

The Swollen Extremity: A Systematic Approach To The Evaluation Of A Common Complaint

It is another busy night in the emergency department; five admitted patients are waiting for beds and three patients are waiting for CT scans. Space and resources are limited. Your next patient is an obese, 35-year-old, female visitor from Australia with no known medical problems. She tells you that she never comes to the emergency room, but decided to come in tonight because the pain in her right leg was keeping her awake. She has had mild to moderate pain in both knees "for a long time," but for the last two days her right lower leg has been progressively painful and swollen. She has been staying off her feet and taking ibuprofen, but the pain and swelling are not getting better. She also complains of a mild discomfort in her chest which she can not characterize. Her blood pressure is 140/90 mmHg, pulse is 100, respiratory rate is 20, temperature is 37.2°C, and her pulse oximetry is reading 95%. You note that her right ankle is diffusely red, swollen, and painful; her right calf measures 28 cm and her left calf measures 25 cm; her thighs are equal in size and there is no Homans' sign or palpable cords. Once again, you find yourself faced with the recurrent clinical decision of pursuing cellulitis vs DVT vs DVT plus PE and must decide how to best utilize your resources while providing quality emergency care. You order a diagnostic test . . .

Patients presenting to the emergency department (ED) with a swollen extremity can be a diagnostic challenge. The differential diagnosis is vast and includes a wide range of diseases from the benign to the potentially life threatening. As an emergency physician, it is crucial to consider all of the dangerous causes of a swollen extremity and to prioritize your diagnostic tests. The history and physical exam may reveal the cause to be related to previous trauma, surgery, systemic disease, infection, malignancy, or radia-

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CME Objectives

Upon completion of this article, you should be able to:

1. Discuss the potential causes of a swollen extremity.
2. Describe the imaging tests available to determine the diagnosis for a swollen extremity.
3. Discuss risk factors for deep venous thrombosis.
4. Evaluate, diagnosis, and treat the patient presenting with a swollen extremity.

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tion therapy. Once a working diagnosis is made, appropriate treatment can be initiated. This issue of *Emergency Medicine Practice* provides a systematic review of the diseases that present with a chief complaint of “swollen extremity” and provides a cost-effective approach to guide in the selection of diagnostic tests to aid in clinical decision-making.

Critical Appraisal Of The Literature

A literature search was performed using Ovid MEDLINE and PUBMED. Searches included articles on deep venous thrombosis, cellulitis, chronic venous insufficiency, acute compartment syndrome, necrotizing fasciitis, and edema. This search provided an enormous number of studies ranging from case series to well-designed, randomized, double-blinded studies. In addition, the Cochrane Database of Systemic Reviews was searched for updates on current management recommendations for deep venous thrombosis, cellulitis, and chronic venous insufficiency. Another source of information was the National Guideline Clearinghouse at www.guidelines.gov, which was created by the US Department of Health and Humans Services' Agency for Healthcare Research and Quality (AHRQ) in partnership with America's Health Insurance Plans (AHIP). This site provided guidelines published by the Infectious Diseases Society of America (IDSA) and the American College of Radiology (ACR), among others.

Abbreviations Used In This Article

CBC – Complete Blood Count
 CRP – C-reactive Protein
 DVT – Deep Venous Thrombosis
 ECG – Electrocardiogram
 ELISA – Enzyme-Linked ImmunoSorbent Assay
 ESR – Erythrocyte Sedimentation Rate
 LMWH – Low Molecular Weight Heparin
 LRINEC – Laboratory Risk Indicator for Necrotizing Fasciitis
 MRSA - Methicillin Resistant Staphylococcus Aureus
 ORIF – Open Reduction and Internal Fixation
 PCT – Procalcitonin
 SVC – Superior Vena Cava
 UFH – Unfractionated Heparin
 VTE – Venous Thromboembolism
 WBC – White Blood Cell

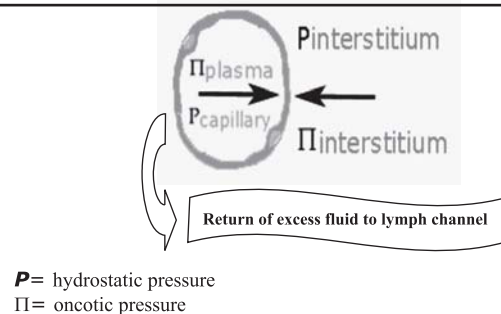
Epidemiology, Etiology, Pathophysiology

A swollen extremity is a frequent ED presentation and is usually associated with a large list of potential etiologies. Patients may complain of unilateral or bilateral swelling of the arms or legs. The swelling may be acute or chronic, painful or painless.

Edema occurs when there is excessive accumulation of fluid in the tissues. Swelling of the extremity results when a physiologic imbalance occurs between fluid pressure, oncotic pressure, capillary permeability, or lymphatic obstruction. The physiologic forces responsible for maintaining homeostasis is described in Starlings Law; see Figure 1.

Total body water is divided between the intracellular and extracellular spaces. The extracellular space, which comprises about one third of total body

Figure 1. Starlings Law: The rate of fluid transfer is a function of the permeability of the membrane and the difference between the hydrostatic pressures and oncotic pressures of fluid on either side of the membrane.



water, is composed of the intravascular plasma volume (25%) and the extravascular interstitial space (75%). Starling defined the physiologic forces involved in maintaining the balance of water between these two compartments which include the gradient between intravascular and extravascular hydrostatic pressures, differences in oncotic pressures within the interstitial space and plasma, and the hydraulic permeability of the blood vessel wall.

There are five common mechanisms of edema formation:

- 1. Plasma volume expansion:** Because interstitial tissue easily accommodates several liters of fluid, a patient's weight may increase nearly 10% before pitting edema is evident. The source of this expansion is the blood plasma. Because the volume of normal blood plasma is only about 3 L, the diffusion of large amounts of water and electrolytes into the interstitial space necessitates

the renal retention of sodium and water to maintain hemodynamic stability. Hence, blood volume and normal osmolality are maintained despite movement of large amounts of fluid into the extravascular space.

- 2. Increased venous pressure/capillary hydrostatic pressure:** In addition to an expansion in plasma volume, increased venous pressures due to central or regional venous outflow obstruction is a process that causes pressure to be transmitted to the capillary bed thereby increasing hydrostatic pressure and predisposing to edema.
- 3. Decreased plasma oncotic pressure:** Albumin is important for maintaining plasma oncotic pressure; low plasma albumin results in a decreased plasma oncotic pressure and filtration out of the capillary. Edema is often seen when the albumin level falls below 2 g/dL of plasma.¹
- 4. Increased capillary permeability:** Changes in capillary wall permeability are mediated by cytokines such as tumor necrosis factor, interleukin 1, and interleukin 10, by circulating vasodilatory prostaglandins and nitric oxide, and by chemical mediators including histamine, leukotrienes, and complement. These factors allow for the leakage of capillary proteins and fluid into the interstitium. Increased vascular permeability is central to edema resulting from local inflammation, infection, allergic reactions, and burns.
- 5. Lymphatic obstruction:** Normally, filtration of fluid out of capillaries is slightly greater than absorption of fluid into the capillaries. The excess filtered fluid is returned to circulation via the lymph channels. Interstitial fluid enters the lymph channels via unidirectional flow through one-way valves. Edema forms when the volume of interstitial fluid exceeds the ability of the lymphatics to return it to the circulation. Conditions such as lymph node resection after cancer surgery, filariasis, or lymphoma impair clearance fluid from the interstitial space by the lymphatic system.

Differential Diagnosis

The differential diagnosis for extremity swelling is extensive because numerous entities cause disruption of the aforementioned physiologic balance of fluid distribution; see Table 1. Often times the generalized swelling may be due to common medications;

see Table 2. In these cases, the diagnosis can often be made based on temporal association with drug administration and the exclusion of other potential acute causes of edema. Stopping these medications often returns extremities to normal.

Prehospital Care

Non-traumatic extremity swelling is an uncommon cause for EMS activation. However, pain or inability to ambulate may prompt a 911 call, placing the prehospital provider in a critical triage role. The EMS provider must identify those causes of a swollen extremity that require transport to a specialized center. For example, a swollen extremity with no pulse should go to a hospital with a vascular service. Likewise, a swollen extremity with ecchymosis and bullae must go to a hospital that can provide immediate surgical intervention for necrotizing fasciitis.

Extremity injuries should be splinted in the field before patient transport to prevent excessive fracture-site motion or to reduce pain in a dislocated joint. Assessment of the limb's neurovascular status must be made before and after application of the splint or realignment of a fracture. Application of splints should be applied as soon as possible, but they must not take precedence over resuscitation.

Emergency transport personnel can also be useful in providing information to the ED staff regarding the injury such as the mechanism of injury, time frame, and delays in extrication or transport. By eliciting the mechanism of injury, suspicion may be raised of other injuries not immediately apparent.

ED Evaluation

Initial Assessment

When a patient presents to the ED for the evaluation of a swollen extremity, the triage nurse must be aware of certain life or limb threatening conditions which require emergent evaluation by the emergency physician. In addition to obtaining a set of vital signs, the triage nurse should be on the alert for patients who present with concerning symptoms or signs, e.g., a swollen leg with shortness of breath (pulmonary embolism), a swollen extremity with ecchymosis and bullae or subcutaneous air (necrotizing fasciitis), or a swollen extremity with pain and pallor (compartment syndrome).

In trauma patients, it is important to completely undress the patient and to note the color of the extremity as well as the presence of pulses. This is

**Table 1. Differential Diagnosis Of The Swollen
Extremity Categorized By Physiologic Mechanisms**

Physiologic Mechanism	Associated Condition
Increased plasma volume	<u>Generalized body swelling</u> ¹⁴¹ Heart failure Renal failure Nephrotic syndrome ¹⁴² Cirrhosis/ liver failure ¹⁴³ Cor pulmonale/COPD ¹⁴⁴ Medications (see Table 2) Pregnancy Premenstrual edema ¹⁴⁵ Secondary aldosteronism ¹⁴⁶
Increased capillary hydrostatic pressure	<u>Systemic venous pressure (generalized body swelling)</u> Restrictive cardiomyopathy Constrictive pericarditis ¹⁴⁷ Tricuspid valvular disease <u>Regional venous pressure (often unilateral)</u> Superior vena cava syndrome Inferior vena cava/iliac vein compression syndrome ¹⁴⁸ Pelvic masses (ovarian cancer, prostate cancer, uterine fibromas, retroperitoneal fibrosis) ^{149, 150, 151} Deep venous thrombosis ¹⁵² Superficial thrombophlebitis Trauma (hematoma, ruptured gastrocnemius, or Achilles tendon) ¹⁵³ Chronic venous insufficiency ¹⁵⁴ Compartment syndrome ¹⁵⁵ Popliteal (Baker's) cyst ¹⁵⁶ Reflex sympathetic dystrophy (RSD) ¹⁵⁷ Pseudoaneurysm ¹⁵⁸
Decreased plasma oncotic pressure	<u>Reduced albumin synthesis (generalized or bilateral lower extremity swelling)</u> Malnutrition (e.g. kwashiorkor) Malabsorption Cirrhosis/ liver failure <u>Albumin loss (generalized or bilateral lower extremity swelling)</u> Preeclampsia ¹⁵⁹ Glomerulonephritis Malabsorption Burns ¹⁶⁰ Inflammatory bowel disease (IBD)
Increased capillary permeability	<u>Generalized, bilateral, or unilateral extremity swelling</u> Allergic reactions (hives, serum sickness, angioedema) Infection (cellulitis, osteomyelitis, abscess, septic arthritis) Vasculitis (erythema nodosum) ¹⁶¹ Inflammatory (burns, arthritis, sprain) Interleukin 2 therapy ¹⁶²
Lymphatic obstruction	<u>Bilateral or unilateral extremity swelling</u> Iatrogenic (postsurgical or radiation) ^{163, 164} Nodal enlargement due to malignancy (especially prostate cancer and lymphoma) Filariasis ¹⁶⁵ Primary lymphedema ¹⁶⁶
Other	<u>Generalized or bilateral extremity swelling</u> Idiopathic edema ¹⁶⁷ Hypothyroidism/pretibial myxedema ¹⁶⁸ Lipidema ¹⁶⁹

particularly important in patients who are non-responsive or intoxicated. If significant injury is suspected, the extremity should be monitored for compartment syndrome.

History

Extremity swelling is due to a wide range of causes including systemic illnesses, local conditions, and medications. The diagnosis can be narrowed by categorizing the edema according to its duration (acute or chronic) and distribution (unilateral or bilateral, upper or lower extremity). Table 3 provides a list of relevant questions that may be helpful in focusing on the likely etiology of a swollen extremity. Relevant questions pertain to the patient's underlying medical condition. Other historical details are also helpful.

Physical Examination

Vital Signs: Initial abnormal vital signs may provide clues to a swollen extremity. For example, the presence of fever may point toward an infection such as cellulitis, abscess, osteomyelitis, or septic joint. However, an elevation in temperature is not a reliable indicator of infection in elderly patients. One Canadian study on the ED management of cellulitis in the elderly showed that fever of greater than 37.8°C was present in only 7% of patients.² Patients with DVT/PE can also present with fever caused by

a systemic inflammatory response as demonstrated in a prospective study of 311 patients in which a temperature greater than or equal to 37.8°C was reported to be present in 14% of patients diagnosed with PE.³

A respiratory rate of 20 per minute or more, and/or a heart rate of greater than 100 beats per minute can be present in a wide variety of conditions. This can be seen in heart failure, liver failure, cor pulmonale, renal failure, fever, dehydration, and pain. The onus is always on the emergency physician to find the etiology of an abnormal vital sign and to never discharge a patient with an unexplained abnormality. Tachycardia and tachypnea are frequently found in PE and should be suspected in patients with these findings.⁴

Hypertension in an edematous, pregnant patient is a concern because of the risk of preeclampsia, which affects 2 to 7% of healthy nulliparous women in the US. However, edema is so prevalent in normal pregnancies that it has been dropped from the current definition of preeclampsia.⁵ Mild edema is likely to be benign, but sudden, severe, generalized edema, associated with hypertension in a pregnant patient, raises concern. Gestational hypertension is defined as a systolic BP of at least 140 mmHg and/or diastolic BP of at least 90 mmHg on at least two occasions at least six hours apart after the 20th week of gestation in a previously normotensive woman.

Table 2. Medications That Cause Bilateral Swollen Extremities

Medication Type	Class of Medication
Psychiatric medications	Monoamine oxidase inhibitors Antipsychotics (olanzapine) ¹⁷⁰
Antihypertensive medications	Calcium channel blockers (nifedipine, felodipine, amlodipine, verapamil, diltiazem) ^{171, 172} Direct vasodilators (hydralazine, minoxidil, diazoxide) Beta-blockers Antiadrenergics (clonidine, reserpine, methyl dopa) ¹⁷³
Hormones	Estrogens/progesterones, testosterone, corticosteroids
Pain relief medications	NSAIDs ¹⁷⁴ Nonselective cyclooxygenase inhibitors Selective cyclooxygenase-2 inhibitors ¹⁷⁵
Diabetic medications	Thiazolidinediones (rosiglitazone, pioglitazone) ^{176, 177}
Chemotherapy	Gemcitabine, docetaxel ^{178, 179}

Preeclampsia is defined as gestational hypertension with proteinuria (300 mg or more in a 24 hour urine collection). Two urine dipsticks with 1+ for protein done at least six hours apart are also suggestive of proteinuria, but a 24 hour urine collection remains the gold standard.⁶

Cardiopulmonary And Abdominal Examination:

Patients, especially those with age greater than 45 or those who have a history of hypertension, coronary artery disease, or congestive heart failure, should receive a cardiopulmonary and abdominal examination. Rales, jugular venous distension, systolic murmur, or pericardial friction rub on exam indicate a cardiac etiology. An electrocardiogram (ECG) may also provide additional clues to a cardiac cause. For example, evidence of an inferior wall myocardial infarction may suggest right sided failure as an etiology and explain why the patient has no pulmonary findings.

Performing an abdominal exam on a patient who has a history of chronic alcohol use, cirrhosis, or hepatitis is necessary. Shifting dullness on abdominal exam, fluid wave in abdominal exam, spider angiomas, or jaundice all point to liver disease and will prompt laboratory testing to investigate the

patient's serum protein level. Palpable abdominal or pelvic masses may cause external venous or lymphatic compression. In these cases, ovarian cancer or prostate cancer should be suspected.

Upper/Lower Extremity Examination: Patients with swelling presenting with a cast or bandage should have it removed immediately in order to reduce external compression and provide full exposure. Note whether the distribution is unilateral or bilateral, localized or diffuse. Assess for warmth and tenderness as well as whether the skin is tense, firm, doughy, thickened, erythematous, or hyperpigmented. The presence of fluctuance, pulsations, and crepitus are additional findings that may direct a diagnosis. Finally, a determination of whether the edema is pitting or non-pitting may help to distinguish vascular (pitting) from lymphatic (non-pitting) pathologies.

Arm swelling may occur alone or in conjunction with facial swelling or jugular venous distension, as in the case of superior vena cava (SVC) syndrome. The veins of the upper extremity are distended in 60 to 70% of patients with SVC syndrome.⁷ For acute unilateral calf swelling, it is essential to consider deep venous thrombosis. Physical findings include

Table 3. Key Questions For History Of Present Illness

Key Questions	Possible Etiologies
Sudden onset of pain?	Muscle or tendon rupture, musculoskeletal injury, vascular catastrophe
Associated shortness of breath?	Congestive heart failure, SVC syndrome, deep venous thrombosis (with associated pulmonary embolism)
Associated fever?	Cellulitis, septic thrombophlebitis, deep venous thrombosis, necrotizing fasciitis
Recent prolonged travel?	Travel-related deep venous thrombosis
Recent surgery?	Deep venous thrombosis, post-surgical infection
Recent trauma or trauma in the past?	Contusions, tendon or muscle rupture, compartment syndrome, deep venous thrombosis, hematoma, reflex sympathetic dystrophy
Recent or current pregnancy?	Deep venous thrombosis, preeclampsia
Any current use or past use of a blood thinner?	Deep venous thrombosis, compartment syndrome in the setting of trauma (with current use of anticoagulants)
Any history of cancer?	Deep venous thrombosis, external venous compression from a tumor (ovarian or prostate), lymphatic obstruction (can occur years after cancer surgery)
Any current use of antibiotics?	Cellulitis or abscess complicating failed treatment of minor skin infection
Have you recently started a new medication?	A long list of culprits; see Table 2
Did you recently come from a developing country?	Filariasis, a parasitic infection transmitted by mosquitoes, affects more than 120 million people worldwide. ¹⁸⁵

unilateral swelling, tenderness, warmth, palpable cord of a thrombosed vein, and Homans' sign (pain on passive dorsiflexion of the foot). When there is clinical suspicion, it must be followed by an appropriate workup; see the Diagnostic Studies section.

Other, less benign causes of lower extremity swelling include Achilles tendon rupture, gastrocnemius rupture, and Baker's cyst rupture. Achilles tendon rupture and gastrocnemius rupture are injuries which generally occur in the setting of sports. Perform the Thompson-Doherty test to help determine the diagnosis; this test involves squeezing the midportion of the calf with the patient lying in the prone position. If the Achilles tendon is torn, plantar flexion of the foot is absent. If the gastrocnemius is ruptured, plantar flexion is present and the pain and swelling involves the proximal medial portion of the calf.⁸

Diagnostic Studies

Laboratory Testing

Complete blood count (CBC): Though an elevated WBC count is associated with infection, its predictive value for bacterial disease is low.⁹ However, an elevated WBC count has been shown to help distinguish necrotizing fasciitis with non-necrotizing soft tissue infection. A study by Wall et al proposed a simple model to serve as an adjunctive tool in diagnosing necrotizing fasciitis. The investigators reported that 90% of necrotizing fasciitis patients and 24% of non-necrotizing fasciitis patients met this model: WBC greater than 15.4 per mm³ or serum sodium less than 135mmol/L.¹⁰ The model had a sensitivity

of 90%, a specificity of 76%, a positive predictive value of 26%, and a negative predictive value of 99%.

Serious bacterial illnesses may also present with a normal WBC count, and noninfectious causes can result in an elevated WBC count. As early as 1919, it was noted that patients with battle injuries, particularly extremity wounds with hemorrhage, had leukocytosis.¹¹ Since then, various studies have looked at the leukocyte count and lymphocyte count in trauma patients as a predictor of mortality, but the results have been inconclusive.¹²⁻¹⁴ A study by Rainer et al sought to characterize the changes in peripheral leukocyte counts in 20 patients over a three hour time period following injury. They found that granulocytosis, lymphocytosis, and monocytosis were evident within 40 minutes of injury and there was no correlation with injury severity.¹⁵

Chemistry Panel: A chemistry panel may be helpful in a variety of conditions. A patient who is suspected of having compartment syndrome from a crush injury may have electrolyte abnormalities from rhabdomyolysis. A chemistry panel may reveal hyperkalemia and abnormal calcium and phosphorus levels. Serum creatinine and blood urea nitrogen are also useful to determine baseline renal status and identify acute renal failure. The serum chemistry panel may also be helpful in the early recognition of necrotizing fasciitis. Wong et al devised the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score to help distinguish necrotizing fasciitis from other soft tissue infections; see Table 4.¹⁶

D-Dimer: There have been a number of studies which have evaluated D-dimer testing as an aid in

Table 4. The Laboratory Risk Indicator For Necrotizing Fasciitis¹⁹

Laboratory Variable	Laboratory Value and Points Assigned
Sodium level	≥135 mmol/L=0 points, <135 mmol/L=2 points
Creatinine	≤141μmol/L=0 points, >141 μmol/L=2 points
Glucose	≤10 mmol/L=0 points, >10 mmol/L= 1 point
WBC count	<15 per mm ³ =0 points, 15-25 per mm ³ =1 point, >25 per mm ³ =2 points
Hemoglobin	>13.5 g/dL=0 points, 11-13.5 g/dL=1 point, <11 g/dL=2 points
C-reactive protein	<150 mg/L=0 points, ≥150 mg/L=4 points

A score of ≥ 6 is suspicious for necrotizing fasciitis and a score of ≥ 8 is strongly predictive

diagnosing deep venous thrombosis.^{17,18,19} Multiple D-dimer assays are available with differing sensitivities and variability. A large systematic review of trials assessed sensitivity, specificity, likelihood ratios, and variability among D-dimer assays.²⁰ This review found that ELISAs, in particular the quantitative rapid ELISA, was superior when compared to other D-dimer assays for sensitivity and negative likelihood ratio. The quantitative rapid ELISA had a negative likelihood ratio similar to those for a normal or near-normal lung scan or negative duplex ultrasonography in patients with suspected deep venous thrombosis or pulmonary embolism. Based on these results, a negative, quantitative, rapid ELISA is as diagnostically useful as a normal lung scan or a negative duplex ultrasonography in ruling out DVT or a pulmonary embolism.

However, D-dimer should not be used alone in diagnosing or excluding deep venous thrombosis. The physician should first estimate the pretest clinical probability of DVT. Wells et al devised a modified scoring system that is based on objective criteria in quantifying the pretest clinical probability for DVT; see Table 5.²¹ They concluded that DVT can be ruled out in a patient who is judged clinically unlikely to have DVT and who has a negative D-dimer and ultrasound testing. There have been a number of studies that have assessed the combination of D-dimer and the pretest clinical probability score for

deep venous thrombosis.²²⁻²⁶ The overall consensus is that a patient with a low pretest clinical probability and a negative D-dimer does not need further testing. This may not hold true in certain subpopulations, such as the elderly. One study investigated whether age has an influence on the performance of the combined D-dimer and pretest clinical probability in evaluating for DVT and found that this strategy is less useful in the elderly since it has been found that D-dimer levels increase with age.²⁷

There have also been studies evaluating D-dimer testing as a diagnostic strategy for follow-up after an initial normal proximal vein ultrasonography. A randomized, multicenter study with 810 patients evaluated patients with suspected deep venous thrombosis and normal results on proximal vein ultrasonography comparing D-dimer testing with repeat ultrasonography after one week. They found that D-dimer testing followed by no further treatment if the result was negative and venography if the result was positive did not differ from withholding anticoagulant therapy and repeating ultrasonography after one week.²⁸ The authors stated that Doppler ultrasonography of the distal (calf) deep veins is more difficult to perform and less than 20% of symptomatic deep venous thromboses are confined to the distal veins. They also stated that there is a very low risk of distal deep venous thrombosis extending into the proximal veins, and when this does occur, it does so within

Table 5. Wells et al Clinical Model For Predicting Pretest Probability For DVT²⁴

Clinical Characteristic	Score
Active cancer (patient receiving treatment for cancer within previous the 6 months or currently receiving palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recent bedridden for greater than 3 days or major surgery within the previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (nonvaricose)	1
Previously documented deep-vein thrombosis	1
Alternative diagnosis at least as likely as deep-vein thrombosis	-2

A total score of two or higher indicates that the probability of deep-vein thrombosis is likely; a total score of less than two indicates that the probability of deep-vein thrombosis is unlikely. In patients with symptoms in both legs, use the more symptomatic leg.

one week of presentation. Their results showed that venous thromboembolism occurred in 1% of patients with a negative D-dimer result.

While D-dimers are widely measured when there is a clinical suspicion of deep venous thrombosis, they are, however, not specific to thrombotic conditions. There are a number of nonthrombotic conditions where D-dimer levels are elevated, such as disseminated intravascular coagulation, sepsis, pregnancy complications, major surgery, and malignant disease.²⁹ In conclusion, D-dimer levels in combination with the pretest clinical probability of deep venous thrombosis appears to be an effective strategy when deciding the further workup and management of a patient with a swollen extremity.

Blood and Tissue Cultures: Blood and tissue cultures may be useful in some infective diseases, but not all. For instance, there are multiple studies that conclude that blood cultures are not necessary in community-acquired cellulitis.^{30,31} Mills et al reviewed the evidence of whether blood cultures were necessary in adults with cellulitis by searching Ovid MEDLINE (1966 to present) which yielded 122 research articles.³² Of these, five articles addressed the question specifically. After reviewing the articles, the authors concluded that blood cultures do not significantly alter treatment or aid in diagnosing the microbial organism in acute adult cellulitis in normal immunocompetent adults.

Opinion differs for non-perineal cutaneous abscesses. While there are some studies that suggest there is a role for culture and sensitivity of pus samples, the Infectious Diseases Society of America (IDSA) states that, in cases of simple abscesses, cultures are not necessary as the bacterial agent is usually *S. aureus*.^{33,34} For a patient presenting with a severe infection or with a progressing infection despite empirical antibiotic therapy, cultures are appropriate.

The practice guidelines published by the IDSA are expert consensus recommendations. IDSA guidelines do recommend blood and wound cultures in certain scenarios; see Table 6. The IDSA reports that, despite their recommendation to obtain cultures, aspiration of the skin is not helpful in 75 to 80% of cases of cellulitis and blood cultures are rarely positive (less than 5% of cases). In the case of diabetic foot infections, the recommendation is to send appropriately obtained specimens for culture prior to starting empirical antibiotic therapy, except in cases of mild infection.^{35,36} It is recommended that aspira-

tion, biopsy, or ulcer curettage are obtained for culture rather than a wound swab specimen.

Acute Phase Reactants (ESR, CRP, PCT): The acute phase reactants are proteins produced by hepatocytes and other cell types in response to infection, inflammation, and tissue injury. These reactants are nonspecific and nonsensitive for identifying individual disease entities. Acute phase reactants include erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin (PCT).

ESR is one of the more commonly measured acute phase reactants in the ED. It remains useful mostly for the diagnosis of a few conditions, such as temporal arteritis, polymyalgia rheumatica, rheumatoid arthritis, septic arthritis, and toxic synovitis. An extreme elevation of ESR (greater than 100 mm/hr) is strongly associated with a more serious underlying disease such as infection, collagen vascular disease, or metastatic malignancy.³⁷ If the ESR is greater than 25 mm/h, patients have a greater risk for septic arthritis. High-risk patients with suspected clinical findings should have the involved joint aspirated and cultured. However, in low-risk patients with a non-elevated ESR, the patient may be closely observed instead. In this instance, the ESR can help distinguish a high-risk from a low-risk patient.

C-reactive protein concentrations tend to increase with acute infections and CRP levels may help suggest the severity of the inflammation or tissue injury.³⁸ CRP is not helpful in distinguishing cellulitis from DVT as there are studies showing that CRP levels are elevated in both conditions.^{39,40}

PCT is an acute phase reactant that may be more

Table 6. Infectious Disease Society of America Recommendations For Scenarios In Which To Obtain Blood And Wound Cultures

- Signs and symptoms of systemic toxicity
 - Fever or hypothermia
 - Tachycardia [HR greater than 100 beats/min]
 - Hypotension [systolic blood pressure less than 90 mmHG or 20 mmHg below baseline]
 - Diffuse cellulitis
 - Trauma; water contact; animal, insect, or human bites
 - Patients who do not respond to initial antibiotics
 - Patients who are immunocompromised
-

useful than CRP measurements. A meta-analysis comparing serum PCT and CRP levels for markers of bacterial infection found that PCT levels were more sensitive and more specific than both ESR and CRP for differentiating bacterial from noninfective causes of inflammation.⁴¹

In conclusion, acute phase reactant determination has limited clinical utility in the ED. They may provide some usefulness in certain circumstances, such as septic arthritis, when the diagnosis is unclear in patients who are considered low-risk.

Radiographic Studies

X-rays are a logical test to order in many patients who present with a painful swollen extremity, especially if there is a history of trauma. When necrotizing fasciitis is in question, an x-ray study of the involved extremity may show gas within the involved muscle and surrounding soft tissue. A CT scan or MRI may also show changes associated with this condition.

Doppler ultrasounds are commonly ordered in the evaluation of a swollen lower extremity when a deep venous thrombosis is being considered. A Doppler ultrasound may also reveal other findings in the differential, such as a Baker cyst, popliteal artery aneurysms, or other vascular masses. In the evaluation of deep venous thrombosis, lower extremity Doppler ultrasonography has replaced contrast venogram as the “gold standard” for diagnosing DVT above the knee. Sonography is up to 97% sensitive for detecting proximal DVT compared with 90% for venography.⁴² MRI, MR venography, and multidetector CT also have up to 97% sensitivity in diagnosing DVT.⁴³ While venography has been the “gold standard” and CT and MRI show promise, Doppler ultrasonography has the advantages of being less expensive, portable, non-invasive, reliable, and easy to perform.

When evaluating for musculoskeletal infection, x-rays are the traditional imaging study performed. CT scans and MRI can further help in delineating many types of musculoskeletal infections. CT scanning and MRI provide excellent anatomic resolution and soft tissue contrast to evaluate for cellulitis, fasciitis, abscess, myositis, and septic arthritis.⁴⁴ Ultrasound may also have a role in the diagnosis and management of patients with clinical cellulitis. A study by Tayal et al was performed to evaluate the effect of diagnostic soft-tissue ultrasound on the management of ED patients with clinical cellulitis. They found that ultrasound changed the management of 48% of

patients who were initially believed to *not* need further drainage. These patients went on to need drainage, further diagnostics, or consultation. They also found that ultrasound changed the management of 73% of patients who were initially believed to *need* further drainage.⁴⁵ In another study, Yen et al prospectively used ultrasound to evaluate 62 patients with suspected necrotizing fasciitis in the ED. In this observational study, the authors compared their results with pathological findings of patients who underwent fasciotomy or biopsy; they reported that ED ultrasound had a sensitivity of 88.2%, a specificity of 93.3%, a positive predictive value of 83.3%, a negative predictive value of 95.4%, and an accuracy of 91.9% for diagnosing necrotizing fasciitis.⁴⁶

The American College of Radiology (ACR) publishes guidelines for a radiological approach to a patient with suspected upper extremity vein thrombosis.⁴⁷ They recommend beginning the workup with a chest x-ray. This is helpful to evaluate for the presence of a mass lesion causing central venous obstruction or to confirm the presence and location of a venous catheter. Rare entities that could be associated with extrinsic compression syndromes such as a cervical rib, could also be detected. The next appropriate test would be a Doppler ultrasound, which would evaluate for the presence of a DVT or a proximal venous obstruction. If the Doppler ultrasonography results are inconclusive, then venography would be the next step. Venography is still considered the “gold standard” for evaluating upper extremity veins. When further evaluation of central veins is needed for obstruction, order MRI or CT scan with contrast of the upper extremity and chest.

Compartment Pressure Measurement

When compartment syndrome is suspected, the tissue pressure should be measured without delay so as to limit any possible nerve dysfunction or muscle death. A number of commercial model tonometers are available (such as Stryker® or ACE®) to measure the compartment pressure. The normal pressure in a muscle compartment is 0 to 10 mmHg. Capillary blood flow may be compromised within a compartment at pressures greater than 20 mmHg.⁴⁸ The critical level of the absolute intra-compartmental pressure remains undecided. Different studies site levels ranging from 30 to 50 mmHg.⁴⁹ Experimental studies have shown a wide range between individuals when correlating absolute pressure levels, clinical signs, nerve functions, and oxygen levels in the muscle.

Whitesides introduced the concept that the level of intra-compartmental pressure which causes ischemic compromise is related to the perfusion pressure.⁵⁰ The concept is similar to the CPP in brain injury: The change in pressure (Δp) is the diastolic pressure minus the intra-compartmental pressure. If the Δp is less than 30 mmHg and/or clinical signs are present, emergent fasciotomy is recommended; for indeterminate pressure measurements and/or early symptoms, careful and frequent reassessments are indicated.

Special Conditions

Deep Venous Thrombosis

Deep venous thrombosis (DVT) affects approximately 200,000 Americans per year.⁵¹ Identifying those at risk is a major component of the risk stratification used in interpreting tests and initiating management for suspected DVT and pulmonary embolus; see Table 7. It is important to assess the patient's risk factors for DVT, such as age, history of cancer, immobilization, recent trauma or surgery, obesity, pregnancy, estrogenic medications, congestive heart failure, diseases that alter blood viscosity (polycythemia, sickle cell disease), and inherited thrombophilias. Approximately 75% of patients with DVT have at least one established risk factor.⁵² This means that 25% of patients with DVT have no established risk factor which signifies that it is absolutely necessary to consider the diagnosis in patients where there is clinical suspicion of DVT.

Thrombophilia (a disorder where there is a tendency for the occurrence of thrombosis), thrombocytosis, and hypercoagulable are predispositions to

venous thromboembolism (VTE) and may be classified as inherited or acquired. There is a strong association between cancer and the development of venous thromboembolism.⁵³ In a cohort study by Cogo et al, the majority of DVT cases were due to major risk factors such as immobilization, trauma, or recent surgery. Factors such as age greater than 60 years and systemic lupus erythematosus also indicate a risk for DVT.⁵⁴ Of patients diagnosed with DVT, approximately 50% have perfusion defects on nuclear lung scanning.⁵⁵

When considering a cause of unilateral upper

Figure 2. Stryker Intracompartmental Pressure Monitor System



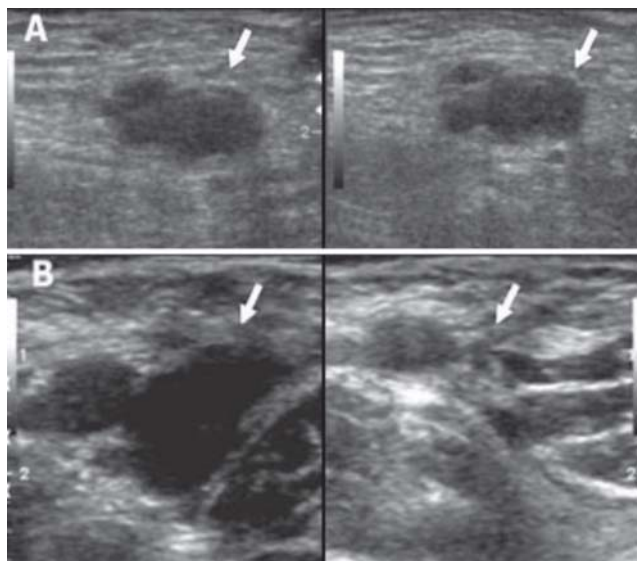
When testing the deep posterior compartment with the Stryker intra-compartmental pressure monitor system, insert the needle just medial and posterior, staying relatively superficial within the posterior tibial muscle belly.

Reprinted from Braver, DPM, Richard. "Surgical Pearls: How To Test And Treat Exertional Compartment Syndrome." *Podiatry Today*. 24 September 2006. <<http://www.podiatrytoday.com/article/%2E%2E%5CPODTD%5CHTML%5Cimages%5Cthumbs%5CPT%2E05%2Esurgfig1.tif%2Ejpg>>.

Table 7. Risk Factors For DVT In Ambulatory Patients

Acquired (persistent)	Advancing age Malignancy Antiphospholipid antibodies Prior history of DVT/PE
Acquired (transient)	Recent surgery or major trauma Pregnancy ^{180, 181} Oral contraceptives/ hormone replacement therapy Prolonged immobilization: bed rest, paralysis, travel ¹⁸² Comorbidities: CHF, myocardial infarction, nephrotic syndrome, IBD ^{183, 184}
Inherited	Antithrombin III deficiency Proteins C and S deficiency Factor V Leiden Prothrombin gene mutation

Figure 3. Lower Extremity Ultrasound



Compression US of the right leg in (A) a patient with and (B) a patient without common femoral vein thrombus. Note that a vein with acute thrombus demonstrates no intraluminal echoes. Thrombus is only detected by lack of compression. In contrast, a normal vein is easily compressible.

Reprinted from Miller, Janet Cochrane. *Diagnosis of Lower Extremity Deep Vein Thrombosis. Radiology Rounds. Vol 3, Issue 5.*

extremity swelling, venous thrombosis is generally at, or near, the top of the diagnostic considerations. As an indwelling catheter is a common cause, their increased utilization for hemodialysis, chemotherapy, or parenteral nutrition has increased the incidence of upper extremity DVT. One registry of 592 patients found that the most powerful independent predictor of upper extremity DVT was the presence of an indwelling central venous catheter.⁵⁶ Many risk factors for upper extremity DVT differ from the conventional risk factors for lower extremity DVT. While inherited thrombophilia and cancer predispose to upper extremity DVT, oral contraceptives did not increase the risk by itself, but did increase the risk when combined with inherited thrombophilia.⁵⁷ Another study showed that the most frequent triggering factor for patients with upper extremity DVT was recent history of strenuous exercise of the muscles in the affected extremity.⁵⁸

When the deep venous system of the arm or leg is occluded by thrombosis, a patient may develop acute pain and swelling.^{59,60} The exam may reveal erythema, warmth, tenderness to palpation, and pitting edema. Historically, the examination of the lower extremity included the elicitation of Homans' sign, which refers to the development of pain in the calf or popliteal region on forceful dorsiflexion of the ankle with the knee in flexed position. However, a systematic review

of the literature reported that Homans' sign has a sensitivity varying between 13 to 48% and specificity from 39 to 84% in the evaluation of DVT.⁶¹ The classic signs and symptoms of calf pain, edema, venous distension, and positive Homans' sign occur in less than one-third of patients.⁶²

Inherited deficiencies of antithrombin III and protein C and S have been recognized for years. For patients with antithrombin III deficiency, the peak age of thrombosis is between 15 and 30.⁶³ Among the most important inherited disorders is factor V Leiden, which is the most common cause of thrombophilia and is identified in about 50% of patients with recurrent DVT. Having the prothrombin gene mutation increases the risk of DVT two to four times.⁶⁴ Patients who develop idiopathic venous thromboembolism at a young age, have recurrent thrombosis, experience recurrent unexplained pregnancy loss, or have a family history of thromboembolic disorders should be worked-up for thrombophilia.⁶⁵

If the patient is a female of childbearing age, it is crucial to inquire about whether she is pregnant or has had a recent delivery or abortion. The literature suggests that women are at greater risk for developing venous thromboembolism postpartum than antepartum. In fact, one study reported the incidence of pregnancy-associated venous thromboembolism at a rate of 1.25 per 1000 deliveries.⁶⁶ The same study noticed a predilection for the left leg (74.3%). This may be due to an anatomical condition where there is compression in the left iliac vein.⁶⁷ Furthermore, the risk of venous thromboembolism is higher after cesarean section than after vaginal delivery.⁶⁸

Other conditions such as abscess, Baker's cyst, superficial thrombophlebitis, muscle rupture, calf hematoma, pseudoaneurysm, cellulitis, and venous stasis may present very similar to DVT. One study looked at Doppler ultrasound to further evaluate non-filling of contrast in deep veins on phlebography in patients with clinical signs of DVT. Ultrasound confirmed DVT in 31% of patients; 38% of patients had other pathology such as edema, bleedings, ligament or muscle rupture, Baker cysts, or superficial thrombophlebitis. The rest of the patients showed no pathology.⁶⁹ Therefore, clinical assessment alone is not satisfactory for detecting the majority of cases of DVT.

Compartment Syndrome

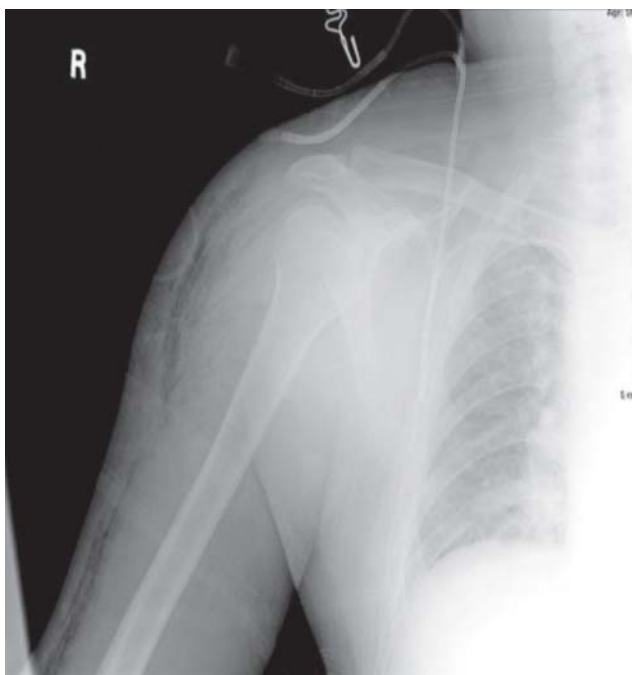
Fractures, crush injuries, burns (thermal and electrical), snakebite, and arterial injuries to any extremity have the potential to cause a compartment syn-

drome. Additional causes to consider in upper extremity compartment syndrome are muscle avulsion, high-pressure injection injuries, infection, and intravenous drug infiltration.^{70,71} The increase in compartmental pressure can also result in the external compression of the compartment from a circumferential cast, burn eschar, or prolonged limb compression after drug or alcohol overdose.⁷²⁻⁷⁶ Dozens of reports have described the development of compartment syndrome after strenuous exercise.⁷⁷ The exact incidence of compartment syndrome in the emergency department is unknown. However, it has been shown that approximately three-quarters of cases are associated with fractures of the arm or leg, with tibial fractures having the highest association.⁷⁸

The 5 P's (pain out of proportion, pallor, paresthesia, paralysis, and pulselessness) are frequently used as a mnemonic for the signs and symptoms of compartment syndrome. Weakness, paralysis of involved muscles, pallor, or loss of pulses in the affected limb are all late signs of compartment syndrome. Clinical diagnosis is based on the history of injury and physical signs coupled with a high index of suspicion.⁷⁹

The development of compartment syndrome can

Figure 4. A Case of Necrotizing Fasciitis Showing Subcutaneous Air On Plain Film Radiograph.



Reprinted from Wikibooks. "Diagnostic Radiology/Musculoskeletal Imaging/Infection/Necrotizing fasciitis." 24 September 2006. <http://en.wikibooks.org/wiki/Diagnostic_Radiology/Musculoskeletal_Imaging/Infection/Necrotizing_fasciitis>.

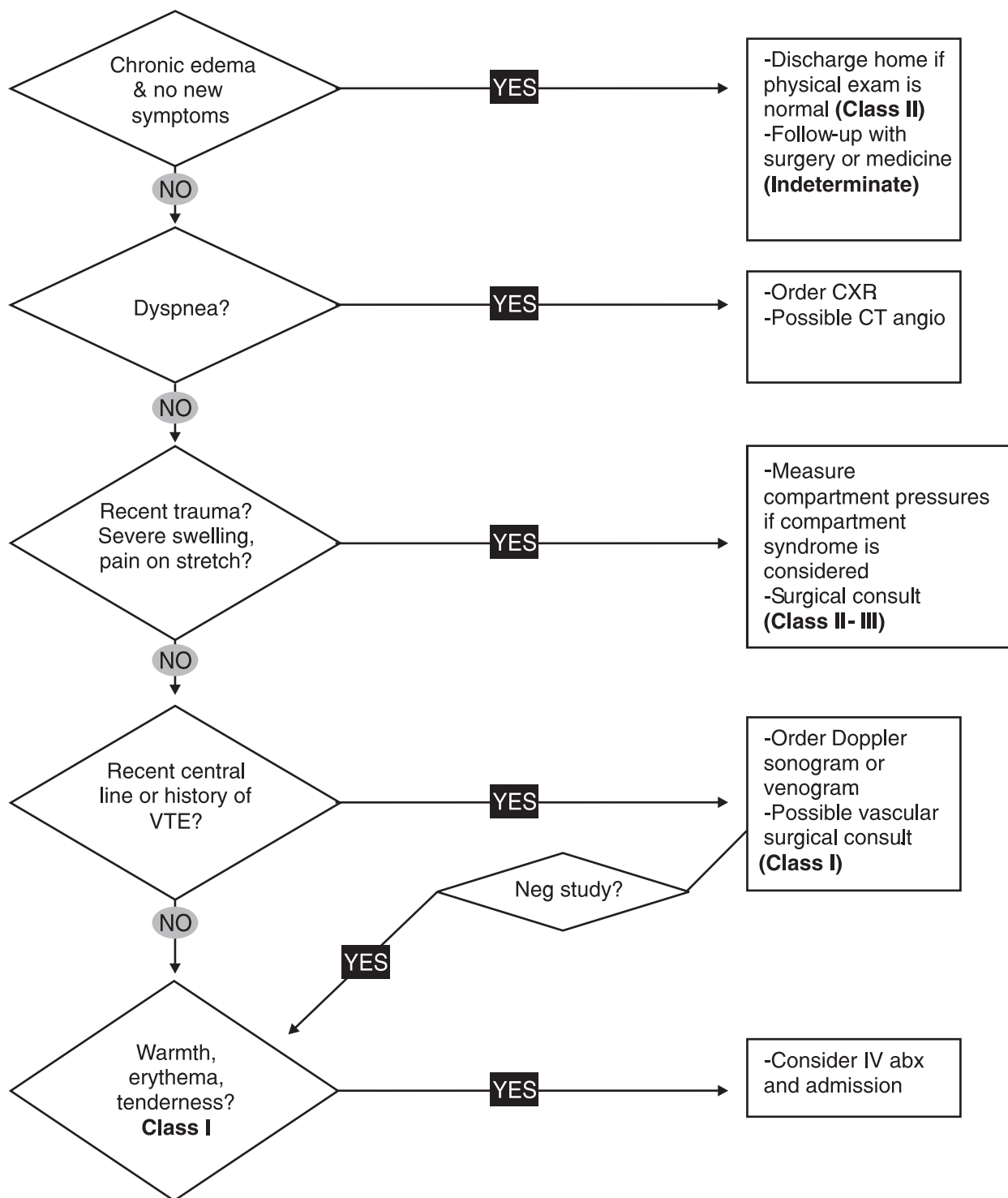
also occur after a contusion to the thigh. It is difficult to differentiate between a severe thigh contusion and compartment syndrome based on clinical presentation alone as both can present with severe pain and swelling. The compartments of the thigh are large and usually compliant enough to allow the expansion of a hematoma; a large amount of bleeding in the potential space may occur prior to a rise in intracompartmental pressure. Delayed presentation of compartment syndrome from persistent muscular hemorrhage in the thigh has been described.⁸⁰ Even in minor trauma to the thigh, compartment syndrome may present with only pain and swelling.⁸¹ The best way to objectively distinguish who needs emergent fasciotomy is by compartment pressure measurements.

Compartment pressure measurements are a consideration in a patient who is not alert or if the clinical examination is inconclusive.^{82,83} The most frequently used device is the Stryker® Intracompartmental Pressure Monitor System (Stryker Instruments, Kalamazoo, MI); see Figure 2 on page 11. Easy to use, the efficacy and accuracy of the device has been validated;⁸⁴ however, when not available, manometer measurements using equipment available in most EDs are an alternative.⁸⁵

Each limb contains a number of compartments that are at risk for compartment syndrome. Thus, all compartments of the involved extremity should be checked for elevated intracompartmental pressure. The upper arm contains the anterior and posterior compartments. The forearm has both a volar and dorsal compartment. In the lower extremity, there are three gluteal compartments, anterior and posterior compartments in the thigh, and the four compartments of the lower leg. The anterior compartment of the lower leg is most frequently involved in compartment syndrome of the lower extremity.^{86,87}

Resting intracompartmental pressure is normally between 0 and 10 mmHg. According to animal studies performed by Heppenstall et al, tissue pressures greater than 30 mmHg suggest impending or ongoing muscle and nerve damage.⁸⁸ The patient's mean blood pressure should also be taken into consideration; the lower the mean blood pressure, the lower the compartment pressure that causes a compartment syndrome.⁸⁹ No absolute threshold of pressure exists for determining when emergent fasciotomy is indicated. Rather, the diagnosis should be made on both the physical exam and the pressure measurements. Serial exams may be indicated in cases where the onset time of injury is unknown and the com-

Clinical Pathway: Swelling Of Upper Extremity

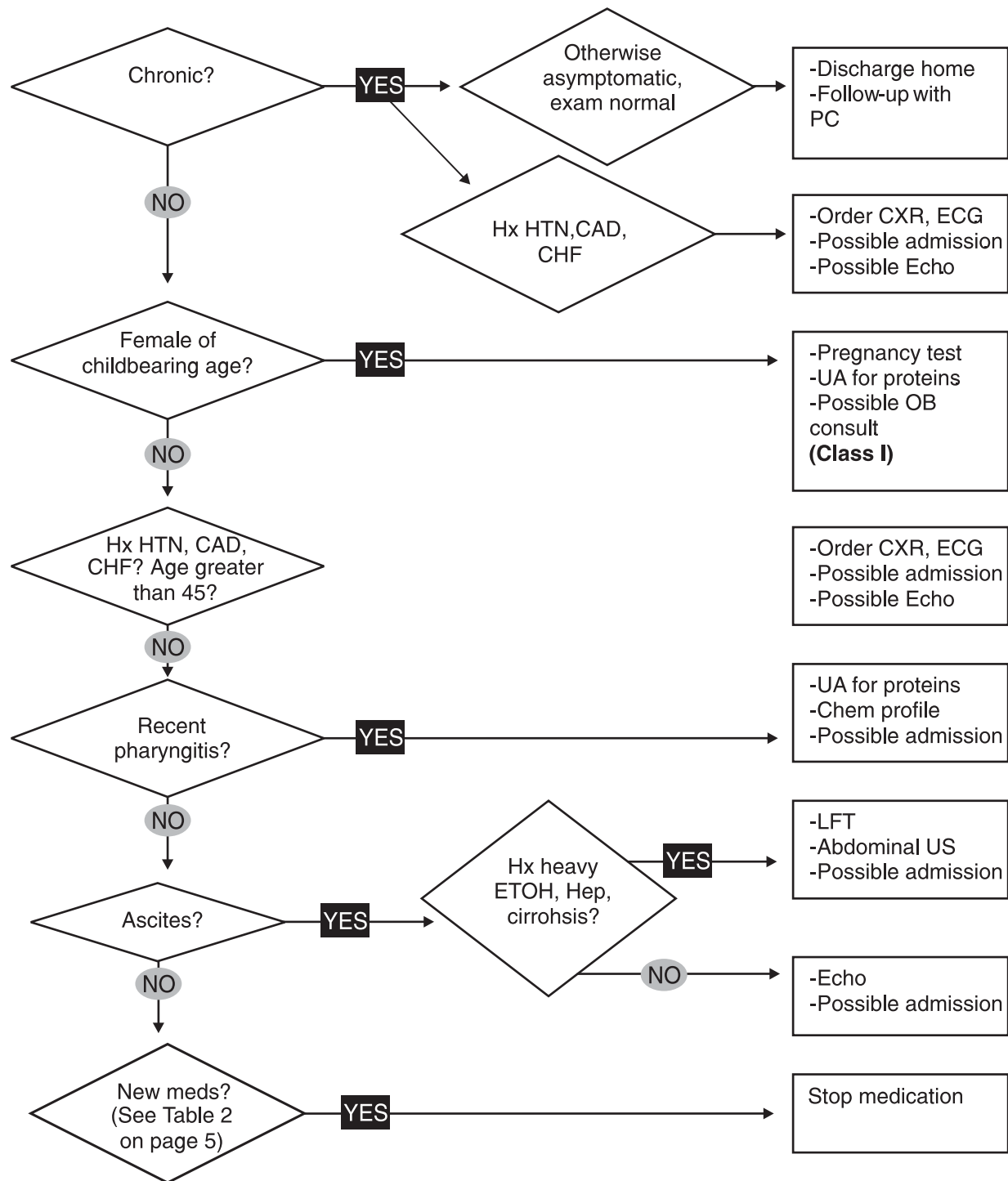


The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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Clinical Pathway: Lower Extremity Swelling Bilateral

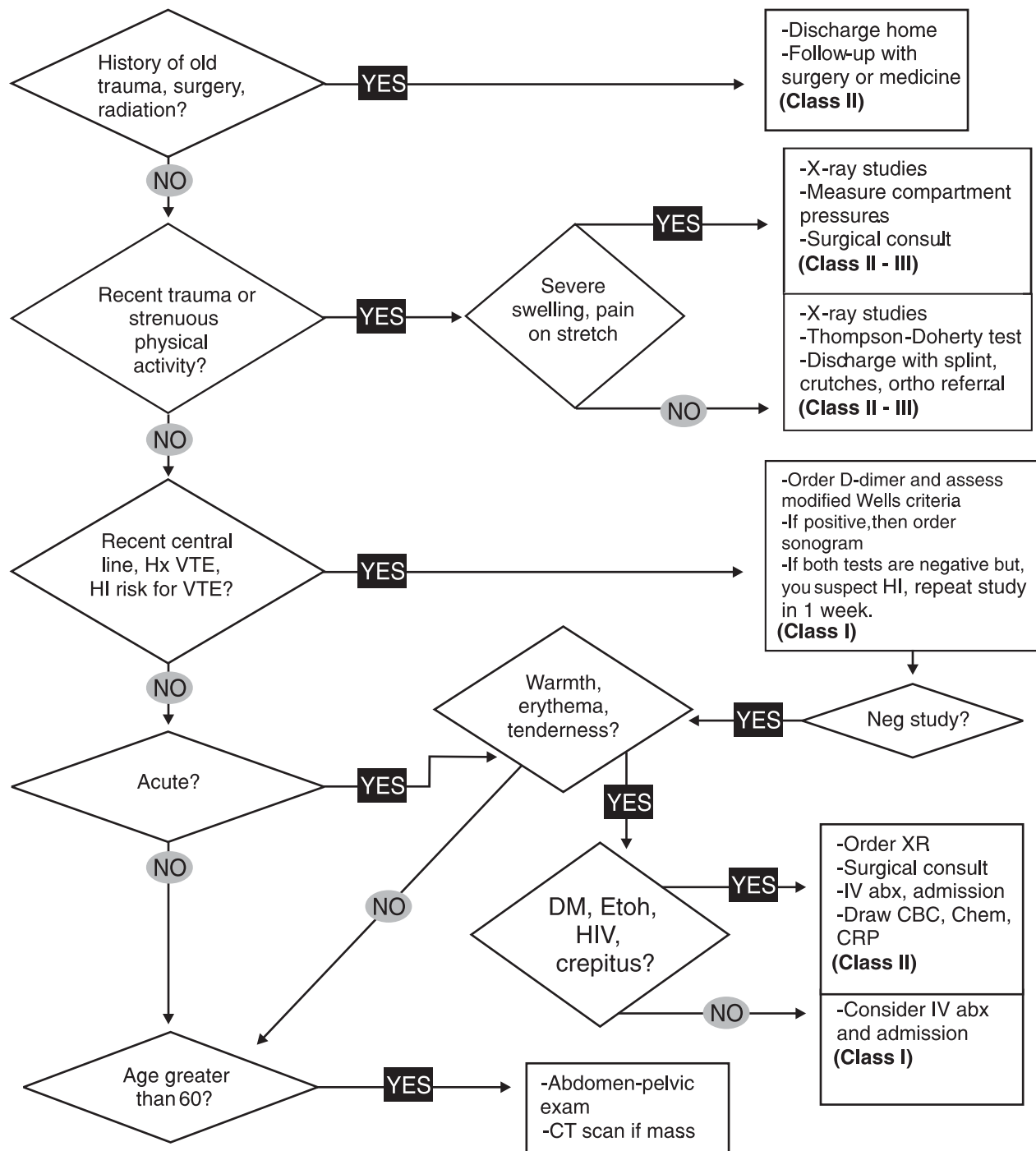


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Clinical Pathway: Lower Extremity Swelling Unilateral



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partment pressures are normal, but the mechanism of injury and physical exam puts the patient at risk for developing compartment syndrome.

Soft Tissue Infection

The typical signs of cellulitis are erythema, warmth, tenderness and swelling. Most cellulitis is mild and results from group A streptococcus or *S. aureus* infections. Diffuse necrotizing infections are serious and, at times, are difficult to distinguish from simple cellulitis. Foul smelling purulent discharge may present in cellulitis or necrotizing infections. Necrotizing fasciitis and clostridial myonecrosis (gas gangrene) should be suspected in patients who are immunocompromised or have peripheral vascular disease. The earliest clinical clues include edema out of proportion to skin erythema, skin vesicles, and crepitus.⁹⁰

Surgery/Radiation Treatment

Lymphedema of an extremity can occur after surgery and radiation for treatment of cancer. Lymphedema after mastectomy plus node dissection occurs in as many as 30% of patients with breast cancer, with higher rates of chronic lymphedema occurring in patients treated with radical mastectomy, and much lower rates in patients who have only sentinel node biopsies.⁹¹ This occurs as a result of disruption or compression of the lymphatics. The combination of surgery and radiation is highly predictive of the occurrence of lymphedema.⁹² A study by Segerstrom evaluated six factors that may increase the likelihood of upper extremity swelling after treatment of breast cancer and found that being overweight, oblique surgical incision, infection in the arm, and radiotherapy correlated with upper extremity swelling.⁹³ The highest incidences were found in patients who had received radiotherapy in high doses (60%) and had a history of one or more infections of the involved arm (89%). Another study found that 80% of patients who had undergone breast conserving surgery, axillary dissection, and breast radiation complained of symptoms such as extremity stiffness (41%), numbness (45.7%), and swelling (14.6%).⁹⁴ A study evaluated patients who received radiotherapy for extremity soft tissue sarcoma and found that edema was more frequent in the postoperative arm (23.3%) than in the preoperative arm (15.5%).⁹⁵ It was also found that patients had greater rates of fibrosis and joint stiffness postoperatively. Therefore, extremity swelling, stiffness and numbness are common sequelae to surgical and radiation therapy in the treatment of cancer.

Treatment And Disposition

Musculoskeletal Trauma

Many cases of soft-tissue trauma and fractures can be managed with pain medications, immobilization for fractures, and orthopedic follow-up after discharge from the emergency department. Emergent orthopedic consultation is necessary for conditions that are limb threatening, involve vascular compromise or open fractures, or when compartment syndrome is being considered. Reduction of displaced fractures and dislocations should be performed in the ED by either the emergency physician or the orthopedic consult physician. The emergency physician should have a knowledge of which fractures require admission for open reduction and internal fixation (ORIF). These include Monteggia and Galeazzi fracture/dislocations, fractures involving the articular surfaces, displaced fractures with epiphyseal injuries known to have a propensity for growth arrest (Salter-Harris types III and IV), and major avulsion fractures associated with disruption of important musculotendinous or ligamentous groups.

Deep Venous Thrombosis

Historically, patients diagnosed with proximal deep venous thrombosis have been admitted to the hospital for anticoagulation. Patients have been initially anticoagulated using unfractionated heparin and then were changed to oral warfarin for continued outpatient therapy; both which required frequent laboratory monitoring. A Cochrane review compared the effect of low molecular weight heparin (LMWH) with unfractionated heparin (UFH) for the initial treatment of venous thromboembolism (VTE) and found that LMWH was more effective than UFH for the initial treatment of VTE. LMWH significantly reduced the occurrence of major hemorrhage during the initial treatment and reduced overall mortality at follow-up.⁹⁶

Another Cochrane review evaluated the efficacy and safety of long-term treatment of VTE with LMWH compared to vitamin K antagonists and found that treatment with LMWH was significantly safer than treatment with vitamin K antagonists.⁹⁷ Other benefits include shortening of hospital stay, no laboratory monitoring required, and overall decreased cost of care. The Cochrane review concluded that LMWH is possibly a safe alternative in those patients who reside in geographically inaccessible places, are reluctant to visit a thrombosis serv-

Ten Pitfalls To Avoid

1. **"He has a negative Homans' sign and I'm not impressed with the swelling."**

The lack of the Homan's sign is not reliable in eliminating DVT as a possibility. The physical examination is only 30% accurate in patients presenting with DVT and should be used to increase clinical suspicion of DVT, but negative exam findings cannot be used to exclude DVT as a possible concern.⁶

2. **"Her breast cancer is in remission and her venous Doppler is negative. I'm not worried about DVT."**

A common pitfall is placing too much confidence in a negative venous Doppler. Though it is highly sensitive (95%) and specific (96%) for a proximal venous thrombosis, the study does not accurately assess calf veins. Doppler ultrasounds of distal veins have shown sensitivity and specificity of 88% and 86% respectively. Also, proximal extension of a thrombus can occur in up to 25% of patients with a calf DVT.¹⁴⁰

3. **"He told me he just banged his elbow. The x-ray was negative for a fracture. When I saw him for the second visit four days later, I just figured the pain and swelling was from the contusion."**

Patients presenting with cellulitis usually have a history of trauma or surgery causing a break in the skin. However, some patients may have no signs of dermal injury. Patients with peripheral vascular disease or diabetes can present with signs of cellulitis after minor injuries. It is important for the clinician to recognize signs of cellulitis and treat appropriately.

4. **"I just thought all her swelling was due to water weight gain."**

Generalized edema is normal in most pregnancies and, though it has been excluded from the definition of preeclampsia, it should be a consideration in the context of a hypertensive pregnant female.

5. **"The x-ray did not show a fracture so I wasn't concerned about compartment syndrome."**

Though compartment syndrome presents after a fracture 75% of the time, it can also occur from a thigh contusion or excessive exercise, as in the

case of body-builders. Patients on coumadin can also have compartment syndrome after very little trauma.

6. **"I felt that the patient's frequent requests for pain meds were simply due to a low pain tolerance . . . and maybe some drug seeking . . ."**

It is a common error to believe that the patient's pain is confined only to the direct injury itself. Pain should improve with time. If a patient has increasing pain or pain out of proportion to the injury, compartment syndrome may be a concern.⁴⁰

7. **"Although she is a diabetic, her blood sugar is under very good control. It seemed like a simple cellulitis of the lower leg."**

Necrotizing infections are difficult to distinguish from cellulitis, especially early in presentation. Immunocompromised patients are susceptible to necrotizing infections; a high index of suspicion is necessary for early diagnosis and treatment.

8. **"He had frequent asthma attacks. I thought his swelling was due to steroid use."**

Although weight gain can occur due to steroid use, the presence of orthopnea, pedal edema, and nocturnal dyspnea are suggestive of congestive heart failure.

9. **"The surgery consult said they were busy. I thought my patient with necrotizing fasciitis would do well in the meantime with IV antibiotics."**

While administration of broad-spectrum antibiotics and resuscitation is important in the management of necrotizing fasciitis, emergent, aggressive surgical debridement is vital in order to reduce the morbidity and mortality of this rapidly progressive infection.

10. **"I didn't know she could have DVT in her upper extremity. I just thought her indwelling catheter had infiltrated."**

DVT's can occur in the upper extremity as well. Risk factors include the presence of an indwelling catheter, inherited thrombophilia, trauma, and cancer.

ice regularly, or have contraindications to vitamin K antagonists. These conclusions only apply for three to six months of treatment following initial treatment. For a definitive answer to which treatment is better for the long-term treatment of VTE, Cochrane concludes that larger, adequately-designed clinical studies need to be performed.

Cellulitis/Abscess

Many cases of cellulitis can be managed on an outpatient basis with orally prescribed antibiotics and follow up. Appropriate antibiotic therapy includes semi-synthetic penicillin, first-generation or second generation oral cephalosporins, macrolides, or clindamycin. In the case of *S. aureus*, the physician should assume that the organism is resistant because of the high prevalence of community-associated MRSA strains.⁹⁸ Studies cite that 25% of MRSA strains are resistant to clindamycin and up to 87% are resistant to erythromycin.^{99,100} Most MRSA strains are susceptible to trimethoprim-sulfamethoxazole and tetracycline.¹⁰¹ Long-acting tetracyclines, such as minocycline and doxycycline, possess greater anti-staphylococcal properties than tetracycline. A small study of 24 patients found that long-acting tetracyclines had a success rate of 83% for MRSA infection and a success rate of 93% for complicated skin and skin-structure infections.¹⁰²

When cellulitis is extensive or is accompanied by signs and symptoms of systemic toxicity (fever or hypothermia, tachycardia [HR greater than 100 beats/min], or hypotension [systolic blood pressure less than 90 mmHg or 20 mmHg below baseline]), hospitalization should be strongly considered. Patients who present with severe infection or with progression of infection despite empirical antibiotic therapy should be treated more aggressively. Antibiotic choice should be based on the results of gram stain, culture, and drug susceptibility analysis. In the case of *S. aureus*, it should be assumed to be a community-acquired MRSA strain and initial antibiotics should have an agent effective against MRSA, such as vancomycin, linezolid, or daptomycin.¹⁰³ In the case of *S. pyogenes*, 99 to 100% of strains are susceptible to clindamycin and penicillin.

Immunocompromised patients presenting with skin and soft tissue infections may present a diagnostic challenge because infection can be caused by a more diverse group of pathogens not normally considered. These infections are often systemic and the degree of infection and type of immune deficiency may attenuate the clinical findings. Many infections

are hospital acquired and may mount resistance to empirical therapy. Admit patients who appear ill or present with signs and symptoms of systemic toxicity and start broad-spectrum antibiotics for resistant gram-positive bacteria, such as MRSA (vancomycin, linezolid, daptomycin), and gram-negative bacteria, such as pseudomonas (carbapenems or combination of fluoroquinolone or aminoglycoside plus either an extended-spectrum penicillin or cephalosporin).

Depending on the severity of infection and on certain comorbidities, patients with skin and soft-tissue infections, osteomyelitis, and joint infections can be managed on an outpatient basis with outpatient parenteral antimicrobial therapy. There are numerous studies which have shown that outpatient parenteral antimicrobial therapy is safe, effective, and cost-effective for carefully selected patients.¹⁰⁴⁻¹⁰⁶ One study randomized 200 patients to receive intravenous antibiotic treatment at home versus inpatient.¹⁰⁷ Patients eligible for the study were 16 years or older, had clinical signs of cellulitis, and required intravenous antibiotics because of severity of cellulitis or failure of oral antibiotics. The two treatment groups did not differ significantly for the primary outcome; patients were followed for four weeks and the recurrence of cellulitis at the same site within one month did not differ between groups. Therefore, carefully selected patients can be safely treated at home with intravenous antibiotics for cellulitis. Patients selected should meet certain criteria, such as having an infection that would require treatment beyond the expected hospitalization, no other need for hospitalization, and no equally safe and effective oral antibiotic therapy available for treatment.

In the treatment of abscesses, it is essential that treatment include incision and drainage, as antibiotic treatment alone will result in a high rate of treatment failure. Debridement of necrotic tissue is also required in diabetic patients who present with infected wounds with retained purulence or advancing infection, despite optimal antibiotic therapy.¹⁰⁸

Necrotizing Fasciitis

Patients presenting with signs of necrotizing fasciitis require immediate surgical consultation and emergent surgical debridement. A study by Wong et al showed that patient outcome was adversely affected when there was a delay in surgery of more than 24 hours, as well as by other factors such as advanced age and two or more comorbidities.¹⁰⁹ This study was

Cost Effective Strategies In Patients With Extremity Swelling

1. Limit the use of blood cultures.

Multiple studies suggest that blood cultures do not significantly alter treatment or aid in diagnosing the microbial organism in acute adult cellulitis in normal immunocompetent adults. They are also not helpful in simple abscesses.

Risk Management Caveat: There are instances where blood cultures would be helpful, such as when a patient presents with a severe infection or with a progressing infection despite empirical antibiotic therapy. Treatment for these patients should be more aggressive and should be based upon results of the appropriate gram stain, culture, and drug susceptibility. Blood cultures should be reserved for patients with severe infections presenting with fever or hypothermia, tachycardia [HR greater than 100 beats/min], hypotension [systolic blood pressure less than 90 mmHg or 20 mmHg below baseline], diffuse cellulitis, trauma, water contact, animal, insect or human bites, who do not respond to initial antibiotics, or who are immunocompromised.

2. Use D-dimer levels in combination with pretest clinical probability for the evaluation of deep venous thrombosis.

The use of D-dimer levels in combination with the pretest clinical probability of deep venous thrombosis appears to be an effective strategy when deciding which patients with a swollen extremity need a Doppler ultrasound for evaluation of DVT. The overall consensus is that a patient with a low pretest clinical probability and a negative D-dimer does not need further testing.

Risk Management Caveat: This may not hold true in certain subpopulations, such as the elderly. It has been found that D-dimer levels increase with age. Also, in the event of a distal (calf) DVT, Doppler ultrasound has a lower, but acceptable, sensitivity and specificity for diagnosing distal DVT while studies show that the D-dimer has no utility in diagnosing distal DVT.

3. X-rays are a logical first test for a swollen extremity.

X-rays can be helpful in diagnosing many patients who present with a painful, swollen extremity, especially if there is a history of trauma; they may also have utility in the nontraumatic state. In the case of trauma, an x-ray will diagnose a fracture, when present. It may have some use in non-traumatic situations as well, such as necrotizing fasciitis. When necrotizing fasciitis is in question, an x-ray study of the involved

extremity may show such signs as gas within the involved muscle and surrounding soft tissue.

Risk Management Caveat: While x-rays have their usefulness, it should not be relied on to rule out all causes of a swollen extremity, even in the case of trauma. Compartment syndrome is a limb-threatening condition which should be considered and may occur when there is no fracture present.

4. Administer the appropriate antibiotics.

When deciding on antibiotics for treatment of cellulitis, assume that, in the case of *S. aureus*, there is resistance because of the high prevalence of community-associated MRSA strains. Studies cite that 25% of MRSA strains are resistant to clindamycin and up to 87% are resistant to erythromycin. Most MRSA strains are susceptible to trimethoprim-sulfamethoxazole and tetracycline. Long-acting tetracyclines, such as minocycline and doxycycline, possess greater anti-staphylococcal properties than tetracycline.

Risk Management Caveat: Do not assume that any patient has appropriate antibiotic coverage and that they will do well. Always schedule follow up for a patient to reassess the cellulitis and the response to prescribed antibiotics. Patients without improvement or worsening of their infection will need admission.

5. Low molecular-weight heparin is easier and more effective than unfractionated heparin for the treatment of DVT.

Low molecular weight heparin (LMWH) is more effective than unfractionated heparin (UFH) for the initial treatment of venous thromboembolism (VTE). LMWH significantly reduced the occurrence of major hemorrhage during the initial treatment and reduced overall mortality at follow-up. Dosing is simple and there is no need to check PTT.

Risk Management Caveat: LMWH has not been studied for long term treatment of DVT. The results of studies advocating the use of LMWH apply for three to six months of treatment following initial treatment. Vitamin K antagonists are still the treatment of choice for long-term treatment. Also, keep in mind that patients with diminished renal function will accumulate LMWH which can increase the risk of bleeding.

a retrospective review of 89 patients. They found that the cumulative survival rate between admission and time to operation was 93.2% at 24 hours and decreased to 75% at 48 hours. Other studies support the absolute need for immediate surgical management.¹¹⁰ Another retrospective review of 68 patients found that those patients who underwent aggressive surgical debridement performed at the initial recognition of the disease process had a mortality rate of 4.2 % while patients with a delay in, or inadequate therapy, had a mortality rate of 38%.¹¹¹ The use of broad-spectrum antibiotics without immediate surgical debridement may mask the severity of the underlying infection and may alter the clinical presentation thus making an early diagnosis difficult. Therefore it is vital to recognize and promptly diagnose necrotizing fasciitis, administer broad-spectrum antibiotics, and initiate emergent aggressive surgical debridement in order to reduce the morbidity and mortality of this rapidly progressive infection.^{112,113}

Controversies/Cutting Edge

Management Of Suspected DVT Below The Knee With A Negative Ultrasound

Doppler venous ultrasound has become the most widely used diagnostic modality for the work-up of a DVT. Ultrasonography of the distal or calf veins is less accurate and is more difficult to perform than evaluation of the proximal veins.^{114,115} However, numerous studies have shown that the sensitivity and specificity of color Doppler in isolated calf veins is at least 88% and 86%, respectively.¹¹⁶⁻¹²⁰ While this is less than the sensitivity (95%) and specificity (96%) for a proximal venous thrombosis, many authors consider the color Doppler ultrasonography for detection of distal DVT to be highly accurate and reliable. A study by Jennersjö et al found that D-dimer levels were not as predictable for diagnosing distal DVT.¹²¹ The study found that 59% of patients being evaluated for DVT had distal DVT. The sensitivity of D-dimer in distal DVT was only 65% compared to 96% for proximal DVT. The negative predictive values were 84% for distal DVT and 99% for proximal DVT. Therefore, D-dimer levels cannot be used together with the pretest clinical probability to reliably rule in or rule out distal DVT. Proximal extension of isolated calf thrombi have been reported to occur in 20% of cases and usually within one week of presentation.¹²² There are some controversies as to the treatment of distal DVT. The American Society

of Chest Surgeons recommends 6 to 12 weeks of anticoagulation in symptomatic patients.¹²³ In contrast, a study by Gottlieb et al recommends withholding anticoagulation in symptomatic patients who have thigh ultrasounds negative for DVT and following up with sonograms to evaluate propagation of calf vein thrombus into the thigh for those patients with persistent symptoms.¹²⁴ In summary, studies show lower but acceptable sensitivity and specificity of color Doppler in diagnosing distal DVT. D-dimer has questionable utility in diagnosing distal DVT, and further studies are needed to evaluate the usefulness of anticoagulation therapy with distal DVT.

Outpatient Management Of DVT With Low Molecular Weight Heparin

It has been more than ten years since low molecular weight heparin (LMWH) has been investigated as a home treatment option for venous thromboembolism. Advantages to outpatient LMWH treatment compared to in-patient unfractionated heparin treatment include no laboratory monitoring with consequent cost savings and no increase in adverse events such as major bleeding, recurrent deep venous thrombosis, pulmonary embolism, and death.¹²⁵ Numerous studies and a Cochrane review of home versus in-patient treatment of deep vein thrombosis found that home management is effective and no more liable to complications than hospital treatment.¹²⁶⁻¹²⁸ A Cochrane review of once versus twice daily LMWH in the treatment of venous thromboembolism found that once daily treatment with LMWH is as effective and safe as the twice daily treatment. However, there was a possibility that patients receiving once daily LMWH were at a higher risk of recurrent venous thromboembolism and the decision to treat with a once daily regimen would have to be balanced with convenience of treatment and the potential for lower efficacy.¹²⁹ Therefore, outpatient treatment of venous thromboembolism with LMWH is a safe and cost-effective option.

Tissue Oxygen Saturation For Diagnosis Of Necrotizing Fasciitis

There is one study that supports the utility of tissue oxygen saturation monitoring in diagnosing necrotizing fasciitis of the lower extremities.¹³⁰ This study was done in an emergency department using near-infrared spectroscopy to measure tissue oxygen saturation over the middle third of possible involved areas. They found that the test had a sensitivity of 100%, a specificity of 97%, and accuracy of 97% for a

cutoff value of a tissue oxygen saturation of less than 70%. This study presented a rapid, reliable, and non-invasive method of assessing lower extremities at risk of necrotizing fasciitis; however, validation of the finding needs to be done before it can be recommended in general clinical practice.

Hyperbaric Oxygen For Treatment Of Necrotizing Fasciitis

Necrotizing fasciitis is a life-threatening bacterial infection of the fascia which progresses rapidly to involve the skin and subcutaneous tissue. The mortality rate for necrotizing fasciitis is 20 to 40%.^{131,132} Hyperbaric oxygen therapy involves the intermittent inhalation of 100% oxygen at increased pressure in either monoplace or multiplace chambers. There has been some promise using hyperbaric oxygen therapy as an adjuvant to standard treatment regimens but the results of studies have been mixed.¹³³ Hyperbaric oxygen therapy acts by decreasing tissue edema and swelling through vasoconstriction; it also leads to increased tissue oxygen tension which is critical for local defense mechanisms, particularly the efficacy of antibiotics.^{134,135} A study by Riseman et al compared a treatment group with a control group, matching groups for age, sex, and bacterial flora. Patients underwent three sessions of hyperbaric oxygen treatments in the first 24 hours which was then continued twice daily until the infection was controlled. They found that, by adding hyperbaric oxygen therapy to the standard surgical management, patients required less debridement and mortality decreased from 66% to 23%.¹³⁶ A study by Korhonen also showed a benefit in patients with Fournier's gangrene where the mortality rate was 9% with the use of hyperbaric oxygen.¹³⁷ However, a retrospective review of 42 patients with Fournier's gangrene found an increase in mortality from 12.5% in the non-hyperbaric oxygen treatment group to 26.9% in the hyperbaric oxygen group.¹³⁸ These results may have been flawed in that hyperbaric oxygen treatment may have been reserved for the more ill patients. Another study by Brown et al found no difference in mortality, need for debridement, or length of hospital stay in patients treated with hyperbaric oxygen compared to controls.¹³⁹ The results of this study may have been influenced by patients in the hyperbaric treatment group having more advanced sepsis and receiving less than four hyperbaric oxygen treatments, which is in contrast to the much more intensive treatments received by patients in the Riseman et al study. The role and ben-

efit of hyperbaric oxygen therapy in patients with necrotizing fasciitis still needs further investigation. There are no prospective, randomized studies and the studies that have been done comparing morbidity and mortality with hyperbaric oxygen therapy are smaller studies with varying treatment protocols. Hyperbaric oxygen therapy may have a role as an adjuvant to standard treatment for necrotizing fasciitis, but large, randomized, controlled studies are needed.

Conclusion

Let us return to our initial patient who traveled from Australia and presented to the ED with the complaint of a progressively painful and swollen right lower leg. After evaluation of the patient, diagnoses of DVT, DVT plus PE, and cellulitis were considered. The modified Well's criteria for predicting pretest probability of DVT was applied and a DVT was considered likely. A lower extremity Doppler ultrasound was initially considered but because of the complaint of chest discomfort, PE was suspected. Consequently, the order for a lower extremity Doppler ultrasound was cancelled and a CT angiogram of her chest was obtained instead. A diagnosis of DVT with PE was made and the patient was treated with low molecular weight heparin. She made an uneventful recovery.

As certain causes of a swollen extremity can be a source of significant morbidity and mortality for the patient, it is crucial for an emergency physician to consider all of the life-threatening causes of a swollen extremity. For example, consider compartment syndrome when the patient presents with any of the 5 P's (pain out of proportion, paresthesia, paralysis, pallor, and pulselessness), especially after trauma, and perform a rapid compartment pressure measurement. Consider necrotizing fasciitis in a patient who has signs of cellulitis but also has edema out of proportion to skin erythema, skin vesicles, and crepitus. These patients need immediate broad spectrum antibiotics and urgent surgical consultation for immediate debridement. DVT is a consideration for patients presenting with pain and swelling to an extremity. Risk factors should be assessed and D-dimer levels in combination with the pretest clinical probability of deep venous thrombosis using the modified Well's criteria should be used as an effective strategy in deciding whether a Doppler ultrasound of the extremity is needed.

Further studies are needed to address issues

such as the long-term prognosis for untreated patients with distal DVT and the usefulness of anticoagulation therapy for distal DVT so that patients are safely managed. Also, larger, randomized control studies are needed to further explore the role of hyperbaric oxygen therapy as an adjuvant to standard treatment for necrotizing fasciitis.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available.

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- c. Pain with passive stretch
- d. Decreased sensation
- e. Tense swelling
52. D-dimers, when positive, make the diagnosis of DVT since they are specific for thrombotic conditions.
 - a. True
 - b. False
53. For patients with antithrombin III deficiency, the peak age of onset for developing a VTE is?
 - a. 15-30
 - b. 30-40
 - c. 40-50
 - d. 50-60
 - e. 60-70
54. Which medical condition is not a risk factor for venous thromboembolism in an ambulatory person?
 - a. Asthma
 - b. Nephrotic syndrome
 - c. Myocardial infarction
 - d. CHF
 - e. IBD
55. The presence of peripheral edema in pregnant patients only occurs in the setting of preeclampsia.
 - a. True
 - b. False
56. Medications that may cause bilateral leg swelling include all of the following EXCEPT:
 - a. Calcium channel blockers
 - b. Thiazolidinediones
 - c. NSAIDs
 - d. Methyl dopa
 - e. Levothyroxine
57. The risk of venous thromboembolism is greatest in which phase of pregnancy?
 - a. 1st trimester
 - b. 2nd trimester
 - c. 3rd trimester
 - d. Post-partum
58. An elderly person living alone was found lethargic on the kitchen floor and presents with a bruised tense thigh. Intracompartmental pressure measurements should be taken in this patient.
 - a. True
 - b. False
59. A 50-year-old male complains of right calf pain and swelling. You perform the Thompson-Doherty test by squeezing his calf in the prone position to diagnose which condition?
 - a. Baker's cyst
 - b. DVT
 - c. Tendon rupture
 - d. Lymphedema
 - e. Pseudoaneurysm
60. Which is the most common cause of thrombophilia?
 - a. Protein C deficiency
 - b. Prothrombin mutation
 - c. Factor V Leiden
 - d. Pregnancy
 - e. Hyperhomocysteinemia
61. A negative venous Doppler is very reliable for ruling out DVT in all patients.
 - a. True
 - b. False

Physician CME Questions

49. Distension of the veins of the upper extremity is rarely seen with SVC syndrome.
 - a. True
 - b. False
50. Which fracture has the highest association with developing compartment syndrome?
 - a. Humerus
 - b. Femur
 - c. Supracondylar
 - d. Tibial
 - e. Radius
51. Which of the following is a late sign of compartment syndrome?
 - a. Erythema
 - b. Pulselessness

62. According to the Infectious Disease Society of America, you should obtain blood and wound cultures in all of the following scenarios except:
- Immunocompromised patients
 - Diffuse cellulitis
 - No response to initial antibiotics
 - History of an animal bite
 - Presence of a simple abscess
63. Early clinical clues for diagnosing necrotizing infections include all EXCEPT:
- Crepitus
 - Skin vesicles
 - Edema out of proportion to erythema
 - Discharge
 - C & D
64. About three fourths of patients who present with suspected DVT have nonthrombotic causes of leg pain.
- True
 - False

Coming in Future Issues:

Thoracic Imaging
Acutely Decompensated Heart Failure
Pediatric Toxicology

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

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- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:

- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II

- Safe, acceptable
- Probably useful

Level of Evidence:

- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case-control studies
- Less robust RCTs
- Results consistently positive

Class III

- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:

- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate

- Continuing area of research
- No recommendations until further research

Level of Evidence:

- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care

Continued in next column.

Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency

Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. JAMA 1992;268(16):2289-2295.

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