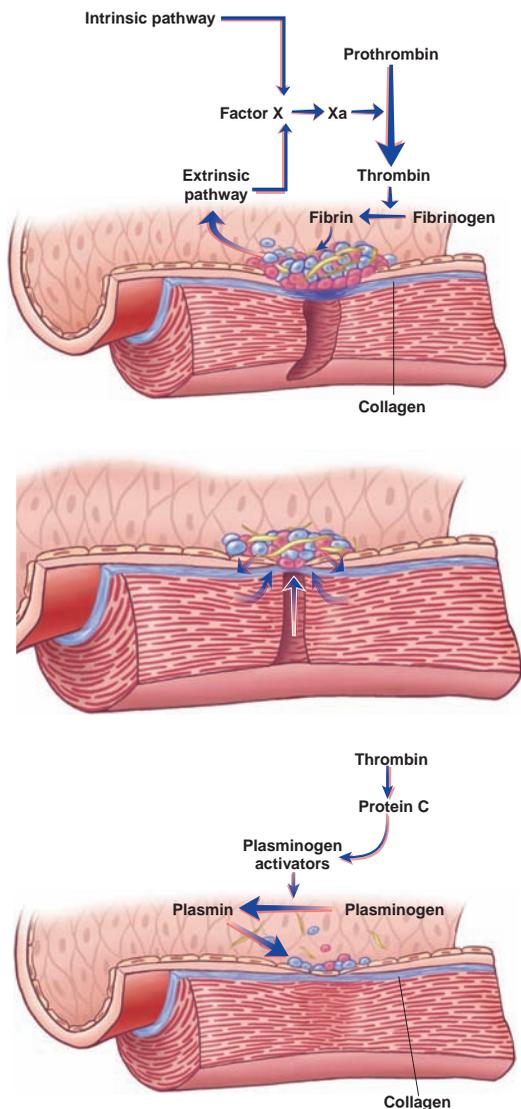
Risk factors associated with venous thrombosis*

These three categories of risk factors for VTE are known as Virchow's triad.

Venous stasis	Hypercoagulability	Vascular endothelial injury
<ul style="list-style-type: none"> • bed rest • immobility • spinal cord injury • acute myocardial infarction • heart failure • shock • venous obstruction 	<ul style="list-style-type: none"> • genetic factors • lower extremity trauma • pregnancy and childbirth • hormonal contraceptive and menopausal hormone therapy use • dehydration • malignancy • antiphospholipid syndrome • hyperhomocysteinemia 	<ul style="list-style-type: none"> • indwelling venous catheter • surgery, especially orthopedic • massive trauma • pelvic and lower extremity fractures • sepsis

*Many of these disorders involve more than one mechanism. This isn't an all-inclusive list of risk factors.

Source: Porth CM. *Essentials of Pathophysiology: Concepts of Altered Health States*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011:442.



3. Blood coagulation. Blood coagulation is a complex process involving the sequential activation of various factors in the blood. There are two coagulation pathways: (1) the intrinsic pathway begins in the circulation and is initiated by activation of circulating factor XII. (2) The extrinsic pathway is activated by a cellular lipoprotein called *tissue factor* that becomes exposed when tissues are injured. Both pathways lead to the activation of factor X, conversion of prothrombin to thrombin, and conversion of fibrinogen to the insoluble fibrin threads that hold the clot together.

4. Clot retraction. Within a few minutes after a clot is formed, the actin and myosin in the platelets that are trapped in the clot begin to contract in a manner similar to that in muscles. As a result, the fibrin strands of the clot are pulled toward the platelets, thereby squeezing serum (plasma without fibrinogen) from the clot and causing it to shrink.

5. Clot dissolution or lysis. Clot dissolution begins shortly after a clot is formed. It begins with activation of plasminogen, an inactive precursor of the proteolytic enzyme plasmin. When a clot is formed, large amounts of plasminogen are trapped in the clot. The slow release of a very powerful activator called tissue plasminogen activator from injured tissues and vascular endothelium converts plasminogen to plasmin, which breaks down the fibrin strands, causing the clot to dissolve.

be inherited or acquired. Its many possible causes include malignancy, pregnancy, and menopausal hormone therapy.⁶

A frequent site of pathologic thrombus formation is the valve cusps of veins where venous stasis occurs. As the thrombus enlarges, blood cells and fibrin collect behind it. This produces a larger thrombus with a “tail” that may eventually totally or partially occlude the vein lumen.⁵ Although upper extremity DVT can occur, lower extremity (LE) DVT is much more common. The two types of LE DVT are distal or calf thrombosis and proximal vein thrombosis. In the first type, thrombi stay in the deep calf veins, but in the second type, thrombi are found in the popliteal, femoral, or iliac veins. An organized throm-

bus becomes a PE when it detaches, travels to, and occludes a pulmonary artery or one of its branches. A proximal vein thrombosis is more likely to lead to a PE.⁸

Nursing assessment

Nurses caring for patients at risk for DVT need to consider their health history, family history, current illness, current medications, and physical assessment data. To effectively advocate for patients and prevent DVT, nurses have a responsibility to assess the patient’s risk factors and identify and promptly report abnormal physical assessment findings. Although a patient may have an asymptomatic DVT, signs and symptoms of DVT in an affected LE may include:

- edema
- a palpable cord indicating a thrombosed vein
- dilated superficial veins
- a sense of fullness in the thigh or calf
- tenderness or pain
- warmth
- erythema.³

One of the most commonly used screening tools for LE DVT is the Wells score.³ (See *Using the Wells prediction rule for DVT*.) This tool quantifies the likelihood of DVT based on the patient’s health history and clinical findings.

Diagnostic testing

One or more of the following studies are indicated for a patient with suspected DVT:³

- **D-dimer assay.** D-dimer is the degradation product of cross-linked fibrin and reflects coagulation system activation. D-dimers are detectable at levels greater than 500 ng/mL in nearly all patients with VTE (normal, <500 ng/mL).³ However, it’s important to note that disorders other than VTE are associated with increased plasma levels of fibrin D-dimer, including sepsis, malignancy, and normal pregnancy.⁹ As a result, although a negative D-dimer test can help to rule out VTE, a positive D-dimer test doesn’t increase the certainty of a VTE diagnosis.⁸

- **Contrast venography.** Venography involves cannulation of the pedal vein in the affected extremity, injection of I.V. contrast media, and serial radiographs of the LE. Although considered the gold standard in diagnosing LE DVT,¹⁰ this imaging study isn’t recommended for initial DVT screening due to associated patient discomfort and contraindications, as well as technical problems.³ In addition, noninvasive studies with nearly equivalent diagnostic accuracy for DVT such as compression ultrasonography,

Using the Wells prediction rule for DVT²³

The key to initiating appropriate preventive therapy is to adopt a robust assessment of at-risk patients before or on admission to the hospital, including elective and emergency admissions, or in the outpatient setting.¹⁰ Appropriate thromboprophylaxis would then be initiated by following one of the evidence-based, nationally recognized risk assessment guidelines, including guidance from National Institute for Health and Care Excellence.¹⁰ The Wells prediction rule for DVT is a commonly used screening tool that quantifies the likelihood of DVT based on the patient’s health history and clinical findings.³ A score of 3 or higher indicates a high probability of DVT; 1 or 2, a moderate probability; and 0 or lower, a low probability. In patients with signs or symptoms in both legs, the more symptomatic leg is used. Depending on the patient’s Wells score, investigation should proceed to either the D-dimer test and/or ultrasonography.^{3,24}

Clinical findings	Score
Active cancer or cancer treated within 6 months	1
Paralysis, paresis, or recent orthopedic casting of the lower extremities	1
Recently bedridden for more than 3 days, or major surgery within past 4 weeks	1
Localized tenderness in the deep vein system	1
Edema of the entire leg	1
Calf edema 3 cm greater than the other leg (measured 10 cm below the tibial tuberosity)	1
Pitting edema greater in the symptomatic leg	1
Collateral nonvaricose superficial veins	1
Alternative diagnosis more likely than DVT (Baker cyst, cellulitis, muscle damage, superficial venous thrombosis, postphlebotic syndrome, inguinal lymphadenopathy, external venous compression)	-2

Source: Wells PS, Anderson DR, Bormanis J, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *Lancet*. 1997;350(9094):1795-1798. With permission.

have greatly decreased the need for venography.³

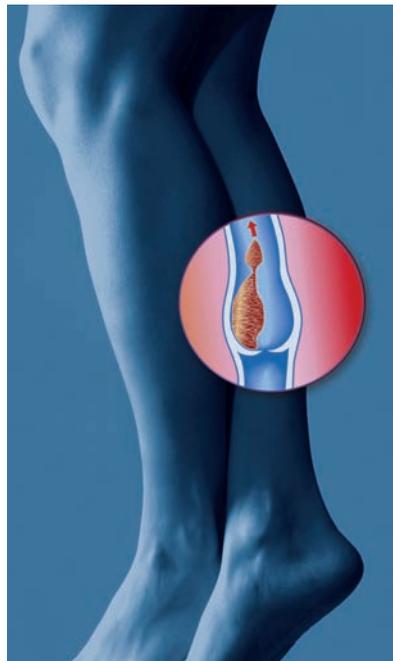
- **Ultrasonography.** This is currently considered the first-line noninvasive imaging study for DVT.¹¹ Research has demonstrated that lack of compressibility of a vein with the ultrasound probe is highly sensitive (>95%) and specific (>95%) for proximal vein thrombosis.³ Doppler color-flow imaging can demonstrate absent or abnormal blood flow in an area where a thrombus might not be visible.

Treating DVT: Initial anticoagulation

Initial anticoagulation refers to systemic anticoagulation administered for the first 5 to 10 days following a diagnosis of DVT. In most patients, anticoagulation should be started immediately because a delay in therapy may increase the risk of potentially life-threatening embolization.¹² Unless there's a contraindication, the mainstay of therapy for DVT is anticoagulation. Patients with DVT will also need anticoagulation to prevent DVT recurrences, embolism, and thrombosis-related death.¹²

Unlike fibrinolytic agents, anticoagulants don't lyse pathologic thrombi, but they can help prevent extension of already existing thrombi and prevent new thrombus formation. Different types of anticoagulants work at different levels of the normal coagulation cascade.

- **Heparins.** These include unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) products. They produce their anticoagulation effects by binding to antithrombin (AT, formerly called AT III, also known as heparin cofactor I) rather than by binding directly to coagulation factors. Binding of heparin to AT converts AT from a slow to a rapid inactivator of coagulation factors (for example, thrombin [factor IIa], factor Xa).¹³ Neither UFH or LMWH crosses the placenta; however, it's important to note that



Among people who've had a DVT, 50% will experience long-term complications.

multiple-dose vials may contain benzyl alcohol, which does cross the placenta and may cause fetal harm. As a result, pregnant women should be given preservative-free preparations.¹³

UFH, which has a rapid onset of action and renal clearance, can be administered subcutaneously or I.V. to treat DVT. Activated partial thromboplastin time (aPTT) results are used to monitor heparin therapy because of its narrow therapeutic window and highly variable dose-response relationship. If bleeding occurs during therapy, heparin's activity can be rapidly reversed by administering I.V. protamine sulfate.^{13,14}

LMWHs are administered subcutaneously, have a longer duration of action, and have a better dose-response relationship without lab monitoring, making them helpful for outpatient

use.¹³ LMWHs include enoxaparin, dalteparin, and tinzaparin. Because few studies have compared clinical outcomes with different LMWHs, the doses of the different LMWHs aren't interchangeable.¹³

- **Warfarin.** Administered orally, warfarin is a vitamin K antagonist that acts by inhibiting the synthesis of vitamin K-dependent clotting factors, which include Factors II, VII, IX, and X, and the anticoagulant proteins C and S. Warfarin has a narrow therapeutic window; therapy is monitored by the prothrombin time (PT) and international normalized ratio (INR).¹⁴ Warfarin can't be administered by itself initially for DVT because the full anticoagulant effect of warfarin doesn't occur until 2 to 3 days of drug administration. Usually heparin or fondaparinux is given along with warfarin for at least 5 days. Expect to adjust the warfarin dose until the INR is therapeutic (2 to 3, with a target of 2.5) for at least 2 days in a row, when the heparin can be stopped.

After oral administration, warfarin is rapidly absorbed in the gastrointestinal tract and its anticoagulant effects persist for 2 to 5 days after discontinuation due to its long half-life.¹⁵ Warfarin dosing is affected by illness and changes in diet, and interacts with several medications and herbal supplements. Warfarin's anticoagulant effects can be reversed with vitamin K, fresh frozen plasma, or prothrombin complex concentrates.¹⁶

- **Direct factor Xa inhibitors.** These oral anticoagulants, including rivaroxaban, apixaban, and edoxaban, prevent factor Xa from cleaving prothrombin to thrombin and bind directly to factor Xa, unlike heparin, which enhances antithrombin III activity. Oral direct factor Xa inhibitors are generally administered at fixed doses without lab monitoring. There's no specific antidote for direct factor Xa inhibitors. Risks of these

agents include bleeding and thrombosis upon discontinuation.¹⁷

• **Direct thrombin inhibitors.**

These drugs include both parenteral and oral agents. Parenteral direct thrombin inhibitors include bivalirudin, argatroban, and desirudin. Dabigatran is the only oral direct thrombin inhibitor available for clinical use. Direct thrombin inhibitors exert their anticoagulation effects by inactivating circulating and thrombus-bound thrombin (factor IIa). Oral direct thrombin inhibitors are generally administered at fixed doses without lab monitoring.¹⁷ Idarucizumab is a humanized monoclonal antibody fragment indicated when reversal of the anticoagulant effects of dabigatran is needed for emergency surgery or urgent procedures or in life-threatening or uncontrolled bleeding.¹⁸

• **Fondaparinux.** This indirect factor Xa inhibitor is administered by subcutaneous injection. It acts indirectly on factor Xa by binding to AT, inducing a conformational change in AT that increases the ability of AT to inactivate factor Xa.¹⁹ Lab monitoring isn't recommended in routine clinical practice, but the drug's anticoagulant activity can be measured using antifactor Xa activity assays if necessary.

Key preventive interventions

To prevent DVT in hospitalized medical patients without risk factors for VTE or who are at high risk for bleeding or in whom anticoagulation is contraindicated, recommendations include early ambulation with or without mechanical methods of thromboprophylaxis with intermittent pneumatic compression (IPC) devices and/or graduated compression stockings (GCS).²⁰

For most patients hospitalized with an acute medical illness who have at least one risk factor for VTE and don't have an increased risk of

bleeding, pharmacologic thromboprophylaxis is recommended, usually LMWH. For most patients hospitalized with an acute medical illness with multiple risk factors for VTE, many experts administer more aggressive prophylaxis with pharmacologic and mechanical thromboprophylaxis.²⁰

Nursing considerations

Patient and family education and engagement in prevention and the treatment plan are important nursing interventions. Patient and family education should include risk factors for thrombus formation, the importance of maintaining adequate hydration, and signs and symptoms of DVT and PE. Follow these steps:

- Identify the patient at high risk for VTE by assessing the patient's health history, family history, and medication record for risk factors.
- Encourage early and aggressive ambulation and active and passive leg exercises to prevent venous stasis.
- Use GCS and IPC devices as prescribed.
- Teach the patient to avoid sitting and lying in bed for prolonged periods, crossing legs, and dangling or placing legs in a dependent position.
- Assess the patient for signs and symptoms of DVT, including unexplained unilateral LE edema.
- Assess the patient for signs and symptoms of PE, including unexplained tachycardia, hypoxemia, and respiratory distress.
- Administer anticoagulation as prescribed.
- Monitor for complications of anticoagulation therapy, especially overt and occult bleeding such as bleeding gums, epistaxis, ecchymoses, hematuria, and melena.
- Monitor lab results such as aPTT and PT/INR as indicated based on the anticoagulant prescribed.

- Monitor hemoglobin and hematocrit values and platelet counts for signs of bleeding or heparin-induced thrombocytopenia.

Prevention strategies

Developing a prevention program will reduce the incidence of VTE in hospitalized patients. Key elements of an optimal VTE-prevention strategy include:

- mandatory VTE risk assessments
- identification of VTE risk factors and contraindications to prophylaxis
- prescription of risk-appropriate VTE prophylaxis
- reassessment of patient risk factors during hospitalization
- collection of patient and provider data to monitor performance
- monitoring of adverse outcomes (for example, hospital-acquired VTE and bleeding)
- regular performance measurement to promote continuous improvement.²¹

The American College of Chest Physicians Antithrombotic Guidelines, as well as those of other national and international societies, provide clear evidence of the effectiveness of prevention strategies in reducing morbidity, mortality, and hospital costs.²¹

Where do we go from here?

Next steps should include a multifaceted approach incorporating data, outcomes, current practice and challenges, and realistic yet aggressive guidelines to be included in a robust DVT prevention program. Creating a preventive program that will not only identify those at risk, but also provide clear guidelines that will be followed from admission to discharge, must be a priority. ■

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