

Venous thromboembolism: Very troubling events

Engage patients to help prevent this possibly deadly condition.

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VENOUS THROMBOEMBOLISM (VTE) is the number-one cause of preventable death in hospitalized patients. (See *VTE facts*.) A thrombus is a clot that forms in a blood vessel, most often in a deep vein, which results in deep vein thrombosis (DVT). The danger lies in the thrombus breaking loose from the vein and traveling through the right side of the heart to the lungs, resulting in a pulmonary embolism (PE). This process is different from a thrombus that forms in an artery and results in a myocardial infarction or cerebral vascular accident. (See *DVT and PE defined*.)

Beyond the immediate dangers, both DVT and PE can produce long-lasting debilitating effects. Chronic thromboembolic pulmonary hypertension, which develops in about 5% of individuals who survive a PE, is characterized by progressive dyspnea, eventually leading to right-sided heart failure. After a DVT, around one-third of patients will develop post-thrombotic syndrome with chronic lower-extremity edema, pain, and skin changes that can progress to weeping ulcerations. More than 20% of patients with proximal DVT (thrombus located in the popliteal, femoral, or iliac veins) or PE will suffer a recurrent event after discontinuing anticoagulation, and patients may experience loss of function, financial burdens from treatment, and fear of recurrence.

VTE risk factors

Virchow's triad illustrates VTE risk factors based on blood flow stasis, endothelial damage, and hypercoagulability. (See *VTE risk factors*.)

Normal venous return of blood from the extremities depends on the pumping action from the muscles and competent one-way valves in the vein. Reduced mobility can result in decreased blood return, and damaged valves can contribute to blood pooling in the distal extremities. Damage to the endothelial layer of the veins from trauma, I.V. catheters, or surgery initiates the coagulation cascade. In addition, inherited hypercoagulable disorders and other conditions—such as dehydration, inflammatory bowel disease, and cancer—can produce varying degrees of hypercoagulability.

Hospitalization is the most important risk factor for VTE. Surgery patients have long been considered at greater risk for VTEs, but recent evidence suggests that they develop equally between patients admitted for medical illness and those admitted for surgery. Overall risk factors include lung disease, prior VTE, family history of VTE, and older age.

Oncology patients are at particular risk for developing VTE because many cancers (pancreatic, lymphoma, brain, liver, leukemia, colorectal, and metastatic) produce a hypercoagulable state. Cancer is so often associated with VTE that the development of a VTE in a patient with no known risk factors may warrant screening for occult cancers. A systematic literature review by van Es and colleagues noted that cancer was found in one in 20 patients within a year of developing an unprovoked (no known risk factor) VTE, with rates seven times higher in patients age 50 years and older. In addition, many patients with cancer are less mobile and have vascular catheters, compounding their risk.

Commitment to prevention

Thromboprophylaxis for at-risk hospitalized patients can reduce VTE by 30% to 65%, has a low incidence of major bleeding complications, and is cost-effective. However, despite widely published guidelines, public reporting, and incremental payment withholding for VTE, prevention recommendations remain largely underused. Because VTE risk factors are spread across patient populations and medical specialties, no one group takes responsibility for addressing prevention; “everyone's problem” becomes “no one's problem.” Passive approaches, such as relying on staff and provider education or order sets have not proven effective.

The Agency for Healthcare Research and Quality (AHRQ) recommends “measure-vention” to boost compliance with adequate prophylaxis.



LEARNING OBJECTIVES

1. Explain how to assess patients for risk of venous thromboembolism (VTE).
2. Describe strategies to prevent VTE.
3. Discuss treatment of VTE.

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laxis and to reduce rates of hospital-acquired VTE. This approach involves active measurement of adherence to and lapses in VTE prevention recommendations, combined with concurrent interventions to correct lapses, including notification of the primary team. The principles of prevention efforts are:

- institutional support and prioritization for the initiative
- a multidisciplinary team focused on reaching VTE prophylaxis targets and reporting to key medical staff committees
- reliable data collection and performance tracking
- specific goals or aims that are ambitious, time defined, and measurable
- proven quality improvement frameworks to coordinate steps toward breakthrough improvement
- evidence-based protocols that standardize VTE risk assessment and prophylaxis
- institutional infrastructure, policies, practices, and educational programs that promote use of the protocol.

A three-bucket model based on risk level (low, moderate, high) may be an effective protocol. (See *Three-bucket model: An example*.) Protocols should be “opt-out” because nearly all hospitalized patients are at risk for developing VTE. In this model, mechanical and pharmaceutical interventions are activated for all patients, with those considered low risk or with contraindications to preventive measures “opted out.” Patients considered to be low risk in this model can ambulate independently and have no other risk factors.

Treatment recommendations

Guidelines published and regularly updated by the American College of Chest Physicians provide recommendations for the choice and duration of anticoagulant therapy to treat VTE, modified based on un-

VTE facts

Numbers—In the United States, venous thromboembolism (VTE) is estimated to affect as many as 600,000 people annually, including at least 100,000 deaths—more than AIDS, breast cancer, prostate cancer, and motor vehicle crashes combined. However, those estimates may be low; VTE may be unrecognized in cases of sudden death or a terminally ill patient who rapidly “takes a turn for the worse.”

Demographics—African Americans are at greater risk of developing VTE than Whites, while Hispanics appear to be at lower risk. Risk increases with age, and men are at greater risk than women.

Costs—The average cost to treat deep vein thrombosis is between \$7,712 and \$10,804; costs to treat pulmonary embolism are between \$9,566 and \$16,644—or a combined total of \$1.5 billion per year in the United States.

DVT and PE defined

Deep vein thrombosis (DVT)

A DVT can develop in the upper extremities, but it’s far more common in the lower extremities. The thrombus can cause varying degrees of partial occlusion to a complete blockage. Proximal DVTs developing above the popliteal trifurcation in the popliteal and femoral veins of the thigh are more dangerous and exhibit more signs and symptoms than distal DVTs forming below the popliteal trifurcation in the veins of the calf. Note that although the name is somewhat misleading, the superficial femoral vein is considered a deep vein.

Signs and symptoms

Suspect a DVT in the presence of unilateral lower-extremity pain, edema, erythema, warmth, and/or tenderness.

Diagnosis

For many years, nurses were taught to check for a Homan’s sign (pain in the calf with dorsiflexion of the foot) as a sign of DVT, but this assessment tool is no longer considered reliable. A serum D-dimer test measures substances released by the thrombus. A negative test essentially rules out a thrombus. A duplex ultrasound can detect occlusions in the deep veins and has replaced the more invasive contrast venography. Some patients develop a DVT in the absence of obvious risk factors (an “unprovoked” DVT). In those cases, thrombophilia testing should be considered; 15% to 20% of these patients will demonstrate a hypercoagulable state.

Pulmonary embolism (PE)

Roughly one-third of patients with a DVT will develop a PE, with sudden death the initial presentation for approximately one-fourth. As the embolism becomes lodged in the lungs, the alveoli distal to the thrombus are ventilated but not perfused, resulting in increased alveolar dead space and increased pulmonary vascular resistance.

Signs and symptoms

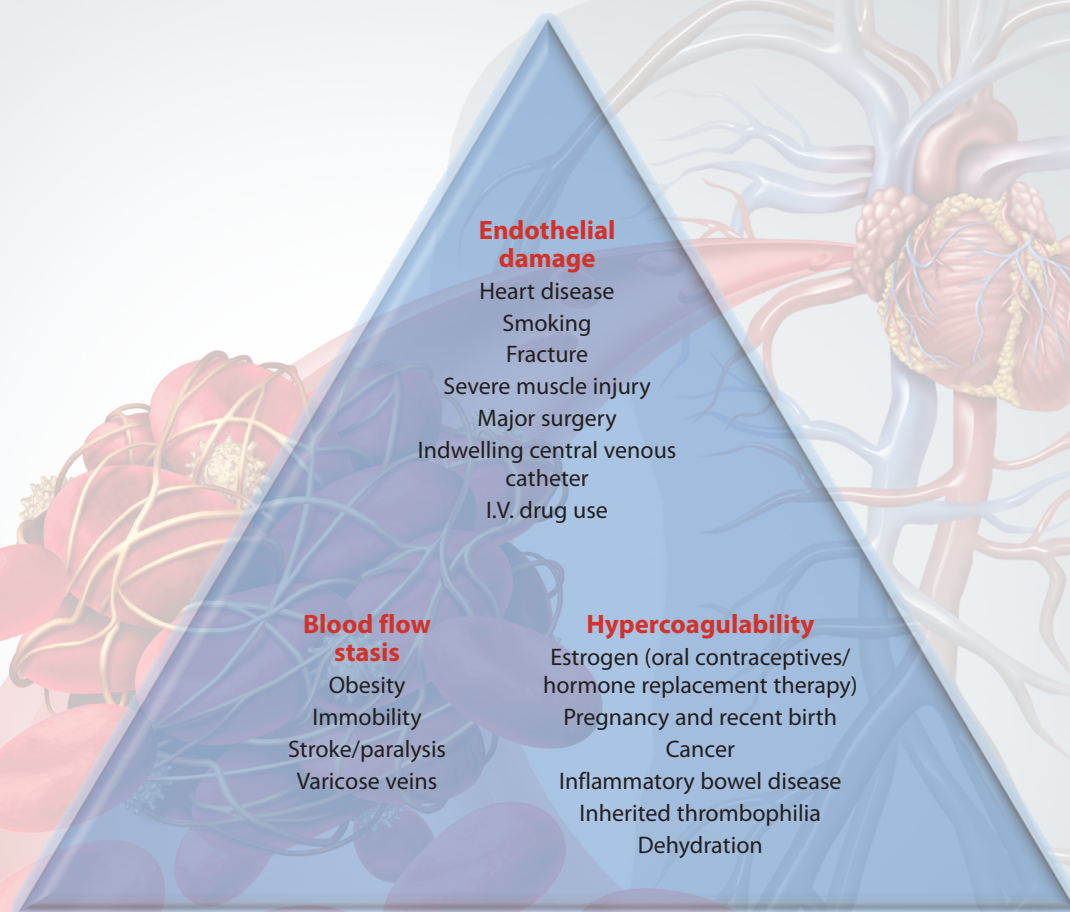
Signs and symptoms of a PE can be vague and nonspecific; they include shortness of breath, pleuritic chest pain, cough, hemoptysis or frothy sputum, tachycardia, diaphoresis, and lightheadedness. Patients may exhibit anxiety and describe a feeling of impending doom.

Diagnosis

Computerized tomography pulmonary angiography is the preferred imaging study to evaluate for a PE. When concerns exist regarding the contrast material injected for the test (for example, allergy to contrast, impaired renal or liver function), a nuclear medicine ventilation-perfusion scan can be used to identify a mismatch between ventilation and perfusion, indicative of a PE.

VTE risk factors

Virchow's triad illustrates venous thromboembolism (VTE) risk factors. Examples are listed for each category.



derlying risk factors. For patients with a PE or proximal DVT, a minimum course of 3 months of anticoagulant therapy is recommended. For patients with underlying cancer, low molecular weight heparin (LMWH) is preferable. For all other patients, direct oral anticoagulants (DOACs, also called NOACs [non-vitamin K antagonist oral anticoagulants]) are preferred over vitamin K antagonist therapy. Dabigatran and edoxaban require initial parenteral anticoagulation. After completing the initial 3 months of treatment, patients with transient risk factors, such as surgery, typically don't need additional therapy. For patients with unprovoked VTE, the provider should evaluate the risks and benefits of continued therapy. Most patients with active cancer will need to continue therapy.

Anticoagulants

Anticoagulants are indicated for the prevention and treatment of VTE. Understanding anticoagulant options will help when educating patients and monitoring for adverse effects. Keep in mind that all anticoagulants carry the risk of bleeding, so monitor for and immediately report any unusual bleeding.

Parenteral anticoagulants

Unfractionated heparin (UFH) and newer LMWHs are the parenteral agents used. UFH was the first parenteral anticoagulant; approved in 1939, it's indicated for VTE prevention and treatment. It can be administered as a subcutaneous injection or I.V. infusion. Patients receiving a continuous infusion should have their partial thromboplastin time (PTT) monitored and dosage adjust-

ed to maintain a PTT 1.5 to 2 times normal range. Most hospitals have a protocol for monitoring and adjusting heparin infusions. Protamine sulfate is the reversal agent.

The LMWH enoxaparin is indicated for DVT prevention in patients who've had abdominal surgery or hip or knee replacement. It's also indicated for patients whose mobility is severely restricted because of acute illness and for treatment of acute DVT, with or without PE. Protamine sulfate is the reversal agent. Other LMWHs approved in the United States include dalteparin and tinzaparin.

When administered subcutaneously, both UFH and LMWH are injected into the abdomen. Hold a skinfold between the thumb and index finger throughout the injection, and don't rub the site.

Oral anticoagulants

Warfarin has been the mainstay of oral anticoagulants for many years, but several new agents have been approved, including DOACs.

The vitamin K antagonist warfarin was approved in 1954. Because warfarin takes several days to become effective, it's generally not used for immediate VTE prevention. Although relatively inexpensive and effective, warfarin requires lab monitoring of the patient's international normalized ratio (INR) and frequent dose adjustments to maintain its narrow therapeutic range. Dosing is further complicated by metabolism variations based on DNA variants in two genes: CYP2C9 and VKORC1. Dosing algorithms are available based on genetic data. Warfarin can be affected by many other medications and foods. It can be reversed with vitamin K.

DOACs address some of the issues surrounding warfarin; for instance, they don't require routine monitoring and have fewer drug interactions. A downside is that they're more expensive than warfarin.

Recent studies suggest similar efficacy rates between warfarin and DOACs. Risks of bleeding appear similar, possibly favoring some of the DOACs over warfarin, even though no reversal agents are available, except for dabigatran. Extensive clinical trials have provided information on the safety and efficacy of DOACs in study populations; specifically, younger and healthier subjects. Post-marketing observational studies involving real-world, older individuals with more comorbidities have been performed primarily in patients with atrial fibrillation taking DOACs because they were approved for that indication before approval for VTE prevention and treatment.

Several DOACs have been approved for VTE prevention, including one that is a direct thrombin inhibitor (dabigatran) and four that are factor Xa inhibitors (apixaban, rivaroxaban, edoxaban, and betrixaban).

Three-bucket model: An example

This three-bucket model for venous thromboembolism (VTE) prevention is in use at the University of California San Diego. University of California Davis Medical Center has developed an algorithm (bit.ly/2yayxWK) based on this model.

Risk level	Recommended intervention
Low risk <ul style="list-style-type: none">• Observation status, expected length of stay (LOS) < 48 hours• Minor ambulatory surgery unless multiple strong risk factors• Medical patients ambulatory in hall and not moderate or high risk• Ambulatory cancer patients admitted for short chemotherapy infusion	<ul style="list-style-type: none">• No prophylaxis• Reassess periodically• Ambulate
Moderate risk <ul style="list-style-type: none">• Most general, thoracic, open gynecologic, or urologic surgery patients• Active cancer or past VTE/known thrombophilia in medical patient with LOS > 48 hours• Medical patients with decrease in usual ambulation and VTE risk factors (myocardial infarction, stroke, heart failure, pneumonia, active inflammation/infection, dehydration, age > 65 years)	<ul style="list-style-type: none">• Unfractionated heparin or low molecular weight heparin (LMWH) prophylaxis*
High risk <ul style="list-style-type: none">• Hip or knee arthroplasty• Hip fracture surgery• Multiple major trauma• Spinal cord injury or major neurosurgery• Abdominal-pelvic surgery for cancer	<ul style="list-style-type: none">• Intermittent pneumatic compression device (IPCD) and LMWH or other anticoagulant*

*For those at moderate or high VTE risk and contraindications to anticoagulation, use IPCD alone until bleeding risk subsides.

ban). Dosages must be adjusted for factors such as decreased creatinine clearance and whether the intention is treatment or prevention.

Dabigatran is indicated for VTE prevention in patients after hip replacement, treatment of VTE after 5 to 10 days of parenteral anticoagulation, and recurrent VTE reduction. Side effects include GI upset. Idarucizumab is the reversal agent.

Rivaroxaban and **apixaban** are indicated for DVT prevention in patients who've had hip or knee replacement, VTE treatment, and recurrence reduction. Patients should avoid concomitant use of rivaroxaban with drugs that are combined

P-gp and strong CYP3A4 inducers (for example, carbamazepine, phenytoin, rifampin, and St. John's wort). Menorrhagia and longer periods have been reported with rivaroxaban use. Andexanet alfa has been approved as a reversal agent for rivaroxaban and apixaban, although its supply is expected to be limited until early 2019.

Edoxaban is indicated for VTE treatment and has no reversal agent.

Betrixaban is indicated for VTE prophylaxis in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications because of moderately or severely restricted mobility

VTE prevention

Venous thromboembolism (VTE) prevention requires nurses to stay current with VTE prevention guidelines and to participate in related quality-improvement projects. Assess your patients for VTE risk factors and take these monitoring and patient education steps:

Increase mobility

- Assist patient with ambulation at least three or four times per day
- Teach patient how to perform lower-extremity range-of-motion exercises and verify completion

Avoid constrictive clothing or devices

- Ensure that any socks or stockings aren't tight around the patient's leg; remeasure for compression stockings if edema develops
- If wrapping the extremity, extend the wrap over a larger area to avoid multiple layers within a small area
- If a leg strap is used to secure urinary catheter tubing or a leg bag, make sure it's not too tight

Promote adequate hydration

- Ask patient for preferred beverage and keep it within reach at the bedside
- Encourage fluid intake throughout the day (unless contraindicated)

Provide mechanical prophylaxis as ordered

- Intermittent pneumatic compression and foot impulse devices
 - Ensure proper fit
 - Encourage consistent use
- Graduated compression stockings (14 mmHg to 15 mmHg)
 - Explain contraindications: arterial disease, significant skin issues, heart failure, unusual leg size or deformity
 - Ensure proper fit and remeasure as indicated
 - Instruct patient to remove daily for skin care and inspection

Monitor closely for any signs of VTE and report immediately

- Deep vein thrombosis—edema, pain, erythema, warmth, or tenderness in an extremity
- Pulmonary embolism—sudden onset of shortness of breath, pleuritic chest pain, cough, hemoptysis or frothy sputum, tachycardia, or lightheadedness

with assistance. You also can teach your patient how to perform lower-extremity range-of-motion exercises and the rationale for compression stockings or lower-extremity mechanical devices. Remind patients to reapply devices after walking, and consistently reinforce your efforts. In addition, ensure patients are well hydrated; dehydration can contribute to hypercoagulability.

Even with preventive measures in place, VTE can develop. Early identification and treatment with anticoagulants can minimize serious long-term consequences.

Immediately report any signs and symptoms of a VTE. DVT symptoms can be subtle, so continually monitor for edema, pain, erythema, warmth, or tenderness in an extremity. Although DVTs typically are unilateral, also evaluate for bilateral symptoms. PE symptoms may be more dramatic, but still nonspecific. Suspect a PE in any patient with a sudden onset of shortness of breath, pleuritic chest pain, cough, hemoptysis or frothy sputum, tachycardia, or lightheadedness. These symptoms can be very distressing for the patient, so reassure him or her that the condition is being addressed and provide emotional support.

Administer treatment for VTE, such as anticoagulants, as instructed, and monitor for adverse effects.

Laying a foundation

Understanding VTE risk factors, prevention measures, and treatment options gives you a foundation for effectively engaging with patients and their families. Provide them with the information they'll need to prevent VTE and to recognize signs and symptoms if they occur. ★

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and other VTE risk factors. It has no reversal agent.

Anticoagulants and discharge

At discharge, provide patients with verbal instructions and supplemental written information about all medications—generic and trade names, dosage, frequency, possible food or drug interactions, and precautions—follow-up appointments, including lab monitoring, and signs and symptoms they should report. Explain the importance of continuing treatment beyond discharge and that patients shouldn't stop anticoagulant therapy without discussing it with their provider. In addition, you can direct patients to resources

to help cover the cost of anticoagulant therapy.

Nursing implications

In addition to administering prophylaxis as ordered by the provider, you can help reduce your patient's risk of developing a VTE. (See *VTE prevention*.) Patients are more likely to engage in prevention measures if they're educated about their individual VTE risk factors, appreciate the consequences of a VTE, and understand the effectiveness of preventive measures.

Maintain and improve your patient's mobility level by helping him or her walk to the bathroom, sit in a chair for meals, and walk in the hall

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Please mark the correct answer online.**1. Risk factors for venous thromboembolism (VTE) are related to the triad of**

- a. endothelial damage, blood flow stasis, and hypocoagulability.
- b. endothelial damage, increased blood flow, and hypercoagulability.
- c. epithelial damage, blood flow stasis, and hypercoagulability.
- d. endothelial damage, blood flow stasis, and hypercoagulability.

2. Demographics related to VTE include which of the following?

- a. Most VTEs occur in patients younger than age 50.
- b. Women are at greater risk than men for VTE.
- c. African Americans are at greater risk of developing VTE than Whites.
- d. Hispanics are at greater risk of developing VTE than Whites.

3. Which statement about the risk of VTE in patients with cancer is correct?

- a. Oncology patients have a low risk of VTE.
- b. An unprovoked VTE is not a sign of cancer.
- c. Oncology patients are at particular risk of VTE.
- d. Few cancers are associated with hypercoagulability.

4. A successful organizational strategy to prevent VTE includes all of the following except:

- a. a nurse-pharmacy team focused on VTE prophylaxis targets.
- b. quality improvement frameworks to coordinate steps.
- c. institutional support and prioritization for the initiative.
- d. reliable data collection and performance tracking.

5. What is the likely VTE risk level for your 70-year-old patient who's undergoing thoracic surgery?

- a. Minimal
- b. Low
- c. Moderate
- d. High

6. Your 64-year-old patient is undergoing knee arthroplasty. What would you expect her VTE prevention to include?

- a. intermittent pneumatic compression device (IPCD) or low molecular weight heparin (LMWH) or other anticoagulant
- b. IPCD and LMWH
- c. None because the risk is low
- d. Unfractionated heparin (UFH) or LMWH

7. For patients with a proximal deep vein thrombosis (DVT) or a pulmonary embolism (PE), anticoagulation therapy should be continued for a minimum of

- a. 1 month.
- b. 3 months.
- c. 6 months.
- d. 1 year.

8. Which statement about parenteral anticoagulants is correct?

- a. Enoxaparin is indicated for DVT prevention in patients who've had abdominal surgery.
- b. In patients receiving LMWH, the partial thromboplastin time (PTT) should be kept at 1.5 to 2 times the normal range.
- c. Idarucizumab is the reversal agent for UFH.
- d. UFH is administered orally or subcutaneously.

9. When administering parenteral anticoagulants subcutaneously, you should

- a. inject the medication into the deltoid muscle.
- b. inject the medication into the abdomen.
- c. stretch the skin tautly.
- d. rub the injection site afterwards.

10. Which statement about warfarin is correct?

- a. It is effective immediately.
- b. It requires no lab monitoring.
- c. It has no reversal agent.
- d. It is a vitamin K antagonist.

11. A direct oral anticoagulant (DOAC) that directly inhibits thrombin is

- a. apixaban.
- b. dabigatran.
- c. edoxaban.
- d. rivaroxaban.

12. Menorrhagia and longer periods have been reported with

- a. apixaban.
- b. dabigatran.
- c. edoxaban.
- d. rivaroxaban.

13. An anticoagulant that has no reversal agent is

- a. apixaban.
- b. dabigatran.
- c. warfarin.
- d. enoxaparin.

14. Which of the following actions that nurses can take to prevent VTE is correct?

- a. Use graduated compression stockings for patients with arterial disease.
- b. Have patients remove compression stockings every 3 days for skin care.
- c. Extend an elastic bandage wrap over a larger area.
- d. Be sure elastic bandages are wrapped tightly.