Clinical manifestations and evaluation of edema in adults

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INTRODUCTION

Edema is defined as a palpable swelling produced by expansion of the interstitial fluid volume; when massive and generalized, the excess fluid accumulation is called anasarca. A variety of clinical conditions are associated with the development of edema, including heart failure, cirrhosis, and the nephrotic syndrome, as well as local conditions such as venous and lymphatic disease (table 1). (See "Pathophysiology and etiology of edema in adults".)

The clinical features and evaluation of generalized edematous states in adults are reviewed here. The general principles of the treatment of edema in adults, including the use of diuretics to remove the excess fluid, the treatment of refractory edema, and the approach to edema in children, are discussed separately. (See "General principles of the treatment of edema in adults" and "Treatment of refractory edema in adults" and "Evaluation and management of edema in children".)

OVERVIEW OF PATHOPHYSIOLOGY

The pathophysiology and etiology of edema formation are discussed in detail elsewhere, but the pathophysiology is briefly reviewed here. (See "Pathophysiology and etiology of edema in adults".)

An increase in interstitial fluid volume that could lead to edema does not occur in normal subjects because of the tight balance of hemodynamic forces along the capillary wall and the function of the lymphatic vessels. For generalized edema to occur, two factors must be present:

- An alteration in capillary hemodynamics that favors the movement of fluid from the vascular space into the interstitium. Such movement requires a change in one or more components of Starling's law: increased capillary hydrostatic pressure, decreased capillary oncotic pressure (ie, hypoalbuminemia), and/or increased capillary permeability. (See "Pathophysiology and etiology of edema in adults", section on 'Capillary hemodynamics'.)

- The retention of dietary or intravenously administered sodium and water by the kidneys. Edema (other than localized edema as with an allergic reaction) does not become clinically apparent until the interstitial volume has increased by 2.5 to 3 L, an amount that is almost equal to the plasma volume. Thus, patients would develop marked hemoconcentration and shock if the plasma volume were not maintained by renal retention of sodium and water to compensate for the shift of fluid to the interstitium.

The retention of sodium and water can either be a primary event, as in renal failure, or a secondary event resulting from a primary reduction in either cardiac output (as in heart failure) or systemic vascular resistance (as in cirrhosis). In the latter settings, fluid retention tends to return the effective circulating volume toward normal. Diuretic therapy in such patients may have a deleterious effect on systemic hemodynamics even though it reduces the edema. Thus, careful monitoring is required. (See "General principles of the treatment of edema in adults", section on 'What are the consequences of the removal of edema fluid?'.)

CLINICAL MANIFESTATIONS AND EVALUATION

Edema in adults can be divided into peripheral edema, pulmonary edema, ascites, and other forms of edema, which include lymphedema, nonpitting edema, and periorbital and scrotal edema.

Peripheral edema — Peripheral edema can be pitting or nonpitting. Pitting edema is more common and is defined by the presence of tissue depression after pressure is applied to the edematous area for at least five seconds (picture 1) [1]. Pitting reflects movement of the excess interstitial water in response to pressure. Nonpitting edema suggests lymphatic obstruction or hypothyroidism. (See 'Nonpitting edema' below.)

Although clinicians commonly grade pitting edema from 1+ to 4+ (mild to severe), there is no agreed-upon definition of these grades. However, this type of grading scheme may help the clinician record relative changes in edema (eg, less edema after diuretic therapy). Documenting weight loss is another component of monitoring the efficacy of diuretic therapy.

Since peripheral edema locates preferentially in the dependent areas, it is primarily found in the lower extremities in ambulatory patients and over the sacrum in patients confined to bed rest. Less commonly, peripheral edema may occur in the upper extremities. (See 'Arm edema' below.)

Leg edema — Our approach to the differential diagnosis of leg edema in adults depends upon whether the patient has unilateral/asymmetric edema or bilateral edema, and upon the acuity of the edema.

Acute onset of unilateral leg edema raises concern for deep vein thrombosis, which must be addressed promptly. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity", section on 'Suspected first DVT (risk stratification)'.)

Bilateral edema is particularly frequent in older adults, and is usually chronic rather than acute. It is often due to chronic venous disease, heart failure, venodilating medications, or pulmonary hypertension (the most commonly missed cause of bilateral edema). The list of etiologies for bilateral edema is extensive (table 2).

Certain infiltrative conditions may be mistaken for edema, such as pretibial myxedema seen with thyroid disease and lipedema (a familial bilateral deposition of excess fat in the lower extremities). (See "Pretibial myxedema (thyroid dermopathy) in autoimmune thyroid disease".)

Patients with unilateral or asymmetric leg edema

Acute unilateral or asymmetric edema — It is essential to consider the diagnosis of deep venous thrombosis (DVT) in patients with acute unilateral or asymmetric leg edema. In addition to edema, patients with a DVT can have calf tenderness, pain or firmness along the course of a vein, or unilateral warmth or erythema. A larger calf circumference in the affected leg is the most useful finding, whereas Homans' sign (calf pain upon passive dorsiflexion of the foot) is **not** a reliable sign of DVT. The findings of DVT may be subtle; patients may present with only unilateral or asymmetric edema. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity", section on 'Clinical presentation'.)

Acute leg swelling may appear asymmetric in patients who have baseline unilateral or asymmetric chronic venous disease. In such patients, causes of acute bilateral edema (eg, drug-induced edema, heart failure) may present with asymmetric leg swelling.

Our approach to patients with acute unilateral or asymmetric leg edema is as follows:

- First, determine the clinical probability of DVT and perform appropriate diagnostic testing depending upon the clinical probability. The Wells score (calculator 1) and modified Wells score (calculator 2) are the best-studied prediction rules. We prefer approaches that combine an assessment of the clinical probability with D-dimer testing in select patients. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity", section on 'Suspected first DVT (risk stratification)'.)

- If DVT has been ruled out based upon the results of testing, it is important to evaluate for other causes of acute unilateral or asymmetric leg edema. DVT is not present in more than three quarters of patients with suspected DVT. In 160 such patients, after exclusion of DVT, the following causes of leg swelling were identified [2,3]:

    - Muscle strain, tear, or twisting injury to the leg – 40 percent
    - Leg swelling in a paralyzed limb – 9 percent
    - Lymphangitis or lymph obstruction – 7 percent
    - Venous insufficiency – 7 percent
    - Popliteal (Baker's) cyst – 5 percent
    - Cellulitis – 3 percent
    - Knee abnormality – 2 percent

- Unknown – 26 percent

Many of these diagnoses are suspected based upon clinical features:

- Calf muscle pull or tear – An inciting injury may be identified in the history, and there may be signs of bleeding (if ultrasonography is performed) or bruising at the ankle. The diagnostic evaluation of patients with a suspected calf muscle pull or tear is presented elsewhere. (See "Calf injuries not involving the Achilles tendon".)

- Cellulitis – Bacterial cellulitis is a common condition of the leg, particularly in patients who have chronic leg swelling due to venous insufficiency or lymphedema. In bacterial cellulitis, the warmth and redness often skip areas and may be associated with constitutional symptoms including fever. Some patients with venous insufficiency develop a low-grade, nonbacterial cellulitis, which resembles infectious cellulitis, but without constitutional symptoms. Although fever increases the suspicion for cellulitis, it can also be present in DVT. The approach to patients with suspected cellulitis is discussed separately. (See "Cellulitis and skin abscess: Clinical manifestations and diagnosis".)

- Superficial thrombophlebitis – Superficial vein thrombophlebitis classically presents with palpable, tender superficial veins. However, since superficial thrombophlebitis is a risk factor for DVT, many such individuals also undergo ultrasound to exclude DVT. (See "Phlebitis and thrombosis of the superficial lower extremity veins".)

- Popliteal (Baker's) cyst – The majority of popliteal cysts are due to either distention of a bursa by fluid originating from a knee joint or posterior herniation of the joint capsule due to increased intra-articular pressure. A popliteal cyst that causes calf symptoms is usually leaking or has ruptured. It is often distinguished from DVT by posterior knee pain, knee stiffness, swelling or a mass behind the knee (especially with the knee in extension), and by bruising around the ankle. However, calf symptoms are common; in addition, compression of the popliteal vein may cause leg swelling or secondary DVT. Evaluation of patients with a suspected popliteal cyst is presented elsewhere. (See "Popliteal (Baker's) cyst".)

- Inflammatory pathology of the knee – Pain, inflammation, and swelling can accompany any knee joint pathology and may be confused with a popliteal cyst or DVT. (See "Approach to the adult with unspecified knee pain".)

- May-Thurner syndrome – May-Thurner syndrome occurs in younger females (second or third decade) who present with acute pain and swelling of the entire left lower extremity, with or without venous thrombosis. The syndrome is most often caused by a compression of the left iliac vein between the overlying right common iliac artery and the fifth lumbar vertebrae. (See "May-Thurner syndrome".)

Chronic unilateral or asymmetric edema — The most common cause of chronic unilateral or asymmetric edema is lower extremity chronic venous disease. (See "Clinical manifestations of

lower extremity chronic venous disease" and "Diagnostic evaluation of lower extremity chronic venous insufficiency" and "Overview and management of lower extremity chronic venous disease".)

Less common causes include primary or secondary lymphedema, a pelvic neoplasm compromising venous return, and complex regional pain syndrome. (See "Clinical features and diagnosis of peripheral lymphedema" and "Complex regional pain syndrome in adults: Pathogenesis, clinical manifestations, and diagnosis".)

Our approach to patients with chronic unilateral or asymmetric leg edema is as follows:

- Chronic venous disease, lymphedema, and complex regional pain syndrome can generally be diagnosed based upon clinical features. Such patients do not usually require additional diagnostic testing or imaging. Suggestive history and physical examination findings include:
    - Chronic venous disease – There may be an antecedent history of thrombophlebitis in the affected leg. If the edema is longstanding, it often leads to characteristic pigmentary changes and skin ulceration (picture 2). (See "Clinical manifestations of lower extremity chronic venous disease".)
    - Lymphedema – Patients with lymphedema may have a history of an ipsilateral inguinal or pelvic lymph node dissection, or of radiation therapy. The edema is initially pitting, but becomes non-pitting as cutaneous fibrosis occurs. (See "Clinical features and diagnosis of peripheral lymphedema".)
    - Complex regional pain syndrome – Complex regional pain syndrome usually occurs four to six weeks after limb trauma, and is characterized by pain, edema, and alteration in skin color and temperature (picture 3). Specific diagnostic criteria are presented elsewhere. (See "Complex regional pain syndrome in adults: Pathogenesis, clinical manifestations, and diagnosis", section on 'Diagnostic criteria'.)
- If the history and examination are not consistent with venous insufficiency, lymphedema, or complex regional pain syndrome, compression ultrasonography (CUS) with Doppler should be obtained. CUS can provide the following information:
    - Confirmation of lower extremity chronic venous disease
    - Suggestion of pelvic outflow obstruction

  A normal study is consistent with either lymphedema or complex regional pain syndrome.
- A neoplasm should be suspected when CUS is suggestive of pelvic outflow obstruction, particularly in patients with a history of cancer or concerning symptoms such as unexplained weight loss. If a neoplasm is suspected, imaging of the pelvis should be obtained. Specifically, if ovarian or endometrial cancer is suspected, a transvaginal ultrasound should be performed. Otherwise, a contrast-enhanced computed tomography (CT) scan of the pelvis is preferred.

A pelvic neoplasm can cause unilateral or asymmetric leg edema by compressing the veins or lymphatic system. The most common etiologies include ovarian cancer, endometrial cancer, bladder cancer, lymphoma, and prostate cancer. Rarely, benign lesions such as uterine fibroids or ovarian cysts can cause unilateral leg swelling.

Patients with bilateral leg edema

Acute bilateral leg edema — Acute bilateral leg edema is uncommon. The most likely etiologies include:

- Side effect of medications, especially dihydropyridine calcium channel blockers (table 3). (See "Major side effects and safety of calcium channel blockers", section on 'Edema'.)
- Acute heart failure. (See "Approach to acute decompensated heart failure in adults", section on 'Clinical manifestations'.)
- Acute nephrotic syndrome. (See "Overview of heavy proteinuria and the nephrotic syndrome".)
- Bilateral DVT, which is often associated with malignancy. (See "Pathogenesis of the hypercoagulable state associated with malignancy".)

Our approach to patients presenting with acute bilateral leg edema is as follows:

- Although much less likely than with acute unilateral leg edema, the possibility of DVT must be considered. If the clinical probability of DVT is high (calculator 1 and calculator 2), we proceed with CUS to evaluate for DVT. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity", section on 'Suspected first DVT (risk stratification)'.)
- If the clinical probability of DVT is low or moderate, we evaluate multiple possible diagnoses simultaneously:
  - We review the patient's medication history and, if a drug known to cause edema has been initiated or dose-escalated (table 3), we discontinue it if possible. Spontaneous resolution of the edema with discontinuation of the potentially offending agent makes drug-induced edema likely.
  - Patients presenting with dyspnea, orthopnea, paroxysmal nocturnal dyspnea, tachypnea, tachycardia, rales, or distended neck veins should be evaluated for acute heart failure. The approach to such patients is presented elsewhere. (See "Approach to acute decompensated heart failure in adults".)
  - A semi-quantitative urine dipstick should be performed; if positive for protein, then a quantitative urine protein-to-creatinine ratio and serum albumin should be measured. (See "Overview of heavy proteinuria and the nephrotic syndrome".)

- A serum D-dimer should be measured. If elevated, a CUS is usually indicated to exclude DVT. (See "Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity", section on 'Suspected first DVT (risk stratification)'.)

Chronic bilateral leg edema — Chronic venous disease is the most common cause of chronic bilateral leg edema. However, chronic venous disease tends to be overdiagnosed in such patients, whereas other important diagnostic considerations, including heart failure and pulmonary hypertension (often related to sleep apnea), tend to be underdiagnosed. In one study, for example, 32 of 45 patients presenting to a primary care practice with chronic bilateral leg edema were initially diagnosed with chronic venous disease (71 percent) and 8 of 45 patients were diagnosed with heart failure (18 percent) [4]. After further evaluation, 15 had heart failure and 19 had pulmonary hypertension as causes of bilateral edema (33 and 42 percent, respectively).

Less common causes of chronic bilateral leg edema include renal disease, liver disease, a pelvic neoplasm, constrictive pericarditis, idiopathic edema, premenstrual edema, and malnutrition. (See "Idiopathic edema".)

Lymphedema and myxedema are not true edematous states. Lymphedema can be primary (usually presenting in childhood) or secondary. At the onset of lymphedema, it may be pitting, but it becomes nonpitting over time as cutaneous fibrosis and adipose tissue deposition occurs. (See "Clinical features and diagnosis of peripheral lymphedema".)

Myxedema is caused by the accumulation of glycosaminoglycans in the dermis. Pretibial myxedema is nonpitting and can be a feature of autoimmune thyroid disease (most often Graves' disease), or may be present in severe hypothyroidism. Myxedema is discussed elsewhere. (See "Pretibial myxedema (thyroid dermopathy) in autoimmune thyroid disease".)

Our approach to patients with chronic bilateral leg edema is as follows:

- The initial history and examination may be suggestive of a particular cause of chronic bilateral leg edema. As examples:
  - Patients with heart failure may present with chronic bilateral leg edema. In most cases, patients have a known history of heart failure and will have associated symptoms and signs such as dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Patients may also note fatigue, anorexia, and abdominal distention. The examination findings in heart failure are varied, but the most specific are extra heart sounds, hepatomegaly, cardiomegaly, lung rales, and elevated jugular venous pressure. Evaluation of patients with suspected heart failure is presented elsewhere. (See "Evaluation of the patient with suspected heart failure", section on 'Clinical presentation'.)
  - Chronic bilateral leg edema may be a manifestation of pulmonary hypertension caused by conditions such as sleep apnea. Sleep apnea should be suspected if the patient has excessive daytime sleepiness or is aware of loud snoring or interruptions of breathing while

sleeping. The evaluation of patients with suspected sleep apnea is discussed separately. (See "Clinical presentation and diagnosis of obstructive sleep apnea in adults".)

- Chronic bilateral leg edema can be a sign of advanced kidney or liver disease. Such patients typically have other clinical features of the underlying disorder as well as suggestive laboratory abnormalities. (See "Diagnostic approach to the patient with newly identified chronic kidney disease", section on 'Clinical manifestations' and "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis", section on 'Clinical manifestations'.)

- If the initial history and examination do **not** suggest a particular cause of chronic bilateral leg edema:

  - We obtain a semi-quantitative urine dipstick for protein, serum creatinine, serum albumin, prothrombin time, liver function tests, and thyroid-stimulating hormone.

  - If these tests are suggestive of renal, liver, or thyroid disease, we pursue these diagnoses. (See "Diagnostic approach to the patient with newly identified chronic kidney disease" and "Cirrhosis in adults: Etiologies, clinical manifestations, and diagnosis" and "Pretibial myxedema (thyroid dermopathy) in autoimmune thyroid disease" and "Clinical manifestations of hypothyroidism", section on 'Skin'.)

  - By contrast, if these tests are unrevealing, we obtain an echocardiogram to evaluate the possibility of heart failure or pulmonary hypertension. (See "Clinical features and diagnosis of pulmonary hypertension of unclear etiology in adults", section on 'Echocardiography'.)

  - If echocardiography is unrevealing, we assess the likelihood of chronic venous disease. In such patients, the examination usually reveals skin findings, such as pigmentary changes, induration, and ulceration (picture 2). If these findings are present, we make a presumptive diagnosis of chronic venous disease. (See "Clinical manifestations of lower extremity chronic venous disease".)

  - If typical skin findings of chronic venous disease are absent, we obtain imaging of the pelvis to exclude a pelvic neoplasm or other lesion-causing venous outflow obstruction. If ovarian cancer is suspected, we start with a transvaginal ultrasound; otherwise, we obtain a contrast-enhanced CT scan of the pelvis.

Arm edema — Our approach to the differential diagnosis of arm edema in adults depends upon the acuity of the edema.

Acute isolated upper extremity edema can be caused by trauma, infection, superficial thrombophlebitis, or inflammatory arthritis of the upper extremity. In such cases, the underlying etiology is typically apparent from the history and examination.

Upper extremity venous thrombosis should be suspected when none of the etiologies noted above are present, or if there are other significant risk factors such as the presence of a venous catheter. Spontaneous thrombosis occurs most often in muscular male athletes engaging in strenuous activity

with the involved arm and usually involves anatomic abnormalities of the thoracic outlet. Acute bilateral upper extremity edema is rare but may be seen with bilateral spontaneous venous thrombosis or superior vena cava syndrome. (See "Catheter-related upper extremity venous thrombosis" and "Primary (spontaneous) upper extremity deep vein thrombosis" and "Malignancy-related superior vena cava syndrome".)

CUS with Doppler is the study of choice for the initial evaluation of patients with possible upper extremity venous thrombosis. (See "Catheter-related upper extremity venous thrombosis", section on 'Diagnostic evaluation' and "Primary (spontaneous) upper extremity deep vein thrombosis", section on 'Diagnosis'.)

More gradual swelling of the arm occurs with lymphedema. Lymphedema can be primary (usually presenting in childhood) or secondary (usually following surgery or radiation treatment). At the onset of lymphedema, it may be pitting, but it becomes nonpitting over time as cutaneous fibrosis and adipose tissue deposition develop. (See "Clinical features and diagnosis of peripheral lymphedema".)

Isolated pulmonary edema — Patients with pulmonary edema complain primarily of shortness of breath and orthopnea. Physical examination usually reveals a tachypneic patient with rales and possibly a diastolic gallop (S3). The diagnosis of pulmonary edema should be confirmed by radiologic studies because other disorders, such as a pulmonary embolus, may produce similar symptoms but will require different therapy (image 1A-B). (See "Approach to acute decompensated heart failure in adults".)

Although cardiac disease (eg, acute myocardial infarction, heart failure, mitral or aortic valvular pathologies) is the most common cause of pulmonary edema, it can also be produced by volume overload due to primary renal sodium retention (such as acute glomerulonephritis) or by increased capillary permeability in the acute respiratory distress syndrome. (See "Glomerular disease: Evaluation and differential diagnosis in adults", section on 'Clinical manifestations of glomerular disease' and "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults".)

There are a number of other less common forms of noncardiogenic pulmonary edema, including high-altitude pulmonary edema (HAPE), neurogenic pulmonary edema, and pulmonary edema related to opioid overdose. (See "Noncardiogenic pulmonary edema".)

In contrast to cardiac and renal disease, uncomplicated cirrhosis is **not** associated with pulmonary edema. The intrahepatic sinusoidal obstruction in this disorder leads to selective increases in venous and capillary pressures **proximal to** the hepatic vein [5]. The systemic vascular resistance decreases in cirrhotic patients, and this generates relatively reduced blood volume in the cardiopulmonary circulation [6]. (See "Hyponatremia in patients with cirrhosis".)

Pulmonary edema also does not occur due to isolated hypoalbuminemia [7]. Thus, in the absence of a concurrent rise in left atrial and pulmonary capillary pressures, pulmonary edema is not usually seen with hypoalbuminemia, even at a plasma albumin concentration low enough to induce peripheral

edema [8]. The reasons for this are presented elsewhere. (See "Pathophysiology and etiology of edema in adults", section on 'Compensatory factors'.)

Ascites — Ascites is associated with abdominal distention and both shifting dullness and a fluid wave on percussion of the abdomen. Causes of ascites include cirrhosis, hepatic veno-occlusive disease (eg, Budd-Chiari syndrome), malignancy, and infection. Right-sided heart failure and constrictive pericarditis can cause ascites, but these processes typically also cause peripheral edema. If ascites is suspected, the diagnosis can be confirmed by ultrasonography. Abdominal paracentesis is used to determine the cause of ascites. (See "Evaluation of adults with ascites".)

Other forms of edema

Lymphedema — The major causes of lymphedema in adults in developed countries are axillary lymph node dissection in patients with breast cancer and axillary or inguinal lymph node dissection in patients with melanoma. However, worldwide, the most common cause is filariasis. The edema in such patients is typically limited to an arm or leg. The clinical hallmark of lymphedema is the presence of cutaneous and subcutaneous thickening, as manifested by cutaneous fibrosis, peau d'orange, and a positive Stemmer sign, which refers to an inability to tent the skin at the base of the digits. (See "Clinical features and diagnosis of peripheral lymphedema" and "Lymphatic filariasis: Epidemiology, clinical manifestations, and diagnosis", section on 'Lymphedema'.)

Nonpitting edema — Pitting reflects movement of the excess interstitial water in response to pressure. Testing for pitting involves applying firm pressure to the edematous tissue for at least five seconds [1]. (See 'Peripheral edema' above.)

Nonpitting edema is primarily due to one of two disorders:

- Moderate to severe lymphedema, as can occur after radical mastectomy or with lymphatic disease. However, pitting does occur in mild (stage I) and some cases of moderate (stage II) lymphedema [9]. (See "Clinical features and diagnosis of peripheral lymphedema".)
- Pretibial myxedema, which occurs in patients with thyroid disease and is associated with localized areas of swelling [5,6,10]. (See "Pretibial myxedema (thyroid dermopathy) in autoimmune thyroid disease".)

Periorbital and scrotal edema — Periorbital and scrotal edema are localized forms of edema that can be seen in systemic edematous states but should **not** be the sole manifestation of edema in these disorders. The differential diagnosis of **localized** periorbital/facial edema and acute idiopathic scrotal edema are discussed separately. (See "An overview of angioedema: Clinical features, diagnosis, and management", section on 'Disorders resembling cutaneous edema' and "Evaluation of acute scrotal pain in adults", section on 'Acute idiopathic scrotal edema'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Fluid and electrolyte disorders".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Swelling (The Basics)")
- Beyond the Basics topics (see "Patient education: Edema (swelling) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Edema is a palpable swelling produced by expansion of the interstitial fluid volume. Generalized edema is produced by one or more of the following: increased capillary hydrostatic pressure, decreased capillary oncotic pressure, and/or increased capillary permeability. The retention of sodium and water by the kidneys must also occur for edema to develop. (See 'Overview of pathophysiology' above.)
- Our approach to the evaluation of leg edema in adults depends upon whether the patient has unilateral/asymmetric edema or bilateral edema, and upon the acuity of the edema.
    - In patients with acute unilateral or asymmetric edema, we first evaluate for deep venous thrombosis (DVT). If DVT has been excluded, we evaluate for other causes of acute unilateral or asymmetric edema. (See 'Acute unilateral or asymmetric edema' above.)
    - In patients with chronic unilateral or asymmetric edema, a diagnosis can generally be made based upon clinical features. If the history and examination are not consistent with a particular diagnosis (eg, venous insufficiency, lymphedema, or complex regional pain syndrome), we obtain compression ultrasonography (CUS) with Doppler. If the CUS suggests pelvic outflow obstruction, we obtain a transvaginal ultrasound or a contrast-enhanced computed tomography (CT) scan of the pelvis. (See 'Chronic unilateral or asymmetric edema' above.)

- In patients with acute bilateral leg edema, we first evaluate for DVT. If DVT has been excluded, we assess for edema as a medication side effect (table 3) or as a manifestation of acute heart failure or acute nephrotic syndrome. (See 'Acute bilateral leg edema' above.)

- In patients with chronic bilateral leg edema, a diagnosis can often be made based upon clinical features. If the history and examination are not consistent with a particular diagnosis (eg, chronic venous disease, heart failure, pulmonary hypertension, renal, or liver disease), we obtain a semi-quantitative urine dipstick for protein, and measure serum creatinine, serum albumin, prothrombin time, liver function tests, and thyroid-stimulating hormone. If those tests are unrevealing, we obtain an echocardiogram. If the echocardiogram does not suggest the etiology of the edema, and chronic venous disease does not seem likely, we obtain imaging of the pelvis to exclude venous outflow obstruction. (See 'Chronic bilateral leg edema' above.)

- Our approach to the differential diagnosis of arm edema in adults depends upon the acuity of the edema.

  - Acute isolated upper extremity edema can be caused by trauma, infection, superficial thrombophlebitis, or inflammatory arthritis of the upper extremity. Upper extremity venous thrombosis should be suspected when none of the etiologies noted above are present, or if there are other significant risk factors such as the presence of a venous catheter. CUS with Doppler is the study of choice for the initial evaluation of patients with possible upper extremity venous thrombosis. (See 'Arm edema' above.)

  - More gradual swelling of the arm occurs with lymphedema. (See 'Arm edema' above.)

- Patients with pulmonary edema complain primarily of shortness of breath and orthopnea. Physical examination usually reveals a tachypneic patient with rales and possibly a diastolic gallop (S3). The diagnosis of pulmonary edema should be confirmed by radiologic studies because other disorders, such as a pulmonary embolus, may produce similar symptoms but will require different therapy. (See 'Isolated pulmonary edema' above.)

- Ascites is associated with abdominal distention and both shifting dullness and a fluid wave on percussion of the abdomen. If ascites is suspected, the diagnosis can be confirmed by ultrasonography. (See 'Ascites' above.)

- Other forms of edema include lymphedema, myxedema, periorbital edema, and scrotal edema. (See 'Other forms of edema' above.)

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GRAPHICS

Major causes of edema by primary mechanism

Increased capillary hydraulic pressure
Increased plasma volume due to renal sodium retention
Heart failure, including cor pulmonale
Primary renal sodium retention
▪ Renal disease, including the nephrotic syndrome
▪ Drugs:* Nonsteroidal antiinflammatory drugs (NSAIDs), glucocorticoids, fludrocortisone, thiazolidinediones (glitazones), insulins, estrogens, progestins, androgens, testosterone, aromatase inhibitors, tamoxifen; and by multiple mechanisms: vasodilators (hydralazine, minoxidil, diazoxide) and calcium channel blockers (particularly dihydropyridines, ie, amlodipine, nifedipine); also refer to "Arteriolar vasodilation" below
▪ Refeeding edema
▪ Early hepatic cirrhosis
Pregnancy and premenstrual edema
Idiopathic edema, when diuretic induced
Sodium or fluid overload: Parenteral antibiotics or other drugs with large amounts of sodium, sodium bicarbonate, or excessive or overly rapid fluid replacement
Venous obstruction or insufficiency
Cirrhosis or hepatic venous obstruction
Acute pulmonary edema
Local venous obstruction
▪ Venous thrombosis
▪ Venous stenosis
Chronic venous insufficiency - post-thrombotic syndrome
Arteriolar vasodilation
Drugs:* Frequent - vasodilators (hydralazine, minoxidil, diazoxide), dihydropyridine calcium channel blockers; less frequent - alpha1 blockers, sympatholytics (ie, methyldopa), nondihydropyridine calcium channel blockers[1]
Idiopathic edema (?)
Hypoalbuminemia
Protein loss
Nephrotic syndrome
Protein-losing enteropathy
Reduced albumin synthesis
Liver disease
Malnutrition
Increased capillary permeability
Idiopathic edema (?)
Burns
Trauma
Inflammation or sepsis
Allergic reactions, including certain forms of angioedema
Adult respiratory distress syndrome
Diabetes mellitus
Interleukin-2 therapy
Malignant ascites

Lymphatic obstruction or increased interstitial oncotic pressure
Lymph node dissection
Nodal enlargement due to malignancy
Hypothyroidism
Malignant ascites
Other drugs* (uncertain mechanism)
Anticonvulsant: Gabapentin, pregabalin
Antineoplastic: Docetaxel, cisplatin
Antiparkinson: Pramipexole, ropinirole

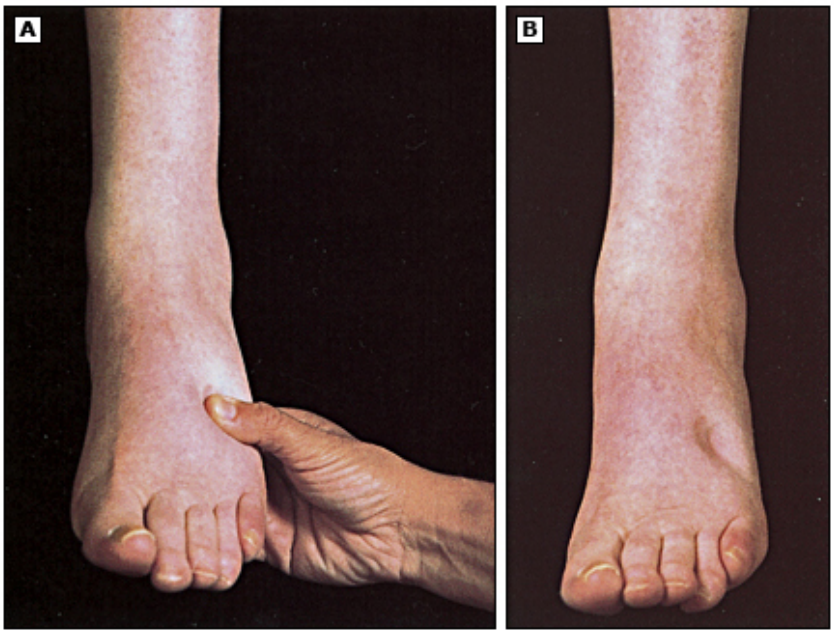
* Patients with decreased cardiac output, preexisting renal insufficiency, and/or receiving higher doses are more likely to experience edema and edema-associated adverse events. This is not a complete list of drugs associated with edema. For additional information, refer to the Lexicomp individual drug monographs included with UpToDate.

Reference:

1. *Messerli FH. Vasodilatory edema: A common side effect of antihypertensive therapy. Curr Cardiol Rep 2002; 4(6):479.*

Graphic 53550 Version 9.0

Pitting edema



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Graphic 118097 Version 1.0

Major causes of bilateral lower extremity edema

Acute edema

- Medications
- Heart failure
- Nephrotic syndrome
- Venous thrombosis
- Acute worsening of chronic causes

Chronic edema

- Venous insufficiency
- Heart failure
  - Left-sided with preserved or reduced ejection fraction
  - Right-sided
    - Pulmonary hypertension (including sleep apnea)
  - Restrictive pericarditis
  - Restrictive cardiomyopathy
- Renal disease (including nephrotic syndrome)
- Liver disease (early cirrhosis)
- Premenstrual edema
- Pregnancy
- Malnutrition (including malabsorption and protein losing enteropathy)
- Pelvic compression (including tumor or lymphoma)
- Dependent edema
- Sodium or fluid overload (including parenteral fluids, antibiotics and other drugs with large amounts of sodium)
- Refeeding edema
- Idiopathic edema
- Inflammation (including sepsis)
- Medications

Chronic lymphedema

- Primary lymphedema (presenting in childhood)
- Secondary lymphedema (including lymph node dissection)
- Thyroid disease (myxedema)

Graphic 118001 Version 1.0

Skin changes of chronic venous insufficiency

Longstanding edema in this patient with chronic venous insufficiency led to moderately advanced pigment changes on the medial and lateral ankles, which extend onto the dorsum of the foot. The left medial ankle displays a healed venous ulcer below the malleolus; the right lateral ankle has a small, active, venous ulcer (arrow).

Courtesy of Patrick C Alguire, MD.

Graphic 56758 Version 2.0

Complex regional pain syndrome of the foot

Courtesy of: David D Sherry, MD.

Graphic 53380 Version 2.0

Medications associated with edema*

Common

Dihydropyridine calcium channel blockers

- Amlodipine
- Felodipine
- Isradipine
- Nicardipine
- Nifedipine
- Nimodipine
- Nitrendipine

Other vasodilators

- Hydralazine
- Minoxidil
- Alpha-blockers

Endocrine

- Thiazolidinediones
  - Rosiglitazone
  - Pioglitazone
- Glucocorticoids
- Fludrocortisone
- Estrogen
- Progesterone
- Tamoxifen
- Aromatase inhibitors
- Testosterone
- Androgens

Less common

Nondihydropyridine calcium channel blockers

- Verapamil
- Diltiazem

Anticonvulsant

- Gabapentin
- Pregabalin

Antineoplastic

- Docetaxel
- Cisplatin
- Interleukin-2 therapy

Antiparkinson

- Pramipexole
- Ropinirole

Antidepressants

- Monoamine oxidase inhibitors
- Trazodone

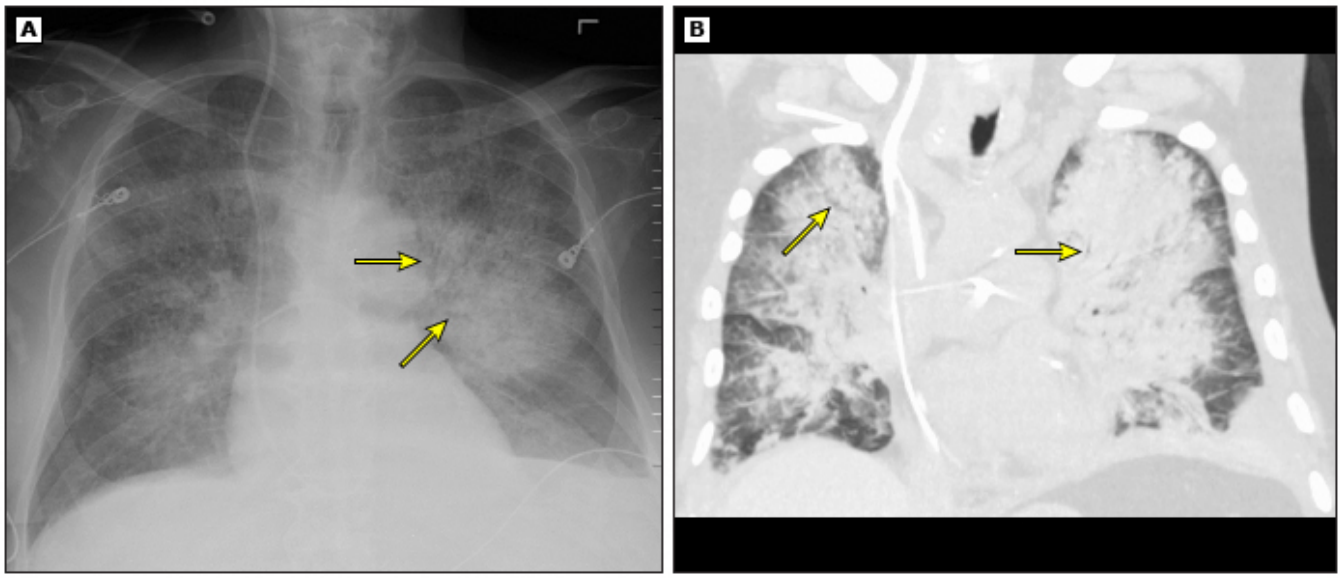
Other

- Diazoxide
- NSAIDs
- Proton pump inhibitors

NSAIDs: nonsteroidal antiinflammatory drugs.
* This is not a complete list of drugs associated with edema. For additional information, refer to the Lexicomp individual drug monographs included with UpToDate.

Graphic 118003 Version 1.0

Radiograph and CT of acute pulmonary edema

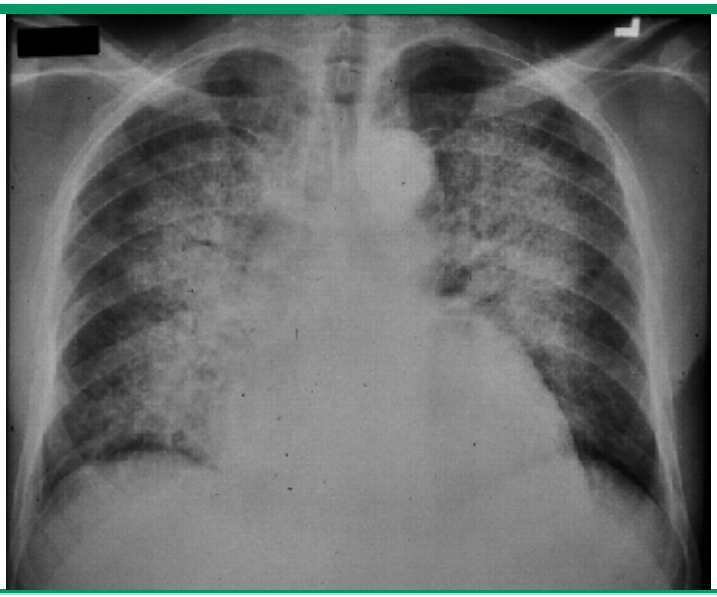


(A) An anteroposterior radiograph shows perihilar consolidations and air bronchograms (arrows) of acute alveolar edema. (B) A coronal reconstruction of a CT scan of the same patient shows acute alveolar edema with diffuse perihilar infiltrates and air bronchograms (arrows).

CT: computed tomography.

Graphic 98495 Version 3.0

Hydrostatic pulmonary edema



Pulmonary edema in a "butterfly distribution" due to left ventricular failure. Chest radiograph shows large perihilar opacities in patient with enlarged cardiac silhouette.

Courtesy of Paul Stark, MD.

Graphic 58394 Version 5.0

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C Christopher Smith, MD Nothing to disclose **Michael Emmett, MD** Consultant/Advisory Boards: AstraZeneca (Lokelma - Zirconium Silicate). **Lisa Kunins, MD** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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