AMERICAN HEALTH CONSULTANTS® A Medical Economics Company

Rapid Reference Card Enclosed

1st Place Winner Best Single Topic Health Newsletter Newsletter Publishers Association

The Practical Guide for Emergency Physicians

Emergency Medicine Reports™

Volume 20, Number 2 January 18, 1999

The management of deep venous thrombosis (DVT) has changed dramatically over the past several years. Advances in both technology and pharmacology have placed the emergency physician in a pivotal role for managing veno-occlusive disease.

DVT is a cause of significant morbidity and mortality.[1-3] Acutely, it causes pain and limits physical activity. A dramatic presentation of DVT known as phlegmasia dolens leads to gangrene, shock, and death. If clots embolize, subsequent pulmonary embolism (PE) can be fatal. Despite resolution of the acute event, destruction of venous valves can lead to recurrent swelling, stasis ulcers, and persistent edema.[1]

Although DVT is a significant cause of mortality in the elderly, even children are not immune. Most patients with venous thrombosis have risk factors, among them: stasis, hypercoagulability, trauma, and/or endothelial injury.

Although the physical examination usually provides clues to the diagnosis, the emergency physician must remember that the clinical examination is neither sensitive nor specific for DVT. Failure to detect a deep venous thrombosis can lead to catastrophic results. A clinical scoring system aids in the diagnosis of patients with leg pain or swelling, and new assays for D-dimer play a growing role. In the past decade, venography has declined, and Duplex ultrasound has become the diagnostic modality of choice.

The emergency physician must aggressively recognize and treat life threats, such as pulmonary embolism and phlegmasia dolens. Heparin is often underdosed, and the use of a weight-based nomogram assists the EP to rapidly achieve a targeted PTT. Low-molecular weight heparin (LMWH) will change practice standards by allowing home treatment of venous thrombosis at lower total cost. The use of thrombolytics remains controversial.

This article outlines an outcome-effective clinical approach for DVT management. It will help emergency departments (EDs) design critical pathways for developing a safe and effective treatment program for this common condition.

—The Editor

Protocols for Deep Venous Thrombosis (DVT): A State-of-the-Art Review

Part I: Risk Factor Assessment, Physical Examination, and Current Diagnostic Modalities

Author: **Stephen A. Colucciello, MD, FACEP,** Assistant Clinical Professor of Emergency Medicine, University of North Carolina Medical School, Chapel Hill, North Carolina; Director, Clinical Services Trauma Coordinator, Deptartment of Emergency Medicine, Carolinas Medical Center, Charlotte, NC.

Peer Reviewer: **Charles Stewart, MD, FACEP,** Emergency Physician, Colorado Springs, CO.

Epidemiology

Approximately 2 million Americans suffer from DVT each year,[4] but, because most DVT is occult, the true incidence is unknown. Approximately 250,000 patients per year require hospitalization for 5-10 days of intravenous heparin therapy.[5] In addition to those with acute thrombosis, millions more suffer from sequelae such as stasis dermatitis and venous ulcers. While the degree of morbidity is significant, mortality rates are equally problematic. Thromboembolic disease is annually responsible for 200,000 deaths in the United States.[6] The elderly are in greatest jeopardy; DVT is associated with a 21% one-year mortality in this age group.[7] Many in this subgroup die from associated PE, while others succumb from comorbid disease, especially cancer. Even children are at risk for venous thrombosis. Pediatric patients at risk include those with spinal

cord injuries, hypercoagulable states, and those with a recent history of central lines.[8]

Etiology and Risk Factors for DVT

Virchow first elucidated the causes of deep venous thrombosis with a description of a classical triad: stasis, hypercoagulability, and endothelial injury. While at least 50% of patients with DVT have risk factors,[9] the strongest risk factor for venous thrombosis is prior thromboembolic disease.[10] *(See Table 1.)* Moreover, risk factors are additive in nature.[11]

Stasis. Stasis may arise from prolonged bed rest (4 days or more) or extended travel in a vehicle such as an airplane or automobile. The principal cause of death related to transatlantic flights is not airplane lasagna, but pulmonary embolism. This is known, among other things, as the "economy class syndrome," in which venous thrombosis is induced by cramped quarters in an airplane, usually during transoceanic flights.[12] A cast on the leg also increases venous stasis and impairs the "muscle pump" mechanism that propels blood into the central circulation. Stasis plays a role in thrombosis encountered in the morbidly obese and in individuals with cardiac disease. Limb paralysis from stroke or spinal cord injury is associated with a difficult-to-evaluate syndrome of painless or occult thrombosis.[13]

Hypercoagulability. Surgery and trauma are responsible for up to 40% of all thromboembolic disease, which results from both a hypercoagulable state and immobility. These insults activate the clotting cascade, and indices of thrombosis and fibrinolysis rise rapidly.[14]

Malignancy also accelerates the coagulation cascade and is responsible for up to 4% of all episodes of DVT.[15,16] Activation of the extrinsic pathway via tissue factor plays an important role in clot generation;[17] breast and prostate cancer are common precipitants. Up to 10% of patients with new onset DVT develop cancer within six months after the diagnosis of DVT.[18,19] Recurrent migratory superficial thrombophlebitis caused by malignancy (usually solid tumors) is called Trousseau's syndrome. This condition is resistant to warfarin therapy and may require long-term heparin prophylaxis.[20]

Increased estrogen predisposes to thrombosis due to a fall in protein 'S,' and cigarette smoking significantly enhances this tendency.[19] Increased estrogen occurs during all stages of pregnancy—the first three months postpartum, after elective abortion, and during treatment with oral contraceptive pills (OCPs). Low-dose estrogen OCPs are not associated with an increased risk of DVT. Women with congenital resistance to activated protein C (factor V Leiden mutation) are especially susceptible to thrombosis due to OCPs.[22] Progesterone-only pills and Norplant may slightly increase the risk of thrombosis.

Ten percent of thromboembolic disease is due to acquired or inherited disorders of coagulation. Three of the most common disorders include deficiencies of protein 'S,' protein 'C,' and antithrombin III. While most patients inherit these conditions, they may also be acquired. Because the nephrotic syndrome results in urinary loss of antithrombin III, this diagnosis should be considered in children presenting with thromboembolic disease.[23] Antiphospholipid antibodies accelerate coagulation and include the lupus anticoagulant and anticardiolipin antibodies.[24] Paradoxically, nearly half of these patients have a prolonged PTT on laboratory testing despite being hypercoaguable.[25] Suspect antiphospholipid antibodies when thrombosis occurs in young patients with no other risk factors. This syndrome is especially likely if the patient has arterial thrombosis or venous clot in unusual locations, such as the mesentery or solid organs.[26] Inflammatory processes, such as systemic lupus erythematosus (SLE), sickle cell disease, and inflammatory bowel disease (IBD), also predispose to thrombosis, presumably due to hypercoagulability.

Endothelial Injury. The third aspect of Virchow's triad is endothelial injury. Trauma, surgery, and invasive procedure may disrupt venous integrity.[27,28] In particular, orthopedic surgery of the hip and lower extremities can incite thrombosis. Iatrogenic causes of venous thrombosis are increasing due to the widespread use of central venous catheters, particularly subclavian and internal jugular lines. These lines are an important cause of upper extremity DVT, particularly in children.[29] Femoral lines also generate thrombus in 14% of patients cannulated.[30]

Emergency Medicine Reports™ (ISSN 0746-2506) is published biweekly by American Health Consultants, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Publisher: Brenda Mooney
Managing Editor: David Davenport
Copy Editor: Suzanne Zunic
Marketing Manager: Deb Zelnio

GST Registration No.: R128870672

Periodical postage paid at Atlanta, GA. **POSTMASTER:** Send address changes to ***Emergency Medicine Reports***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $21. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Multiple copy prices: One to nine additional copies, $87 each; 10 or more additional copies, $58 each.

Accreditation

Emergency Medicine Reports™ continuing education materials are sponsored and supervised by American Health Consultants. American Health Consultants designates this continuing education activity as meeting the criteria for 52 credit hours in Category 1 for Education Materials for the Physician's Recognition Award of the American Medical Association, provided it has been completed according to instructions.

This CME activity was planned and produced in accordance with the ACCME Essentials. ***Emergency Medicine Reports*** also is approved by the American College of Emergency Physicians for 52 hours of ACEP Category 1 credit and has been approved for 52 Category 2B credit hours by the American Osteopathic Association. This program has been reviewed and is acceptable for up to 52 Prescribed credit hours by the American Academy of Family Physicians. Term of approval is for one year from beginning distribution date of 1/98 with option to request yearly renewal.

American Health Consultants is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail: custserv@ahcpub.com
Editorial E-Mail: david.davenport@medec.com

World Wide Web page: http://www.ahcpub.com

Subscription Prices

1 year *with* 52 ACEP/AMA/52 AAFP Category 1/Prescribed credits (52 AOA Category 2B credits): $387
1 year *without* credit: $287

2 years *with* 104 ACEP/AMA/104 AAFP Category 1/Prescribed credits (104 AOA Category 2B credits):$814
2 years *without* credit:$574

3 years *with* 156 ACEP/AMA/156 AAFP Category 1/Prescribed credits (156 AOA Category 2B credits): $1221
3 years *without* credit: $861
Resident's' rate $143.50

All prices U.S. only.
U.S. possessions and Canada, add $30 plus applicable GST. Other international orders, add $30.

Questions & Comments

Please call **David Davenport,** Managing Editor, at (404) 262-5475 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Statement of Financial Disclosure

American Health Consultants does not receive material commercial support for any of its continuing medical education publications. In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Colucciello (author), and Dr. Stewart (peer reviewer) report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

Clinical Pathophysiology

Anatomists describe the venous drainage of the lower extremity in relationship to the muscle fascia. The superficial veins include the greater and lesser saphenous veins, which drain into the deep system via the perforating or communicating veins. A series of valves direct blood flow toward the heart. The pump action of the thigh and calf muscles powers this flow.[31] While some view anatomists as humorless, they have perpetuated a dangerous joke on emergency physicians. The have named a major vessel of the lower extremity the "superficial" femoral vein. However, this structure is a *deep* vein! Three quarters of primary care physicians do not realize this fact and may neglect to anticoagulate the patient when this vein is involved.[32]

The nidus for a clot is often an intimal defect. For example, intravenous catheters, irritating medications, or illicit drugs precipitate superficial thrombophlebitis.[33-35] When a clot forms on an intimal defect, the coagulation cascade promotes clot growth proximally. Thrombus can extend from the superficial veins into the deep system from which it can embolize to the lungs. Nearly 25% of all patients with superficial phlebitis have involvement of the deep system.[36] Males older than age 60, patients with systemic infection, and patients on prolonged bed rest are most likely to develop DVT.[37]

While the vast majority of pulmonary emboli arise from the iliofemoral system, patients with calf vein involvement are also at risk. While *isolated* calf thrombi are unlikely to produce significant pulmonary emboli, up to 15-20% can later propagate and then embolize.[38-40] Once a clot develops, whether proximal or distal, venous hypertension frequently leads to pain and/or swelling. Extensive deep venous thrombosis can even result in compartment syndrome of the thigh and leg.[41] However, many cases of DVT remain asymptomatic until embolization occurs. Anticoagulation of superficial vein thrombosis remains controversial.

Opposing the coagulation cascade is the endogenous fibrinolytic system. After the clot organizes or dissolves, most veins will recanalize in several weeks.[42] Residual clots retract as fibroblasts and capillary development lead to intimal thickening.[43] Venous hypertension and residual clot may destroy valves, leading to the postphlebitic syndrome, which develops within 5-10 years.[44] Edema, sclerosis, and ulceration characterize this syndrome, which develops in 40-80% of patients with DVT.[45,46] In addition to the chronic changes of the postphlebitic syndrome, patients also can suffer exacerbations of swelling and pain, probably as a result of venous dilatation and hypertension. These exacerbations are clinically indistinguishable from recurrent DVT.[47] Accordingly, episodes of acute swelling and pain should be attributed to the postphlebitic syndrome *only after* objective tests confirm no recurrence of DVT.

Pulmonary embolism (PE) is a serious complication of DVT. Many episodes of pulmonary embolism go unrecognized, and at least 40% of patients with DVT have clinically silent PE on VQ scanning, [48] which is not the gold standard for diagnosis of PE. Most cases of PE arise from the iliofemoral system. Massive occlusion of the iliofemoral system can be life- and limb-threatening. Patients who have malignancy, congestive heart failure, massive obesity, or prior DVT are most susceptible to this complication.

Table 1. Risk Factors for Thromboembolic Disease

STASIS
- Immobility
  - Four days bed rest
  - Long plane ride (economy class syndrome)
  - Long train or car ride (many hours)
- Paralysis: stroke, spinal cord injury
- Cast on leg

HYPERCOAGULABILITY (UNDERLYING DISEASE)
- Previous thromboembolic disease
- Malignancy
- Inflammatory conditions (SLE, IBD, PVD)
- Nephrotic syndrome (loss of antithrombin III)
- Sepsis

COAGULATION DISORDERS—INHERITABLE VS. ACQUIRED
- Resistance to activated Protein C
- Protein S deficiency
- Protein C deficiency
- Antithrombin deficiency
- Disorders of fibrinogen or plasminogen
- Antiphospholipid antibodies (lupus anticoagulant and anticardiolipin)

INCREASED ESTROGEN (CAUSES URINARY LOSS OF PROTEIN S AND ANTITHROMBIN III)
- Pregnancy
- Post-partum < 3 months
- Elective abortion or miscarriage
- Oral contraceptive pills, other exogenous estrogens

INTIMAL DAMAGE
- Intravenous drug abuse
- Trauma
- Recent surgery
- Central lines

MULTIFACTORIAL
- Trauma
- Recent surgery
- Age > 60
- Cardiac disease
- Obesity
- Heart failure
- Lower limb arteriopathy

Presentation and Physical Examination

Symptomatic patients typically complain of lower extremity pain or swelling. They may report a sense of fullness, which increases with standing or walking.[49] Some individuals may complain of pain in the lower extremity when coughing or sneezing, which is different from electric type pain with cough or sneeze that is associated with sciatica. Venous involvement is usually unilateral unless the vena cava occludes, a rare and catastrophic event. In one study, DVT never occurred in the patients with bilateral symptoms.[50] However, bilateral involve-

ment can occur.

It is important to determine the time course of symptoms and to elicit a history of recent trauma. As a rule, venous thrombosis occurs over several days, and sudden, severe pain is more compatible with muscle rupture or injury. Associated symptoms are also important, especially the presence of chest pain or shortness of breath, which may suggest PE. The medical history should be used to assess risk factors for thromboembolic disease. A history of prior DVT is important, as up to 26% of patients with DVT have had a previous episode.[10] *(See Table 2.)*

Physical Examination. A caveat that is nearly 20 years old remains valid today. "A combination of clinical signs and symptoms that included tenderness, swelling, redness, and the assessment of Homans' sign [can] not adequately differentiate patients with or without DVT."[51]

This is not to imply that physical examination is useless, but that a number of physical findings in combination with risk factors assist in the diagnosis of a patient with leg complaints.

Occasionally, a rectal temperature can help distinguish cellulitis from DVT. While patients with DVT may have a low grade fever due to a systemic inflammatory response, this fever rarely exceeds 102°F. To help make this differentiation, it is essential to completely undress the patient with leg symptoms and inspect for lymphangitis, erythema, and ulcerations. Clots may become infected, especially in patients with intravenous drug abuse. Remember to examine the entire limb for abnormalities, as lymphangitis may have large "skip" areas. Be alert for psychiatric patients or prisoners who may tie a tourniquet around their thigh to produce factitious DVT.

Lack of discrepancy in calf size does not rule out DVT. Some researches have standardized calf measurements at 10 cm below the tibial tuberosity. While asymmetry of the calves of 1 cm or more is abnormal, such asymmetry does not definitively distinguish between patients with thromboembolic disease and those without.[52] However, asymmetric calf swelling of greater than 3 cm is almost always a significant finding.[53]

Examine the legs for pitting edema; extremities affected by acute thrombosis are frequently warmer than the opposite limb. Palpation includes a search for "cords," which are very specific, although insensitive for thrombosis. Cords are most often detected in the popliteal fossa. Palpate distal pulses and evaluate capillary refill to assess limb perfusion. Pulses may also be diminished in long-standing arterial disease. The presence of pain with passive range of motion of the toes or ankle is an important clue to compartment syndrome. Move and palpate all joints to detect acute arthritis or other joint pathology. Neurologic evaluation may detect nerve root irritation; sensory, motor, and reflex deficits should be noted. Search for a thrill or bruit which is associated with arteriovenous (AV) fistulas. Patients with large fistulas have abnormally high cardiac output, and manual compression of the fistula reflexively slows the heart by reducing the shunt (Branham's sign).[54] Patients with a remote history of a gunshot wound to the extremity are most likely to present with a fistula. Bony tenderness does not rule out DVT. Indeed, up to 65% of patients with DVT will have pain with percussion of the medial tibia.[49] Bancroft or Moses' sign is pain with compression of the calf against the tibia. Some patients with DVT will have more pain with this maneuver than with transverse compression of the gastrocnemius.[55]

A review of venous thrombosis would not be complete without mention of Homans'' sign: pain in the posterior calf or knee with forced dorsiflexion of the foot. It is often present in patients with sciatica. Despite numerous references to Homans'' sign in the medical literature, this finding is inaccurate and unreliable.[56]

Examination of the patient with DVT does not end with evaluation of the extremity. Search for stigmata of PE such as tachycardia (common), tachypnea or chest findings (rare), and exam for signs suggestive of underlying malignancy.[18]

Diffuse swelling can indicate the presence of an upper extremity DVT. Effort-induced thrombosis occurs in young, active males, while catheter-related thrombosis is limited to patients with prior instrumentation or intravenous drug abuse. Dilated collateral veins are frequent, but these are more easily seen in Caucasians. Look for arm discoloration and palpable axillary veins.[57]

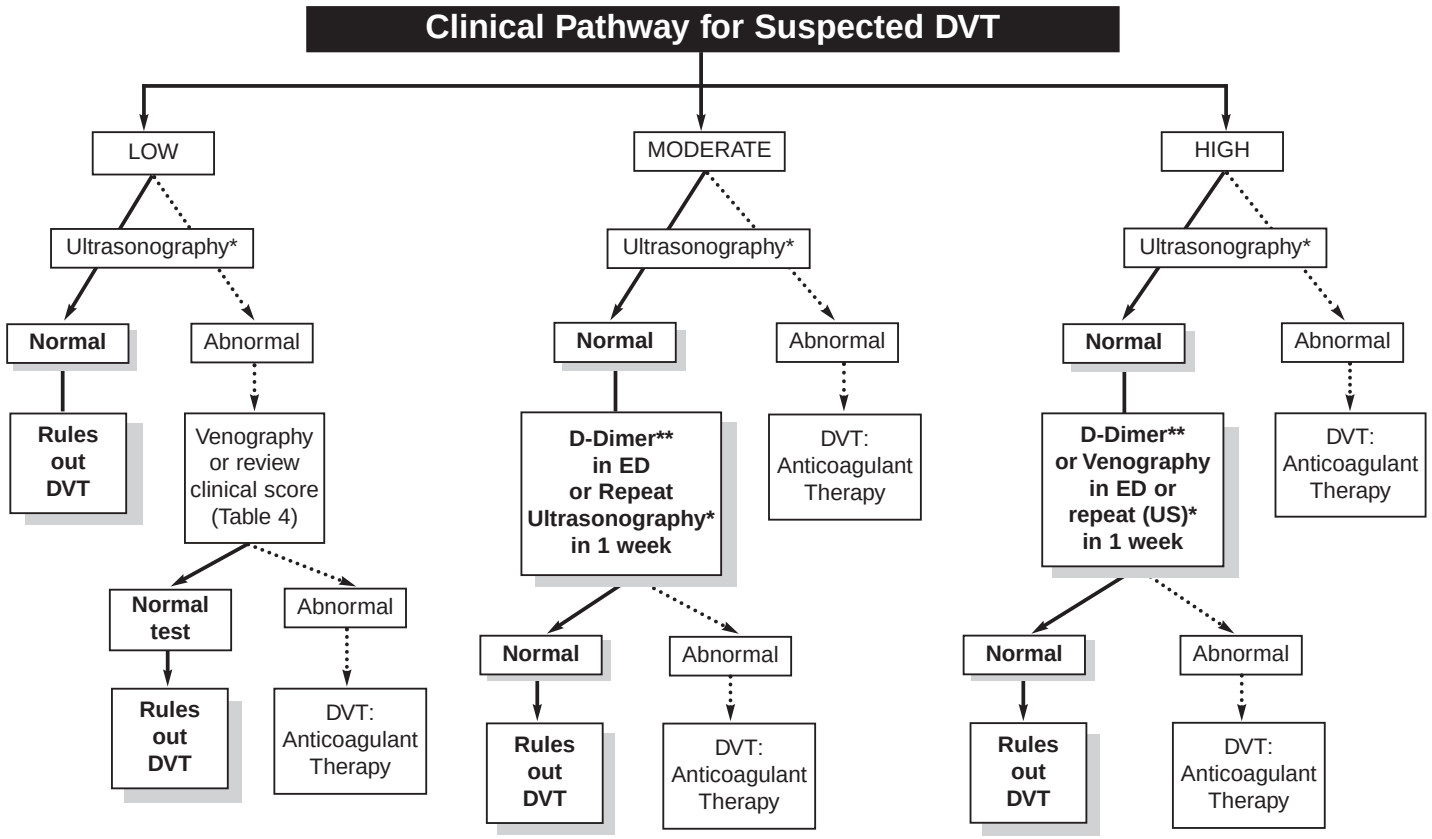
Table 2. Important Historical Questions

1. Have you or anyone in your family ever had a blood clot in their leg or lung?
2. Have you been on a long trip (e.g., car, plane, etc.)?
3. Have you recently been bedridden for more than three days?
4. Have you had surgery or trauma in the last 2-3 months?
5. Have you been pregnant in the last three months (Therapeutic abortion, miscarriage, current pregnancy)?
6. Are you on birth control pills and do you smoke?
7. Do you have any medical problems (e.g., malignancy, SLE, CHF)?
8. Have you had chest pain or shortness of breath?

Diagnostic Studies

Clinical examination alone is able to confirm only 20-30% of cases of DVT.[58] *(See Figure 1.)* Because of the limitations associated with the physical examination and history, the diagnosis of DVT must be pursued in any patient who presents with unexplained extremity pain or swelling. A patient who presents with symptoms in both arms or both legs, usually will not be suffering from bilateral thrombosis. Patients with risk factors for bilateral thrombosis, however, who present with bilateral findings, need careful examination. Patients with unilateral complaints and no clear explanation, such as a direct blow to the extremity, twisted ankle, etc., require further evaluation. The presence of risk factors for DVT must decrease the threshold for obtaining imaging studies. Accordingly, nearly all patients with complaints compatible with venous thrombosis, and who have no typical alternative diagnosis, require an imaging study.[59] Patients with suspected DVT who complain of

Figure 1. Clinical Suspicion for DVT



This Clinical Pathway is a suggested approach for suspected DVT patients, and is intended to supplement rather than substitute for professional judgement. The physician may change this plan at any time depending upon the patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

* Ultrasonography = Color flow Duplex study
** D-Dimer red cell agglutination study

Source: Adapted from Anand. *JAMA* 1998;279:1094-1099.

chest pain or shortness of breath should have a VQ CT scan to expedite the diagnosis.

Blood Tests. Two blood tests are valuable in the management of thromboembolic disease: the D-dimer and the INR. Current D-dimer assays have predictive value for DVT, and the INR is useful for guiding the management of patients with known DVT who are on warfarin (Coumadin). While no blood test can conclusively rule in or rule out venous thrombosis, a normal D-dimer in a patient with no risk factors for thrombosis makes proximal DVT extremely unlikely. Despite the fact that it is frequently ordered, a complete blood count (CBC) rarely provides useful information in patients with leg signs or symptoms. The leukocyte count cannot distinguish between DVT and cellulitis and is neither sensitive nor specific for either condition.

Coagulation Studies. Coagulation studies rarely are required as part of the initial evaluation of venous thrombosis. Occasionally, these studies may be valuable after Doppler demonstrates an acute clot, and in patients who develop a clot while on warfarin.

Although most physicians order a PTT *before* starting heparin for DVT, interestingly, this practice is not justified by the literature. For patients not on warfarin, assessment of the PTT will almost never affect management.[60] Obviously, a PTT should be obtained six hours after standard heparin in begun.

PT and INR. If a patient with acute DVT is currently on warfarin, an International Normalized Ratio (INR) is essential for management. It is now well documented that the prothrombin time (PT) is both antiquated and inaccurate, primarily because the sensitivity of thromboplastin reagents differs from batch to batch. Fortunately, the INR adjusts for this lack of standardization by comparing each batch with an International Sensitivity Index.[61,62] Measurement of the PT could be eliminated from clinical practice if replaced by the INR. Adequate anticoagulation for DVT is reflected by an INR between two and three.[61] If a patient with a *sub-therapeutic* INR develops a DVT, they will require more aggressive anticoagulation—first with heparin, and then an increased dose of warfarin. However, a patient who is on warfarin, but sustains an acute clot and has a *therapeutic* INR, requires a Greenfield filter.

Table 3. Diagnostic Modalities

TEST	ADVANTAGES	DISADVANTAGES	COMMENTS
D-dimer	Rapid, inexpensive, 93% sensitive	Only 77% specific	May be useful screen for DVT when other tests are unavailable
Venography	Traditional gold standard 90-95% accurate	Precipitates DVT and phlebitis in 1-3% of cases expensive; invasive	May be useful if doppler is equivocal especially if doppler cannot distinguish between acute and chronic changes
Radiolabeled fibrinogen	Sensitive for distal thrombi	Poor sensitivity for proximal thrombi; many false positives; time consuming	Not indicated as emergency department study
Impedance plethysmography	Noninvasive, rapid	Variable sensitivity 65-85% Many false positives and false negatives	Modern studies demonstrate low accuracy. Used more in Canada than United States
Duplex scanning	Rapid, relative inexpensive, noninvasive; highly accurate	Can miss small calf thrombi	Initial procedure of choice for the diagnosis of DVT
MRI	97% sensitive; 95% specific Noninvasive; may be useful pregnancy	Expensive	Growing role in detecting thrombi in pelvic and renal veins. May play role of evaluation of thromboembolic disease in pregnancy

Up to 10% of patients with DVT have an underlying coagulation disorder such as antiphospholipid syndrome or protein 'S,' protein 'C,' or antithrombin III deficiency.[1-3] However, measurements of these levels usually are not necessary for emergency management. On occasion, the admitting internist may screen young adults with unexplained thrombosis for more common coagulation disorders.[63]

D-dimer. If an emergency physician wishes to use a single blood test in order to exclude the diagnosis of DVT, the D-dimer assay would be that test. Only 2% of patients with a negative D-dimer (measured by the whole blood agglutination assay) will have DVT. In patients with a low pretest probability, the negative predictive value is 99.4%.[64]

D-dimer is a specific degradation product of cross-linked fibrin. Because concurrent production and breakdown of clot characterize thrombosis, patients with thromboembolic disease have elevated levels of D-dimer. There are three major approaches for measuring D-dimer. The two older tests include the sensitive, but time consuming, enzyme-linked immunoabsorbent assay (ELISA) and a rapid, but less sensitive, latex agglutination.[65] These tests suffered from a specificity of as low as 15-38% in DVT and PE.[66-68] Currently, the most useful assay is the whole blood agglutination test (SimpliRED). This five minute, bedside test is both rapid and sensitive.[69] In one study, this technique had a sensitivity of 93% for proximal DVT, 70% for calf DVT, and an overall specificity of 77%.[69] All D-dimer tests, regardless of the process, are more sensitive for proximal than distal clot, and may miss as many as 30% of calf DVTs.[70,71] False-positive D-dimers occur in patients with recent (within 10 days) surgery or trauma, recent myocardial infarction or stroke, acute infection, disseminated intravascular coagulation, pregnancy or recent delivery, active collagen vascular disease, or metastatic cancer.[69]

In a patient with no risk factors for DVT, a negative D-dimer measured by the whole-blood agglutination assay almost rules out the diagnosis (i.e., there will be less than a 1% chance of proximal DVT).[64] While some physicians may opt to forgo imaging studies in patients with a negative D-dimer, others may be reluctant to rely entirely upon a blood test. It seems reasonable that a negative D-dimer may obviate the need for off-hour Doppler studies in low-risk patients. If a patient presents at night with a swollen leg and a negative red cell agglutination test, imaging usually can be safely postponed until the morning.

Imaging Studies

Imaging studies include both invasive (venography, radiolabeled fibrinogen) and noninvasive (ultrasound, plethysmography, MRI) techniques. *(See Table 3.)* Current options are discussed in the next sections.

Venography. While venography aspires to be the "gold standard" modality for the diagnosis of DVT, it is a "gold-plated" standard at best.[72] First, radiologists disagree on interpretation in at least 10% of cases, and 5-15% of all studies are technically inadequate.[72,73] Moreover, side effects are significant and 2-5% of patients develop phlebitis from this painful procedure. The rare case of anaphylaxis remains a significant clinical concern. For the most part, ultrasound has supplanted venography for the initial evaluation of the patient with suspected DVT. If the ultrasound is equivocal or unavailable, venography may be useful. Venography is also useful if the patient has a high clinical probability of thrombosis and a negative ultrasound, and it is also valuable in symptomatic patients with a history of prior thrombosis in whom the ultrasound is non-diagnostic. In these patients, it usually can distinguish between acute events and chronic changes seen on ultrasound. A contrast study can delineate occlusion, recanalization, and collateral channels. Since neither ultrasound nor impedance plethysmography (IPG) is accurate for clot in

asymptomatic postoperative patients, venography is the only test that is reliable for the diagnosis of DVT in this population.[74] Fortunately, the emergency physician is rarely faced with this dilemma.

Nuclear Medicine Studies. Because the radioactive isotope incorporates into a growing thrombus, this test can distinguish new clot from an old clot.[75] Despite this fact, I-125 labeled fibrinogen is not a valuable ED study. It is insensitive for detection of proximal thrombi, it takes 24 hours to perform, and is plagued by a high, false-positive rate.[76] For these reasons, nuclear medicine studies should be reserved for the admitting physician.

Plethysmography. Plethysmography measures change in lower extremity volume in response to certain stimuli. By using a tourniquet and respiratory variation, the operator can detect changes in leg volume as a function of venous outflow.[77] Changes in such objective variables as calf circumference, cutaneous blood flow, or electrical resistance occur when there is obstruction of venous return. IPG is based upon changes in electrical resistance, and is the most widely used and accurate form of plethysmography.

IPG is very operator dependent, and early literature displayed a 95% correlation with venography for proximal DVT.[76] However, recent literature shows that the sensitivity of IPG is generally around 65-70%.[78-80] Because any impairment of venous outflow affects plethysmography results, many false positives occur. Postphlebitic syndrome, abdominal tumors, pregnancy, and congestive heart failure (CHF) can produce inaccurate results.[78-80]

Ultrasonography. From an emergency medicine perspective, in most clinical encounters, color-flow Duplex scanning is the imaging test of choice for patients with suspected DVT.[81,82] This test is inexpensive, noninvasive, and widely available. Its name derives from the dual use of Doppler flow with two-dimensional scanning. The Doppler component evaluates blood flow for proximal obstruction, and the addition of color flow technology provides the most accurate images. Changes in flow that occur with respiration and from calf compression (phasicity and augmentation) differentiate obstructing from non-obstructing thrombi.[83] The B-mode, or 2-D echo, provides a two-dimensional image of the vein and surrounding structures. The sonographer detects thrombus in the vein by directly visualizing and then compressing the vein with a transducer. Veins filled with clot do not collapse like a normal vein. In addition, the sonographer can distinguish fresh clot from an old clot based upon echogenicity, homogeneity, and collateral flow.[84] The color-flow duplex scan can detect 95-99% of acute thrombi above the knee.[85,86] Ultrasound can also distinguish other causes of leg swelling, such as tumor, popliteal cyst, abscess, aneurysm, or hematoma.[87] Pain, edema, dyspnea, and a history of DVT are most predictive of positive scans.[88]

It should be stressed that ultrasound does have its clinical limitations. High sensitivity testing requires sophisticated, (i.e., expensive) diagnostic equipment. Moreover, scans are very reader dependent and some institutions do not achieve optimal accuracy because of a lack of radiographic expertise. Duplex scanning is less sensitive for clots below the knee and detects only 80% of distal thrombi.[83,89] Supra-inguinal veins are also hard to visualize. In addition, Duplex scans are less likely to detect non-occluding thrombi. During the second half of pregnancy, ultrasound becomes less specific, because the gravid uterus compresses the inferior vena cava, thereby changing Doppler flow in the lower extremities.[90] However, an experienced sonographer may still detect a clot in a pregnant patient by demonstrating a non-compressible vein.

Table 4. Scoring System for Risk of DVT

CLINICAL FEATURE	SCORE
Active Cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremeties	1
Recently bedridden for more than 3 days or major surgery, within 4 weeks	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling by more than 3 cm when compared to the asymptomatic leg (measured 10 cm below tibial tuberosity)	1
Pitting edema (greater in the asymptomatic leg)	1
Collateral superficial veins (non-varicose)	1
Alternative diagnosis as likely or greater than that of deep-vein thrombosis	-2

Low probability ≤ 0
Moderate probability 1 or 2
High probability ≥ 3

Source: Anand SS, et al. Does this patient have deep vein thrombosis? *JAMA* 1998;279:1094-1099.

Outcome-Effective Evaluation: A Multi-Modal Approach

Studies suggest that a limited examination of only the common femoral and popliteal veins may be as sensitive as the traditional venous survey and may be performed in half the time.[91] Another approach to saving cost is to limit use of the ultrasound to the symptomatic extremity. This also cuts scanning time by half while maintaining acceptable accuracy.[92]

When the emergency physician suspects DVT and the ultrasound is positive, subsequent treatment is automatic. But what about the patient with a suspected thrombosis who has a negative Doppler? Two to three percent of such patients later prove to have DVT, and some suffer fatal pulmonary embolism.[93,94] For this reason, many authorities recommend at least one additional ultrasound or IPG within the first week of presentation, in all patients with a negative study.[95] In this regard, two normal ultrasounds one week apart essentially exclude the diagnosis of DVT.[96] Serial testing, however, is costly; many patients are lost to follow-up,

Table 5. Differential Diagnosis of a Swollen Leg

DVT	Abscess
Post-phlebitic syndrome	hypoproteinemia
Cellulitis—most important	Congestive heart failure
Muscle injury/hematoma	Lymphedema
Popliteal cyst (Baker's cyst)	Malignancy
Superficial phlebitis	Factitious
Capillary leak syndrome	AV fistula
Fracture	Acute arthritis
Compartment syndrome	Myositis
Nerve root irritation	

and the vast majority of patients who do undergo serial studies are disease free. As a result, if a definitive diagnosis can be made in the ED without serial studies, it would save time, money, and perhaps lives. One such strategy is the use of pretest probabilities, a strategy that relies on the patient's risk factors

Risk Factor Analysis and Pretest Probability. Patients with suspected DVT may be divided into those with low, moderate, and high pretest probability. The scoring is based on risk factors, symptoms, and physical signs. *(See Table 4.)* In a prospective study, the prevalence of DVT was 85% in the high pretest probability category, 33% in the moderate, and 5% in the low category.[97] If the pretest probability was high and the ultrasound was positive, or if the pretest probability was low and the ultrasound was negative, the results were deemed *concordant*. Patients with ultrasounds concordant with the pretest probability were treated according to the ultrasound results. A patient with a high pretest probability and a positive ultrasound required anticoagulation, while a patient with a low pretest probability and a negative ultrasound required no further treatment. The authors demonstrated that "only 0.6% (3) of 481 (95%; CI, 0.1-1.8) patients with low or moderate pretest probability with a negative initial or serial ultrasound, respectively, developed DVT or PE in the three months of follow-up."[97]

Patients with *discordant* results (i.e., high pretest probability and negative Doppler, or low pretest probability and positive Doppler) were subject to immediate venography. This strategy resulted in the highest diagnostic accuracy rate. Since only 6% of patients with high pretest probability and negative ultrasounds had DVT on venography, the authors suggested such patients might be safely managed with a repeat ultrasound in one week instead of immediate venography. However, they did not test this hypothesis. This study also demonstrated that patients with a low pretest probability and a negative ultrasound did not require serial studies.

Combination D-dimer and Impedance Plethysmography. While using pretest probabilities is one way to eliminate the need for serial studies, the addition of the D-dimer test may be another. One study examined the utility of combining the D-dimer test with IPG. The combination of a negative D-dimer and a negative IPG had a negative predictive value of 98.5% for DVT over the subsequent three months.[64] There is no reason why such results should not apply to patients imaged with Doppler as well. Using this logic, the combination of a negative D-dimer and negative ultrasound may obviate serial studies.

Magnetic Resonance Imaging. Magnetic Resonance Imaging (MRI) represents a significant advance in the diagnosis of DVT. It detects leg, pelvis, and pulmonary thrombi and is 97% sensitive and 95% specific for DVT.[98,99] It distinguishes a mature from an immature clot.[100] Because it is expensive and requires significant patient cooperation, it should not replace ultrasound as the primary screening tool. It is most useful in the second and third trimester of pregnancy when ultrasound becomes less accurate. MRI is safe in all stages of pregnancy.[101]

Differential Diagnosis

The differential diagnosis of the swollen or painful leg is broad. *(See Table 5.)* Many conditions can cause bilateral leg edema, secondary to either hypoproteinemia or an increase in venous or lymphatic pressure. Pregnancy, CHF, nephrotic syndrome, liver disease, or capillary leak syndrome can all produce bilateral leg swelling.[47] If prior DVT has unilaterally damaged venous valves, asymmetric swelling will occur with all of these conditions. Abdominal masses such as gravid uterus, hematoma, malignancy, or abscess, can compress a single iliac vein leading to ipsilateral venous stasis.[56]

Patients with the postphlebitic syndrome develop recurrent unilateral pain and swelling that is clinically indistinguishable from acute DVT. Such patients require objective testing for diagnosis. Recognize that ultrasound, IPG, and even venography will be abnormal and difficult to interpret in the presence of chronic changes.

Cellulitis is an important consideration and may be clinically difficult to distinguish from DVT.[102] While fever, chills, and leukocytosis are more common with cellulitis, these findings can occur with DVT. Duplex scanning is the best method to differentiate cellulitis from DVT. One study suggests that a needle aspirate of the edema fluid can identify cellulitis. A protein level greater than 10 g/L of edema fluid denotes infection.[103]

Lymphedema may also produce unilateral leg swelling. In the United States, malignancy is the most likely cause of lymphedema, while in third world countries filariasis is a common cause. Unlike DVT, septic arthritis and other causes of monoarticular arthritis are characterized by joint pain on range of motion. A Baker's cyst is a popliteal cyst filled with synovial fluid that may present as a mass behind the knee.[104] It usually occurs in association with chronic arthritis. Rupture of a popliteal this cyst may produce pseudothrombophlebitis clinically indistinguishable from acute DVT.[105] A ruptured Baker's cyst is best diagnosed by MRI, knee arthrogram, or duplex sonography.[106-108] A tear of the Achilles tendon or a calf muscle (usually soleus) causes acute pain and may be associated with a hematoma or ecchymosis.[109] Arterio-venous (AV) fistula also produces unilateral pain and swelling. A positive straight leg raise sign signals nerve root irritation, while elevations of creatinine kinase characterize significant myositis.

References

1. Milne AA, Stonebridge PA, Bradbury AW, et al. Venous function and clinical outcome following deep vein thrombosis. *Br J Surg* 1994;81(6):847-849.
2. Zamorski MA, Opdycke RA. Advances in the prevention, diagnosis, and treatment of deep venous thrombosis. *Am Fam Physician* 1993;47:457-469.
3. Carter CJ. The natural history and epidemiology of venous thrombosis. *Prog Cardiovasc Dis* 1994;36:423-438.
4. Hirsh J, Hoak J. Management of deep vein thrombosis and pulmonary embolism. A statement for healthcare professionals. Council on Thrombosis (in constitution with the Council on Cardiovascular Radiology), American Heart Association. *Circulation* 1996;93:2212-2245.
5. Lensing AWA, Hirsh J, Buller HR. Diagnosis of venous thrombosis. In: Colman RW, Hirsh J, Marder VJ, et al, eds. H*emostasis and thrombosis: Basic principles and clinical practice*. 3rd ed. Philadelphia, PA: J.B. Lippincott; 1994:1297-1321.
6. Ferris EJ. Deep venous thrombosis and pulmonary embolism: Correlative evaluation and therapeutic implications. *Am J Roentgenol* 1992;159:1149-1155.
7. Kniffin WD, Jr., Baron JA, Barrett J, et al. The epidemiology of diagnosed pulmonary embolism and deep venous thrombosis in the elderly. *Arch Intern Med* 1994;154:861-866.
8. Radecki RT, Gaebler-Spira D. Deep vein thrombosis in the disabled pediatric population. *Arch Phys Med Rehabil* 1994;75:248-250.
9. Cogo A, Bernardi E, Prandoni P, et al. Acquired risk factors for deep-vein thrombosis in symptomatic outpatients. *Arch Intern Med* 1994;151:164-168.
10. Coon WW, Willis PWI, Keller JB. Venous thromboembolism and other venous disease in the Tecumseh: Community health study. *Circulation* 1973;48:839.
11. Dunmire SM. Pulmonary embolism. *Emerg Med Clin N Am* 1989;7:339-354.
12. Sahiar F, Mohler SR. Economy class syndrome. *Aviat Space Environ Med* 1994;65:957-960.
13. Weingarden SI. Deep venous thrombosis in spinal cord injury. Overview of the problem. *Chest* 1992;102:63, 6S-9S.
14. Sharrok NE, Go G, Sculco TP, et al. Changes in circulatory indices of thrombosis and fibrinolysis during total knee arthroplasty performed under tourniquet. *J Arthroplasty* 1995;10:523-528.
15. Prins MH, Lensing AW, Hirsh J. Idiopathic deep venous thrombosis. Is a search for malignant disease justified? *Arch Intern Med* 1994;154:1310-1312.
16. Dhami MS, Bona RD. Thrombosis in patients with cancer. *Postgrad Med* 1993;92:131-133, 137-140.
17. Kakkar AK, DeRuvo N, Chinswangwatanakul V, et al. Extrinsic pathway activation in cancer with high factor VIIa and tissue factor. *Lancet* 1995;346:1004-1005.
18. Nordstrom M, Lindblad B, Anderson H, et al. Deep venous thrombosis and occult malignancy: An epidemiological study. *BMJ* 1994;308:891-894.
19. Prandoni P, Lensing AWA, Buller HR, et al. Deep-vein thrombosis and the incidence of subsequent symptomatic cancer. *N Engl J Med* 1992;327:1128-1133.
20. Callander N, Rapaport SI. Trousseau's syndrome. *West J Med* 1993;158:364-371.
21. Alving BM, Comp PC. Recent advances in understanding clotting and evaluating patients with recurrent thrombosis. *Am J Obstet-Gyncol* 1992;167:1184-1191.
22. Vandenbroucke JP, Koster T, Briet E, et al. Increased risk of venous thrombosis in oral contraceptive users who are carriers of factor V Leiden mutation. *Lancet* 1994;344:1453-1457.
23. DeMattia D, Penza R, Giordano P, et al. Thromboembolic risk in children with nephrotic syndrome. *Haemostasis* 1991;21: 300-304.
24. Ginsberg KS, Liang MH, Newcomer L, et al. Anticardiolipin antibodies and the risk for ischemic stroke and venous thrombosis [see comments]. *Ann Intern Med* 1992;117:997-1002.
25. Bick RL, Baker WF, Jr. The antiphospholipid and thrombosis syndromes. *Med Clin North Am* 1994;78:667-684.
26. Provenzale JM, Ortel TL. Anatomic distribution of venous thrombosis in patients with antiphospholipid antibody: Imaging findings. *Am J Roentgenology* 1995;165:365-368.
27. Geerts WH, Code KI, Jay RM, et al. A prospective study of venous thromboembolism after major trauma [see comments]. *N Engl J Med* 1994;331:1601-1606.
28. Schmidt U, Enderson BL, Chen Jp, et al. D-dimer levels correlate with pathologic thrombosis in trauma patients. *J Trauma* 1992;33:312-319.
29. Andrew M, David M, Adams M, et al. Venous thromboembolic complications (VTE) in children: First analyses of the Canadian Registry of VTE. *Blood* 1994;83:1251-1257.
30. Meredith JW, Young JS, O'Neil EA, et al. Femoral catheters and deep venous thrombosis: A prospective evaluation with venous duplex sonography. *J Trauma* 1993;35:187-190.
31. Menzoian JO, Doyle JE. Venous insufficiency of the leg. *Hosp Pract* 1989;24:109.
32. Bundens WP, Bergan JJ, Halasz NA, et al. The superficial femoral vein. A potentially lethal misnomer. *JAMA* 1995;274: 1296-1298.
33. Lisse JR, Davis CP, Thormond-Anderle M. Cocaine abuse in deep venous thrombosis. *Ann Intern Med* 1989;110:571.
34. Samlaska CP, James WD, Simel DL. Superficial migratory thrombophlebitis and factor XII deficiency. *J Am Acad Dermatol* 1990;22:939.
35. Villavicencio JL, Gonzalez-Cerna JL. Acute vascular problems of children. *Curr Probl Surg* 1985;22:1.
36. Jorgensen JO, Hanel KC, Morgan AM, et al. The incidence of deep venous thrombosis in patients with superficial thrombophlebitis of the lower limbs. *J Vasc Surg* 1993;18:70-73.
37. Lutter KS, Kerr TM, Roedersheimer LR, et al. Superficial thrombophlebitis diagnosed by duplex scanning. *Surgery* 1991;110:42-46.
38. Philbrick JT, Becker DM. Calf deep venous thrombosis. A wolf in sheep's clothing? *Arch Intern Med* 1988;148:2131-2138.
39. Saeger W, Genzkow M. Venous thromboses and pulmonary embolisms in post-mortem series: Probable causes by correlations of clinical data and basic diseases. *Pathol Res Pract* 1994;190: 394-399.
40. Giachino A. Relationship between deep-vein thrombosis in the calf

and fatal pulmonary embolism. *Can J Surg* 1988;31:129-130.
41. Rahm M, Probe R. Extensive deep venous thrombosis resulting in compartment syndrome of the thigh and leg. A case report. *J Bone Joint Surg—American volume*. 1994;76:1854-1857.
42. van Ramshorst B, van Bemmelen PS, Hoeneveld H, et al. Thrombus regression in deep venous thrombosis. Quantification of spontaneous thrombolysis with duplex scanning. *Circulation* 1992;86:414-419.
43. Lipchik EO, DeWeese JA, Rogoff SM. Serial long-term phlebography after documented lower leg thrombosis. *Radiology* 1976;120:563.
44. Hopkins NFG, Wolfe JHN. Deep venous insufficiency and occlusion. *Med J* 1992;304:107.
45. Cronan JJ, Leen V. Recurrent deep venous thrombosis: Limitations of ultrasound. *Radiology* 1989;170:739.
46. Colucciello SA, Plotka M. The Patient with Chronic Venous Insufficiency. In: Herr R, Cydulka R, eds. *Emergency Care of the Compromised Patient*. Philadelphia, PA: JB Lippincott; 1994:370-382.
47. Barnes RW, Wu KK, Hoak JC. Fallibility of the clinical diagnosis of venous thrombosis. *JAMA* 1975;234:605.
48. Moser KM, Fedullo PF, LitteJohn JK, et al. Frequent asymptomatic pulmonary embolism in patients with deep venous thrombosis [published erratum appears in *JAMA* 1994;271:1908] [see comments]. *JAMA* 1994;271:223-225.
49. DeGowin RL. *DeGowin and DeGowin's Diagnostic Examination* 6th Ed. New York: McGraw Hill, Health Professionals Division; 1994.
50. Sheiman RG, Weintraub JL, McArdle CR. Bilateral lower extremity US in the patient with bilateral symptoms of deep venous thrombosis: Assessment of need. *Radiology* 1995;196:379-811.
51. O'Donnell T, Abbott W, Athanasoulis C, et al. Diagnosis of deep venous thrombosis in the outpatient by venography. *Surg Gynecol Obstet* 1980;150:69-74.
52. Stein PD, Henry JW, Gopalakrishnann D, et al. Asymmetry of the calves in the assessment of patients with suspected acute pulmonary embolism. *Chest* 1995;107:936-939.
53. Anand SS, Wells PS, Hunt D, et al. Does this patient have deep vein thrombosis? *JAMA* 1998;279:1094-1099.
54. Anonymous. *Cecil Textbook of Medicine.* Philadelphia, PA: W.B. Saunders; 1988.
55. Sapira JD. *The Art and Science of Bedside Diagnosis.* Baltimore, MD: Urban & Schwarzenberg; 1990.
56. Hirsh J, Hull RD, Raskob GE. Clinical features and diagnosis of venous thrombosis. *J Am Coll Cardiol* 1986;8:114B.
57. Prescott SM, Tikoff G. Deep venous thrombosis of the upper extremity: A reappraisal. *Circulation* 1979;59:350-355.
58. Huisman MV, Buller HR, ten Cate JW. Utility of impedance plethysmography in the diagnosis of recurrent deep-vein thrombosis. *Arch Intern Med* 1988;148:681.
59. Cronan JJ. Venous thromboembolic disease: The role of US. [Review]. *Radiology* 1993;186:619-630.
60. McKinley L, Wrenn. Are baseline prothrombin time/partial thromboplastin time values necessary before instituting anticoagulation? *Ann Emerg Med* 1993;22:697-702.
61. Hirsh J, Poller L. The International Normalized Ratio. A guide to understanding and correcting its problems. *Arch Intern Med* 1994;154:282-288.
62. Greenspan RH. Pulmonary angiography and the diagnosis of pulmonary embolism. [Review]. *Prog Cardiovasc Dis* 1994;37:93-105.
63. Levi PJ, Gonzalez FM, Rush DS, et al. Hypercoagulable states as an evolving risk for spontaneous venous and arterial thrombosis. *J Am Coll Surg* 1994;178:266-270.
64. Ginsburg JS, Kearon C, Douketis J, et al. The use of D-dimer testing and impedance plethysmographic examination in patients with clinical indications of deep vein thrombosis [see comments]. *Arch Intern Med* 1997;157:1077-1081.
65. de Moerloose P, Minazio P, Reber G, et al. D-dimer determination to exclude pulmonary embolism: A two-step approach using latex assay as a screening tool. *Thromb Haemost* 1994;72:89-91.
66. van Beek EJ, van den Ende B, Berkmans RJ, et al. A comparative analysis of D-dimer assays in patients with clinically suspected pulmonary embolism. *Thromb Haemost* 1993;70:408-413.
67. Bounameaux H, Cirafici P, de Moerloose P, et al. Measurement of D-dimer in plasma as diagnostic aid in suspected pulmonary embolism. *Lancet* 1991;337:196-200.
68. Ginsberg JS, Brill-Edwards PA, Demers C, et al. D-dimer in patients with clinically suspected pulmonary embolism. *Chest* 1993;104:1679-1684.
69. Wells PS, Brill-Edwards P, Stevens P, et al. A novel and rapid whole-blood assay for D-dimer in patients wit clinically suspected deep vein thrombosis. *Circulation* 1995;91:2184-2187.
70. Wells PS, Brill-Edwards P, Stevens P, et al. A novel and rapid whole-blood assay for D-dimer in patients with clinically suspected deep vein thrombosis. *Circulation* 1995;91:2184-2187.
71. Bounameaux H, Cirafici P, de Moerloose P, et al. Measurement of D-dimer in plasma as a diagnostic aid in suspected pulmonary embolism. *Lancet* 1991;337:196-200.
72. Redman HC. Deep venous thrombosis: Is contrast venography still the diagnostic "gold standard?" *Radiology* 1988;168:277.
73. Hirsh J. Clinical utility of impedance plethysmography in the diagnosis of recurrent deep-vein thrombosis. *Arch Intern Med* 1988;148:519.
74. Kearon C, Julian JA, Newman TE, et al. Noninvasive diagnosis of deep venous thrombosis. McMaster Diagnostic Imaging Practice Guidelines Initiative. *Ann Intern Med* 1998;128:663-677.
75. Wu KK, Hoak JC, Barnes RW. A prospective comparison of four methods for the diagnosis of deep vein thrombosis. *Thromb Diath Haemorrh* 1974;32:260.
76. White GH. Chronic venous insufficiency. In: Wilson SE, ed. *Vascular surgery principles and practice.* New York: McGraw-Hill; 1987:736.
77. Warwick DJ, Thornton MJ, Freeman S, et al. Computerized strain-gauge plethysmography in the diagnosis of symptomatic and asymptomatic venous thrombosis. *Br J Radiol* 1994;67: 938-940.
78. Ginsberg JS, Wells PS, Hirsh J, et al. Reevaluation of the sensitivity of impedance plethysmography for the detection of proximal deep vein thrombosis [see comments]. *Arch Intern Med* 1994;154:1930-1933.
79. Anderson DR, Lensing AW, Wells PS, et al. Limitations of imped-

ance plethysmography in the diagnosis of clinically suspected deep-vein thrombosis. *Ann Intern Med* 1993;118:25-30.
80. Heijboer H, Buller HR, Lensing AWA, et al. A comparison of real-time compression ultrasonography with impedance plethysmography for the diagnosis of deep-vein thrombosis in symptomatic outpatients. *N Engl J Med* 1993;329:1365-1369.
81. Vogel P, Laing FC, Jeffrey RB, et al. Deep venous thrombosis of the lower extremity: US evaluation. *Radiology* 1987;163:747.
82. Kristo DA, Perry ME, Kollef MH. Comparison of venography, duplex imaging, and bilateral impedance plethysmography for diagnosis of lower extremity deep vein thrombosis. *South Med J* 1994;87:55-60.
83. Polak JF. Doppler ultrasound of the deep leg veins: A revolution in the diagnosis of deep vein thrombosis in monitoring of thrombolysis. *Chest* 1991;99:165S.
84. Abu Rahma RF, Kennard W, Robinson PA, et al. The judicial use of venous duplex imaging and strain gauge plethysmography (single or combined) in the diagnosis of acute and chronic deep venous thrombosis. *Surg Gynecol Obstet* 1992;174:52.
85. Rose SC, Zwiebel WJ, Nelson BD, et al. Symptomatic lower extremity deep venous thrombosis: Accuracy, limitations, and role of colored duplex flow imaging in diagnosis. *Radiology* 1990;175:639.
86. Lewis BD, James EM, Welch TJ, et al. Diagnosis of acute deep venous thrombosis of the lower extremities: Prospective evaluation of color Doppler flow imaging versus venography. *Radiology* 1994;192:651-655.
87. Buchbinder D, McCullough GM, Melick CF. Patients evaluated for venous disease may have other pathologic conditions contributing to symptomatology. *Am J Surg* 1993;166:211-215.
88. Hill SL, Holtzman GI, Martin D, et al. Selective use of the duplex scan in the diagnosis of deep venous thrombosis. *Surg* 1995;170:201-205.
89. Messina LM, Sarpa MS, Smith MA, et al. Clinical significance of routine imaging of iliac and calf veins by color flow duplex scanning in patients suspected of having acute lower extremity deep venous thrombosis. *Surgery* 1993;114:921-927.
90. Douketis JD, Ginsberg JS. Diagnostic problems with venous thromboembolic disease in pregnancy. [Review]. *Haemostasis* 1995;25:58-71.
91. Pezzullo JA, Perkins AB, Cronan JJ. Symptomatic deep vein thrombosis: Diagnosis with limited compression US. *Radiology* 1996;198:67-70.
92. Sheiman RG, Weintraub JL, McArdle CR. Bilateral lower extremity US in the patient with bilateral symptoms of deep venous thrombosis: Assessment of need. *Radiology* 1995;196:379-381.
93. Cogo A, Lensing AW, Koopman MM, et al. Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein thrombosis: Prospective cohort study. *BMJ* 1998;316:17-20.
94. Ginsberg JS. Management of venous thromboembolism. *N Engl J Med* 1996;335:1816-1828.
95. Koopman MM, van Beek EJ, ten Cate JW. Diagnosis of deep vein thrombosis. *Prog Cardiovasc Dis* 1994;37:1-12.
96. Birdwell BG, Raskob GE, Whitsett TL, et al. The clinical validity of normal compression ultrasonography in outpatients suspected of having deep vein thrombosis. *Ann Intern Med* 1998;128:1-7.
97. Wells PS, Hirsh J, Anderson DR, et al. Accuracy of clinical assessment of deep vein thrombosis. *Lancet* 1995;345:1326-1330.
98. Spritzer CE, Norconk JJ, Jr., Sostman HD, et al Detection of deep venous thrombosis by magnetic resonance imaging. *Chest* 1993;104:54-60.
99. Evans AJ, Sostman HD, Knelson MH, et al. 1992 ARRS Executive Council Award. Detection of deep venous thrombosis: Prospective comparison of MR imaging with contrast venography. *Am J Roentgenol* 1993;161:131-139.
100. Erdman WA, Jayson HT, Redman HC, et al. Deep venous thrombosis of extremities: Role of MR imaging in the diagnosis. *Radiology* 1990;174:425.
101. Spritzer CE, Evans AC, Kay HH. Magnetic resonance imaging of deep venous thrombosis in pregnant women with lower extremity edema. *Obstet-Gynecol* 1995;85:603-607.
102. Nordestgaard AG, Williams RA. Varicose veins. In: Wilson SE, ed. *Vascular surgery: Principles and practice*. New York; McGraw-Hill: 1987:711.
103. Berlyne GM, Kwan T, Li J, et al. Oedema protein concentrations for differentiation of cellulitis and deep vein thrombosis. *Lancet* 1989;2:728-729.
104. Rosian R, Mandell BF. A 47-year-old woman with a swollen leg. *Cleve Clin J Med* 1995;62:281-284.
105. Gomez J, Kattamis A, Scheneck Jr. Pseudothrombophlebitis in an adolescent without rheumatic disease. A case report. *Clin Ortho Rel Res* 1994;3308:250-253.
106. Lazarus ML, Ray CE Jr, Maniquis CG. MRI findings of concurrent acute DVT and dissecting popliteal cyst. *Magn Reson Imaging* 1994;12:155-158.
107. Soriano ER, Catoggio LJ. Baker's cysts, pseudothrombophlebitis, pseudo-pseudothrombophlebitis: Where do we stand? *Clin Exp Rheumatol* 1990;8:107-112.
108. Brady HR, Quigley C, Stafford FJ, et al. Popliteal cyst rupture and

the pseudothrombophlebitis syndrome. *Ann Emerg Med* 1987;16:1151-1154.

109. Thompson JS, Kaufman RL, Beardmore TD. Pseudothrombophlebitis in neuropathic arthropathy. *J Rheumatol* 1989;16:1606.

Physician CME Questions

9. Surgery and trauma are responsible for what percent of all thromboembolic disease resulting from hypercoagulable state and immobility?
   A. 10%
   B. 40%
   C. 90%
   D. 75%
   E. 80%

10. Increased estrogen occurs in a patient:
   A. during all stages of pregnancy.
   B. after elective abortion.
   C. during treatment with oral contraceptive pills.
   D. during the first three months post-partum.
   E. all of the above.

11. Clinical examination alone is able to confirm what percent of DVT cases?
   A. 20-30%
   B. 50%
   C. 5%
   D. 60-70%

12. Radiologists disagree on the interpretation of what percent of venography cases?
   A. 50%
   B. Less than 5%
   C. At least 10%
   D. 75%

13. A sonographer can distinguish a fresh clot from an old clot based on:
   A. collateral flow.
   B. echogenicity.
   C. homogeneity.
   D. all of the above.

14. Duplex scanning:
   A. is most sensitive for clots below the knee.
   B. is less sensitive for clots below the knee.
   C. detects 30% of distal thrombi.
   D. is more likely to detect non-occluding thrombi.

15. What percent of patients with suspected thrombosis and a negative ultrasound later prove to have DVT?
A. 10%
B. 25%
C. 2-3%
D. 40-45%

16. Bilateral leg swelling can be caused by:
   A. liver disease.
   B. nephrotic syndrome.
   C. capillary leak syndrome.
   D. pregnancy.
   E. all of the above.

In Future Issues

DVT: Part II