# Deep venous thrombosis

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## Background

Deep venous thrombosis, a condition of active thrombosis in the deep venous system of one or both lower extremities, is associated with a high likelihood of extension of the thrombotic process and subsequent embolism. Deep venous thrombosis may occur spontaneously, after prolonged stasis (bed rest), or in association with various clinical disorders, including neoplasms, hypercoagulable states, and with estrogen use.

Lower-extremity deep venous thrombosis is associated with significant morbidity and mortality, principally from the complications of pulmonary embolism and chronic venous insufficiency. More than 90% of pulmonary emboli originate in lower extremity sites. The thrombotic process begins in the deep veins of the calf[1,2]. If the process remains confined to the tibial-soleal systems, the chance for subsequent embolic episodes is low; but if such episodes do occur, they usually result in small, asymptomatic pulmonary emboli. However, when thrombi extend into the popliteal and femoral venous systems, the likelihood for further extension and clinically significant embolic events increases markedly.

## Diagnosis

### Estimating pretest probability

Only half of all patients with active venous thrombosis present with signs or symptoms referable to the involved limb[3,4]. Conversely, in almost one third of patients with signs suggestive of deep venous thrombosis (e.g., pain, swelling, tenderness, edema), there is no venographic evidence of clots[3]. Therefore, the presence or absence of signs and symptoms does not correlate well with the presence or absence of active deep venous thrombosis. Thus, when deep venous thrombosis is considered a reasonable probability, objective testing is necessary.

### The modified Wells clinical score

| Clinical characteristic | Score |
|---|---|
| Active cancer (treatment ongoing, within 6 months, or palliative) | 1 |
| Paralysis, paresis, or recent plaster immobilization of the lower extremities | 1 |
| Recently bedridden >3 days or major surgery within 12 weeks requiring general or regional anaesthesia | 1 |
| Localized tenderness along the distribution of the deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swelling 3 cm larger than asymptomatic side (measured 10 cm below the tibial tuberosity) | 1 |
| Pitting edema confined to the symptomatic leg | 1 |
| Collateral superficial veins (nonvaricose) | 1 |
| Previously documented DVT | 1 |
| Alternative diagnosis at least as likely as DVT | -2 |

| Score | Probability | Likelihood ratio for DVT |
|---|---|---|
| >2 | High | 5.2 |
| 1 or 2 | Intermediate | - |
| <1 | Low | 0.25 |

Patients are Categorized as high, intermediate, or low probability, according to the Wells clinical score[5,6]. D-dimer testing is recommended to exclude DVT in patients with a low or intermediate clinical probability score[7,8]. Venous ultrasound is the investigation of choice in patients with a high clinical score or a positive D-dimer result (or all patients if D-dimer is unavailable or unreaiiable). Ultrasound is highly sensitive and specific for detection of proximal (popliteal or above) DVT[9,10]. About 1% to 2% of patients with a normal initial ultrasound have calf vein thrombosis that is destined to extend into the proximal veins, generally within 5 to 8 days. Hence, if the clinical suspicion is strong, ultrasound should be repeated in 1 week[10].

Plethysmography is a suitable alternative to venous ultrasonography if venous ultrasound is not available[11]. If the initial test result is normal, serial testing is recommended.

It should be recognized that in patients with peripheral arterial disease, congestive heart failure, or venous outflow obstruction due to pelvic mass or pregnancy, plethysmography may yield false-positive results.

Ascending functional venography or MRV should be considered if the diagnosis is equivocal after ultrasound or plethysmography[12,13].

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## Laboratory and other studies for suspected DVT[14]

| Test | Sensitivity (%) | Specificity (%) | Likelihood ratio positive | Likelihood ratio negative | Notes |
|---|---|---|---|---|---|
| D-dimer (ELISA) | All DVT: 94<br>Proximal: 98<br>Distal: 86 | 45 | | | Usually used in combination with ultrasound or clinical scoring. The laboratory results should be available within 2 hours of blood draw for adequate clinical utility |
| D-dimer (latex) | All DVT: 89<br>Proximal: 94<br>Distal: 79 | 55 | | | Usually used in combination with ultrasound or clinical scoring. The laboratory results should be available within 2 hours of blood draw for adequate clinical utility |
| D-dimer (whole blood) | All DVT: 87<br>Proximal: 84<br>Distal: 64 | 68 | | | Usually used in combination with ultrasound or clinical scoring. The laboratory results should be available within 2 hours of blood draw for adequate clinical utility |
| Duplex Doppler ultrasound | All DVT: 92<br>Proximal: 96<br>Distal: 71 | 94 | Proximal: 19 | Proximal: 0.05 | Combines Doppler audio measurements of blood flow with visual ultrasound imaging. |
| Compression ultrasound | All DVT: 90<br>Proximal: 94<br>Distal: 57 | 98 | | | The compressibility of the proximal veins is assessed with the ultrasound probe. |
| Impedance plethysmography | All DVT: 75<br>Proximal: 88<br>Distal: 57 | 90 | Proximal: 16 | Proximal: 0.09 | Impedance plethysmography measures the electrical resistance (impedance) in blood from changes in volume and flow rate in the leg with a pneumatic thigh cuff. This noninvasive test cannot distinguish acute DVT from other conditions that affect venous outflow, such as right-sided heart failure, peripheral arterial disease, or an external mass compressing the vein. |

| | | | |
|---|---|---|---|
| Strain-gauge plethysmography | All DVT: 83<br>Proximal: 90<br>Distal: 56 | 81 | Utilizes a strain gauge around the calf to measure changes in venous outflow and capacitance after release of the tourniquet. |
| Venography | 100 | 100 | This test can be of limited value if there is poor contrast filling of the deep veins, however it is the historical criterion standard for DVT. |
| MRV | All DVT: 92<br>Proximal: 94<br>Distal: 62 | 95 | MRV is more expensive than ultrasound imaging. Patients with metal devices such as pacemakers may not be able to undergo MRV imaging. |
| CBC | | | Obtain baseline before initiating anticoagulation therapy. |
| PT/PTT, INR level | | | Obtain baseline before initiating anticoagulation therapy |
| Stool guaiac | | | Obtain baseline before initiating anticoagulation therapy |
| ECG | | | Sinus tachycardia is most common electrocardiographic finding for pulmonary embolus. S wave in lead I with Q wave and inverted T wave in lead III suggests pulmonary embolus; however, sensitivity and specificity are poor |

**CBC = complete blood count; DVT = deep venous thrombosis; ECG = electrocardiography; ELISA = enzyme-linked immunosorbent assay; INR = international normalized ratio; MRV = magnetic resonance venography; PTT = partial thromboplastin time.**

### Differential diagnosis of DVT

It should be recognized that the differential diagnosis of DVT is extensive. Venous reflux, orthopedic problems, and other medical problems come in to the differential diagnosis in patients with suspected DVT.

### Differential diagnosis of DVT[14]

| Disease | Characteristics | Notes |
|---|---|---|
| Venous insufficiency (venous reflux) | Usually due to venous hypertension from such causes as venous reflux or obesity | Obtain ultrasound evaluation of venous reflux |
| Superficial thrombophlebitis | Firm, tender, varicose vein | Superficial thrombosis is rarely associated with DVT |
| Muscle strain, tear, or trauma | Pain occurring with range of motion more characteristic of orthopedic problem due to trauma. Usually history of leg injury. | Order appropriate radiological studies to evaluate for orthopedic problem such as bone fracture |
| Leg swelling in a paralyzed limb | History of hemiplegia | Patients with a paralyzed limb may develop edema without DVT |
| Baker's cyst | Frequent pain localized to popliteal region of leg | Seen on ultrasonography |
| Cellulitis | Skin erythema and warmth | Consider antibiotic treatment |
| Lymphedema | Toe edema is more characteristic of lymphedema than of venous edema. | Lymphedema can occur in one or both legs |

DVT = deep venous thrombosis.

### Treatment

Most patients with DVT can be safely treated as outpatients with LMWH unless they have signs and symptoms of pulmonary embolus. However, certain categories of people should be hospitalized for treatment.

- History of hemorrhagic stroke
- Hematuria, melena, or recent GI bleed
- Hemoglobin <8.0 or thrombocytopenia in history or on laboratory tests
- Major trauma within previous 2 weeks
- Major surgery within previous 2 weeks
- Severe, uncontrolled hypertension (systolic pressure >180 mm Hg or diastolic pressure >110 mm Hg)
- Serum creatinine level >200 μmol/L
- Hepatic failure
- Patient or visiting nurse unable to complete 5-day course of subcutaneous injections
- Potential for nonadherence (e.g., patient is confused, has poor vision, or cannot take care of self)
- Symptomatic pulmonary embolism

### Non-drug therapy

All patients with DVT should wear graduated compression stockings as it has been shown to reduce risk of post-thrombotic syndrome[15]. Graduated compression stocking of appropriate size should be selected (to fit the patient's calf). Patients should be reminded that compression stockings lose elasticity after 6 months of repeated use.

### Drug therapy

Traditionally, intravenous unfractionated (standard) heparin is considered as a first-line therapy for DVT in hospitalized patients because of the rapid onset of action[16,17]. Unfractionated heparin is given as a bolus followed by continuous infusion to achieve an APTT ratio 1.5 to 2.5 times normal; possible dosing regimens are:

- Initial bolus of unfractionated heparin of 5000 units followed by at least 30,000 units for the first 24 hours and according to the APTT thereafter
- A weight-based approach, in which an 80 U/kg bolus is followed by an 18 U/kg/hour infusion.

In patients who do not require hospitalization, outpatient therapy using subcutaneous LMWH is the option of choice as results of clinical trials show that LMWH is as effective as UFH[18,19,20]. Treat acute DVT with one of the following LMWH preparations:

- Enoxaparin: 1 mg/kg subcutaneously every 12 hours, or 1.5 mg/kg subcutaneously every 24 hours.
- Tinzaparin: 175 IU/kg subcutaneously once daily.
- Dalteparin 200 U/kg subcutaneously once daily.

## Drug treatment for DVT[14]

| Agent | Mechanism of Action | Dosage | Benefits | Side Effects | Notes |
|---|---|---|---|---|---|
| Unfractionated heparin | Enhances antithrombin activity, thereby inhibiting thrombin activity | Give iv infusion or intermittent sc doses to keep APTT 1.5 times control value (correlates with plasma heparin level between 0.2-0.4 U/mL by protamine titration or 0.3-0.7 U/mL by antifactor-Xa assay). Consider nomograms for dose adjustment. Continue therapy at least 5 days with an overlap with warfarin for at least 4 to 5 days until INR is therapeutic for 2 consecutive days | Prevents thrombus propagation and pulmonary embolus | Bleeding, thrombocytopenia, hypersensitivity reaction, HIT, osteoporosis after long-term use, elevation of liver enzymes and hyperkalemia | Antidote for bleeding is protamine sulfate. One milligram of protamine neutralizes 90 U of heparin activity. APTT may not correlate with antithrombotic activity or heparin levels and varies with different test reagents and increased levels of certain plasma proteins. Therapeutic range of APTT that corresponds to therapeutic plasma heparin levels should be determined in each laboratory. Monitoring plasma heparin levels may be helpful in patients who require large doses (>35,000 U/day) of heparin |
| LMWH | Inhibits thrombin generation by acting on factor Xa; also acts on antithrombin to inhibit factor IIa activity (anti Xa to anti IIa ratio of 2:1-4:1) | The regimen varies by agent. Dosage for enoxaparin is 1 mg/kg sc every 12 hours | At least as effective as unfractionated heparin in preventing thrombus propagation and pulmonary embolus. Outpatient care may allow for cost savings | Bleeding, thrombocytopenia, hypersensitivity, osteoporosis, HIT | The incidence of HIT and osteoporosis is lower than that associated with unfractionated heparin. Reduced nonspecific binding allows greater bioavailability and longer half-life. This yields a more predictable dose-response relationship than with unfractionated heparin, so laboratory monitoring is not necessary. Proceed cautiously in patients with renal disease, obesity, or pregnancy |

| | | | | | |
|---|---|---|---|---|---|
| Direct thrombin inhibitors: Recombinant hirudin | Directly inhibit thrombin activity | Loading: 0.4 mg/kg iv; Maintenance: 0.15 mg/kg/h | Useful in patients with HIT | Bleeding | APTT is not accurate in measuring anticoagulant activity. Ecarin clotting time is more helpful. Half-life is approximately 1.3 hours and there is no antidote. Proceed cautiously in patients with renal failure |
| Coumarin derivatives: Warfarin | Inhibits hepatic γ-carboxylation of glutamic acid residues of vitamin K-dependent coagulation factors II, VII, IX, and X. Inhibits production of antithrombotic proteins C and S | Give initial dose of 10 mg per day on day 1 of heparin, overlap for 4-5 days until INR becomes therapeutic for 2 consecutive days. Adjust dose to keep INR between 2.0 and 3.0. Continue for at least 6 months | Prevent recurrent DVT and pulmonary embolus | Hypercoagulability during first 24-36 hours of therapy; bleeding; hypersensitivity; teratogenicity; many drug interactions; skin necrosis associated with malignancy and protein C and S deficiency; bleeding associated with malignancy | Causes relative hypercoagulability in first 24-36 h of therapy, despite a prolonged INR, due to decreased factor VII and protein C levels but high factor II, IX and X levels (because of differing kinetics in plasma clearance rates). Contraindicated in pregnancy. Counsel patient to include a stable amount of vitamin K in diet and to avoid all alcohol. Because of drug interactions, patient should be on as few medications as possible. In patients with antiphospholipid antibody syndrome, consider maintaining INR ≥ 3.0 |
| Catheter-directed thrombolytic therapy (Alteplase) | Accelerates thrombolysis by activating plasminogen and therefore lysis of fibrin | Few dosing regimens available | Rapid lysis of ileo-femoral DVT | Bleeding | Venography usually used to monitor thrombolysis. Indicated for patients with ileofemoral DVT. Thrombolysis with secondary venous patency probably reduces the risk of postthrombotic syndrome. Severe postthrombotic syndrome probably more common in patients with iliofemoral vein thrombosis |

APTT = activated partial thromboplastin time; DVT = deep venous thrombosis; HIT = heparin-induced thrombocytopenia; iv = intravenous; INR = international normalized ratio; LMWH = low-molecular-weight heparin; sc = subcutaneous.

Long-term warfarin is indicated to reduce the risk of recurrent venous thromboembolism unless it is contraindicated. Warfarin (initial dose 5 mg) is commenced simultaneously with heparin and duration of therapy is determined based on patient risk factors. Heparin is continued concomitantly with warfarin until the therapeutic potential of warfarin is achieved for 2 consecutive days. An INR of 2 to 3 is the goal.

**Recommendations for the duration of anticoagulant therapy for patients with DVT[14]**

| Characteristics of patient† | Risk of recurrence in the year after discontinuation (%) | Duration of therapy |
|---|---|---|
| Major transient risk factor | 3 | 3 months |
| Minor risk factor; no thrombophilia | <10 if risk factor avoided<br>>10 if risk factor persistent | 6 months. Until factor resolves |
| Idiopathic event; no thrombophilia or low-risk thrombophilia | <10 | 6 months‡ |
| Idiopathic event; high-risk thrombophilia | >10 | Indefinite |
| More than one idiopathic event | >10 | Indefinite |
| Cancer; other ongoing risk factor | >10 | Indefinite |

† Examples of major transient risk factors are major surgery, a major medical illness, and leg casting. Examples of minor transient risk factors are the use of an oral contraceptive and hormone-replacement therapy. Examples of low-risk thrombophilias are heterozygosity for the factor V Leiden and G20210A prothrombin-gene mutations. Examples of high-risk thrombophilia are antithrombin, protein C, and protein S deficiencies; homozygosity for the factor V Leiden or prothrombin-gene mutation or heterozygosity for both; and the presence of antiphospholipid antibodies.

‡ Therapy may be prolonged if the patient prefers to prolong it or if the risk of bleeding is low

### Other options in the initial treatment of DVT

In patients with DVT, the routine use of IV thrombolytic treatment is not recommended. In selected patients, such as those with massive ileofemoral DVT at risk of limb gangrene secondary to venous occlusion, IV thrombolysis is indicated[21]. Catheter-directed thrombolysis in the initial treatment of DVT should be confined to selected patients such as those requiring limb salvage.

Catheter extraction or fragmentation and surgical thrombectomy is another option that is available for the initial treatment of DVT and it is indicated in selected patients such as patients with massive ileofemoral DVT at risk of limb gangrene secondary to venous occlusion[22,23].

Vena caval interruption by placement of an inferior vena caval filter as initial treatment of DVT is recommended in patients with a contraindication for, or a complication of anticoagulant treatment, as well as in those with recurrent thromboembolism despite adequate anticoagulation.

### Prevention

As low-dose subcutaneous unfractionated heparin has been shown to reduce the risk of fatal pulmonary embolism from 0.7% to 0.1%[24,25], it should be considered for primary prophylaxis for DVT in high-risk medical patients and in all surgical patients except those at highest risk (e.g., hip or knee replacement and neurosurgery): 5000 units of unfractionated heparin should be administered preoperatively and then every 8 to 12 hours postoperatively. Prophylaxis is contraindicated in patients with heparin-induced thrombocytopenia or active bleeding.

Randomized trials and meta-analysis show superior efficacy of LMWH over unfractionated heparin[26]. The incidence of adverse effects is low and not significantly different between warfarin and LMWH[27,28]. Warfarin or LMWH is recommended for primary prophylaxis for DVT in patients at highest risk (those undergoing hip or knee replacement or neurosurgery, patients >40 years undergoing general surgery for malignancy, and patients with an inhibitor deficiency state). Warfarin is given to reach a target INR of 1.8 to 3: Enoxaparin: 30 mg subcutaneously every 12 hours. Dalteparin: 2500 U daily for abdominal surgery; 5000 U daily for high-risk patients. In patients undergoing elective knee replacement prophylaxis with LMWH may be initiated 12 to 48 hours postoperatively.

A meta-analysis has shown that mechanical compression methods reduce the risk of DVT by about two thirds when used as monotherapy and by about half when added to a pharmacologic method. These benefits are similar irrespective of the particular method used (graduated compression stockings, intermittent pneumatic compression, or foot pumps) and are similar in each of the surgical groups studied[29]. In the absence

of a clear contraindication (such as severe peripheral arterial disease), mechanical compression with graduated compression stockings is recommended for primary prophylaxis against postoperative DVT.

Below-knee compression socks, producing 14 to 17 mm Hg pressure, starting 2 to 3 hours before the flight are also recommended for individuals at low to medium risk for DVT, going on long-haul flights. For patients at high risk for DVT, consider a single does of LMWH subcutaneously 2 to 4 hours before the flight in addition to compression socks.

### Follow-up

**Ongoing anticoagulation should be monitored for the duration of therapy in patients with DVT.** INR is monitored every 4 weeks for the duration of warfarin therapy, once the level of anticoagulation is stable. Warfarin is given at full therapeutic doses for 3 to 6 months in patients with a first episode of proximal DVT, but long-term, low-dose warfarin (INR, 1.5 to 2) is considered to prevent DVT recurrence.

**Patients should be monitored and treated for postthrombotic syndrome.** Graduated compression stockings are prescribed with a pressure of 20 to 30 mm Hg for moderate edema, 30 to 40 mm Hg for severe edema, and 40+ mm Hg for severe edema not responding to the lower level of pressure. Patients are instructed to replace stockings after 6 months of repeated use because the stockings lose the elasticity needed to maintain adequate pressure.

**Elements of follow-up for DVT[14]**

| Category | Issue | How? | How often? | Notes |
|---|---|---|---|---|
| History and physical exam | Recurrent disease or postphlebtic syndrome | Look for recurrent pain and swelling | As needed and each visit | Often requires imaging to differentiate new thrombosis from post-phlebtic sequellae |
| History and physical exam | Disease complications | Look for stasis skin changes and ulceration | Every 3 months after DVT for 1 year | |
| History and physical exam | Disease complications | Ask about dyspnea and chest pain and examine for signs consistent with pulmonary embolism | As needed and each visit | |
| Laboratory testing | Monitoring of anticoagulation | Measurement of prothrombin time/INR | 2-3 times weekly until maintenance dosage determined, then once weekly; then once every 4 weeks if levels are stable. Change in dosage or addition of other medications should prompt more frequent monitoring until INR is stable | Change in dosage or addition of other medications should prompt more frequent monitoring until INR is stable |
| Laboratory testing | Recurrent disease or complication | Imaging studies of extremities and lungs | As needed | |
| Laboratory testing | Development of chronic thromboembolic pulmonary hypertension | Echocardiography | If patient develops unexplained dyspnea | |
| Non-drug therapy | Local care | Recommend graduated compression stockings | After acute episode of DVT | |
| Drug therapy | Anticoagulation | Adjust warfarin dose on the basis of INR | At least every 4 weeks if INR is stable | |
| Patient education | Overall management | Educate patients about symptoms of recurrent VT or PE, drug or food interactions with warfarin, and potential bleeding complications | | |

DVT = deep venous thrombosis; INR = international normalized ratio; PE = pulmonary embolism.

**Screening for thrombophilias**

Routine screening for thrombophilias in patients who develop venous thrombo-embolism (VTE) is not recommended. However, screening is indicated in following patients.

- patients with idiopathic venous thromboembolic events.
- women who develop VTE while receiving the oral contraceptive pill, HRT, or while pregnant.
- first-degree relatives of patients with thrombophilia or recurrent venous thrombosis.
- women with unexplained complications of pregnancy.
- women with a family history of VTE or thrombophilia (but do not screen all healthy women for thrombophilias before oral contraceptive use).

These patients should be screened for

- Factor V Leiden mutation
- Protein C deficiency
- Protein S deficiency
- Antithrombin deficiency
- Prothrombin gene mutation A20210
- Anticardiolipin antibodies
- Lupus anticoagulant
- Hyperhomocystinemia

**Drug therapy**

Patients with VTE and certain thrombophilias are at especially high risk for recurrent VTE. The benefit of VTE prevention with long-term anticoagulation in these high-risk patients may outweigh the risk for bleeding complications. The risk for VTE during high-risk situations is increased. Maintaining the INR higher than normal in patients with lupus anticoagulant or anticardiolipin antibodies may also prevent recurrent VTE in this group. Instead of maintaining the INR between 2.0 to 3.0, there may be some benefit to keeping it between 3.0 to 4.0[30,31]. However, recent work suggests that this may not be true. Patients with VTE and antiphospholipid antibodies did just as well with an INR of 2.0 to 3.0[32].

Reviews suggest that antithrombin, protein C, or protein S deficiency carries recurrence rates of 5% to 15% per year with a relative risk of 2.5 compared to other patients with VTE[33].

Prolonged (lifelong) therapeutic anticoagulation should be in patients with VTE and any of the following:

- o Lupus anticoagulant
- o Anticardiolipin antibodies
- o Homozygosity for the factor V Leiden mutation
- o Homozygosity for prothrombin gene defect
- o Combined heterozygosity for factor V Leiden mutation and prothrombin gene defect
- o Antithrombin III deficiency
- o Recurrent VTE

Prophylactic anticoagulation is recommended in all patients with thrombophilias during high-risk situations:

- o Surgery
- o Prolonged immobilization
- o Pregnancy

Anticoagulation is provided for VTE prophylaxis under certain circumstances to pregnant women with a history of VTE.

- Recommend heparin for VTE prophylaxis in pregnant women with an underlying thrombophilia and history of VTE.
- Consider heparin prophylaxis in pregnant women with previous idiopathic VTE.
- Consider close observation or heparin prophylaxis in a pregnant woman with previous secondary VTE.

Antithrombin III concentrates should be considered in patients with antithrombin III deficiency, who develop recurrent VTE despite adequate ongoing anticoagulation.

**Differential diagnosis of underlying causes of venous thromboembolism**

It should be remembered that diagnoses other than thrombophilia may predispose to VTE in patients with VTE.

**Differential diagnosis of underlying causes of venous thromboembolism[14]**

| Disease | Characteristics | Notes |
|---|---|---|
| Malignancy | Any malignancy can result in increased risk for VTE (includes solid and hematologic cancers, especially myeloproliferative disorders). | Screen all patients with VTE for malignancy with a complete history and physical.<br>Direct diagnostic tests towards abnormalities in history and physical exam.<br>Normal screening procedures should be followed (e.g., mammograms for women over age 50 and Pap smears for women over age 18).<br>Perform CBC and liver function tests on all patients. Order a chest x-ray for all smokers.<br>Conduct more thorough blood tests and imaging procedures in patients who present with recurrent VTE with no other explanation (73).<br>The true utility of screening these patients for malignancies, with regard to morbidity and survival, is not known |
| Surgery | All but minor procedures in the last month represent an increased risk for VTE | Hip, knee, and pelvic surgeries are highest risk |
| Trauma | Trauma (especially of the lower limb, with or without plaster immobilization) within the last month represents an increased risk for VTE.<br>Spinal injuries also represent an increased risk | |
| Immobility | Prolonged immobilization (>72 hours) increases the risk for VTE | Particularly true for patients with recent cerebrovascular accident with paresis, myocardial infarction, congestive heart failure, and pulmonary disease |
| Previous thrombosis | Even in the absence of a recognized thrombophilic condition, the risk for VTE increases in any patient with a history of thrombosis | |
| Rare thrombophilias not tested for in initial screen | Rare thrombophilias should be considered in patients with unexplained VTE | Consider testing for factors VIII, IX, XI, and also for dysfibrinogenemias |
| Undefined thrombophilia | New thrombophilic states are being described on a regular basis.<br>Even though patients do not have an identifiable thrombophilia now, new testing in the future may demonstrate an as yet unknown condition | Consider storing the blood of certain patients for future testing |

CBC = complete blood count; MI = myocardial infarction; VTE = venous thromboembolism.

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## Questions

### Question 1

A 58-year-old man is evaluated in the emergency department because of dyspnea and hypotension of 3 hours' duration. Three weeks ago, he fractured his right tibia in a motor vehicle accident, requiring open reduction and fixation. A cast was placed that included ankle and knee joints. On physical examination, his pulse rate is 120/min and blood pressure is 95/55 mm Hg (preoperative blood pressure was 135/85 mm Hg). Chest radiography shows no infiltrates. The $SaO_2$ when the patient is breathing room air is 89%. Ventilation-perfusion scanning shows two unmatched lobar defects and two segmental defects. A Doppler study shows a deep venous thrombosis in the femoral vein of the right leg.

**Which of the following therapies is most likely to restore hemodynamic stability within the first 24 hours?**

(A) Unfractionated heparin
(B) Low-molecular-weight heparin
(C) Tissue plasminogen activator (t-PA) followed by heparin
(D) Unfractionated heparin plus an inferior vena cava filter
(E) Warfarin

### Question 2

A 56-year-old man is evaluated in the emergency department because of progressive swelling of the right lower extremity during the previous 5 days and right-sided pleuritic chest pain and dyspnea beginning 1 to 2 hours ago.

On physical examination, his temperature is 38.2 °C (100.8 °F), pulse rate is 105/min, respiration rate is 28/min, and blood pressure is 160/80 mm Hg. Cardiac and pulmonary examinations are unremarkable.

Arterial blood gases with the patient breathing room air are $PO_2$, 78 mm Hg; $PCO_2$, 30 mm Hg; and pH, 7.48. Electrocardiography shows sinus tachycardia and nonspecific ST-T wave changes, and chest radiography is normal. Ventilation-perfusion scanning shows two unmatched segmental defects. The D-dimer value is three times the upper limit of normal.

**Which of the following is the most appropriate course of action?**

(A) Heparin
(B) Helical computed tomography with contrast
(C) Noninvasive studies of the lower extremities
(D) Pulmonary angiography

## Question 3

A 35-year-old woman is evaluated for treatment of a pulmonary thromboembolism. Four days ago she was involved in an automobile accident resulting in fractures of the left lower ribs and required an emergency splenectomy. Two hours ago she developed pleuritic chest pain and dyspnea. Noninvasive ultrasound and Doppler studies of the leg veins show a deep venous thrombosis in the right leg extending beyond the femoral vein into the iliac system. Ventilation-perfusion lung scanning shows two segmental unmatched perfusion defects in the right lung and a similar defect in the left lung. On physical examination, her heart rate is 120/min, respiration rate is 24/min, and blood pressure is 95/60 mm Hg. Arterial blood gases when the patient is breathing room air are $PaO_2$, 58 mm Hg; $PaCO_2$, 28 mm Hg; and pH, 7.44.

**Which of the following is the most appropriate next step?**

(A) Tissue plasminogen activator
(B) Pulmonary angiography
(C) Unfractionated heparin
(D) Inferior vena cava filter
(E) Warfarin