MSD MANUAL
Professional Version

Edema

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Edema is swelling of soft tissues due to increased interstitial fluid. The fluid is predominantly water, but protein and cell-rich fluid can accumulate if there is infection or lymphatic obstruction.

Edema may be generalized or local (eg, limited to a single extremity or part of an extremity). It sometimes appears abruptly; patients say that an extremity suddenly swells. More often, edema develops insidiously, beginning with weight gain, puffy eyes at awakening in the morning, and tight shoes at the end of the day. Slowly developing edema may become massive before patients seek medical care.

Lower Extremity Edema

IMAGE

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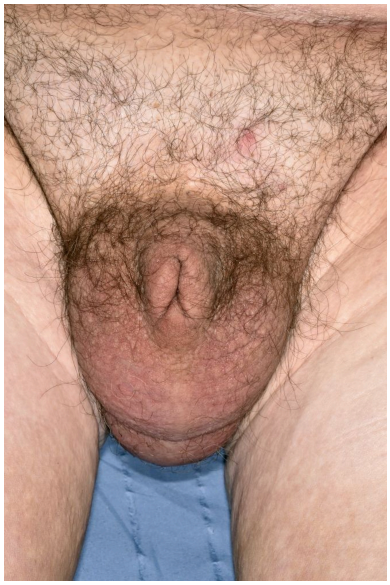
Edema itself causes few symptoms other than occasionally a feeling of tightness or fullness; other symptoms are usually related to the underlying disorder. Patients with edema due to heart failure (a common cause) often have dyspnea during exertion, orthopnea, and paroxysmal nocturnal dyspnea. Patients with edema due to deep venous thrombosis (DVT) often have leg pain.

Scrotal Edema

IMAGE



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Edema due to extracellular fluid volume expansion is often dependent. Thus, in ambulatory patients, edema is in the feet and lower legs; patients requiring bed rest develop edema in the buttocks, genitals, and posterior thighs. Females who lie on only one side may develop edema in the dependent breast. Lymphatic obstruction causes edema distal to the site of obstruction.

Pathophysiology of Edema

Edema results from increased movement of fluid from the intravascular to the interstitial space or decreased movement of water from the interstitium into the capillaries or lymphatic vessels. The mechanism involves one or more of the following:

- Increased capillary hydrostatic pressure
- Decreased plasma oncotic pressure
- Increased capillary permeability
- Obstruction of the lymphatic system

As fluid shifts into the interstitial space, intravascular volume is depleted. Intravascular volume depletion activates the renin-angiotensin-aldosterone- vasopressin (ADH) system, resulting in renal sodium retention. By increasing osmolality, renal sodium retention triggers water retention by the kidneys and helps maintain plasma volume. Increased renal sodium retention also may be a primary cause of fluid overload and hence edema. Excessive exogenous sodium intake may also contribute.

Less often, edema results from decreased movement of fluid out of the interstitial space into the capillaries due to lack of adequate plasma oncotic pressure, as in nephrotic syndrome, protein-losing enteropathy, liver failure, or starvation.

Increased capilliary permeability occurs in infections or as the result of toxin or inflammatory damage to the capillary walls. In angioedema, mediators, including mast cell–derived mediators (eg, histamine,

leukotrienes, prostaglandins) and bradykinin and complement-derived mediators, cause focal edema.

The lymphatic system is responsible for removing protein and white blood cells (along with some water) from the interstitium. Lymphatic obstruction allows these substances to accumulate in the interstitium.

Etiology of Edema

Generalized edema is most commonly caused by

- Heart failure
- Liver failure
- Kidney disorders (especially nephrotic syndrome)

Localized edema is most commonly caused by

- DVT or another venous disorder or venous obstruction (eg, by tumor)
- Infection
- Angioedema
- Lymphatic obstruction

Chronic venous insufficiency may involve one or both legs.

Common causes are listed by primary mechanism (see table Some Causes of Edema).

TABLE

Some Causes of Edema

Cause	Suggestive Findings	Diagnostic Approach*
Increased hydrostatic pressure, fluid overload		
	Symmetric, dependent, painless, pitting edema; often with left-sided heart failure, with dyspnea during exertion, orthopnea, and paroxysmal nocturnal dyspnea	
Right heart failure (primary or secondary to left-sided disease or to constrictive pericarditis or pericardial effusion) directly increasing venous pressure	Commonly, lung crackles, S3 or S4 gallop or both (due to left heart failure); jugular venous distention, hepatojugular reflux, and Kussmaul sign With constrictive pericarditis or pericardial effusion, in addition to jugular venous distention, hepatojugular reflux, and Kussmaul sign; may note distant or weak heart sounds.	Chest radiography and ECG Usually echocardiography
Pregnancy and premenstrual state	Symmetric, dependent, painless, usually mild pitting edema Apparent by history	Clinical evaluation
Medications (eg, minoxidil, NSAIDs, estrogens, fludrocortisone, dihydropyridine, diltiazem, other calcium channel blockers)	Symmetric, dependent, painless, usually mild pitting edema	Clinical evaluation
Iatrogenic (eg, excessive intravenous fluids)	Symmetric, dependent, painless, usually mild pitting edema	Clinical evaluation

	Apparent by history and medical record	
Increased hydrostatic pressure, venous obstruction		
DVT	Acute, pitting edema in a single, usually lower extremity, usually with pain; sometimes Homans sign (pain in the calf when the foot is dorsiflexed) Redness, warmth, and tenderness; possibly less marked than in soft-tissue infection Sometimes a predisposing factor (eg, recent surgery, trauma, immobilization, hormone replacement, cancer)	Ultrasound D-dimer testing
Chronic venous insufficiency	Chronic edema in one or both lower extremities, with brownish discoloration, discomfort but not marked pain, and sometimes skin ulcers Often associated with varicose veins	Clinical evaluation
Extrinsic venous compression (eg, by tumor, a gravid uterus, or marked abdominal obesity)	Nonpainful, slowly developing edema If tumor compresses the superior vena cava, usually facial plethora, distended neck veins, and absent venous pulse waves above the obstruction	Clinical evaluation Ultrasound or CT if tumor is suspected
Prolonged absence of skeletal muscle pumping activity on extremity veins	Prolonged immobility (eg, being bedbound or on a long airline flight) Painless, symmetric, dependent edema	Clinical evaluation

Decreased plasma oncotic pressure†		
Nephrotic syndrome	Diffuse edema, often significant ascites, and sometimes periorbital edema	24-hour urine collection to check for protein loss Serum albumin level
Protein-losing enteropathy	Significant diarrhea	Testing for cause Sometimes endoscopy Sometimes serum and 24-hour stool testing for alpha-1-antitrypsin
Reduced albumin synthesis (eg, in liver disorders or undernutrition)	Often with significant ascites Causes often apparent by history If cause is a chronic liver disorder, often jaundice, spider angiomas, gynecomastia, palmar erythema, and testicular atrophy	Serum albumin, liver tests, PT/PTT
Increased capillary permeability		
Angioedema (allergic, idiopathic, hereditary)	Sudden, focal, asymmetric, nondependent subcutaneous or submucosal edema, more often involving the face, lips, oral mucosa, extremities, or genitals	Clinical evaluation
Injury (eg, burns, chemicals, toxins, blunt trauma)	Focal edema, sometimes erythematous; causes apparent by history	Clinical evaluation
Severe sepsis (causing vascular endothelial leakage)	Obvious sepsis syndrome with fever, tachycardia, focal infection Painless, symmetrical edema	Cultures Imaging studies as needed
	If due to cellulitis, usually redder (or darker on dark skin) and more painful and tender than that due to	Clinical evaluation

Soft-tissue infection (eg, cellulitis, necrotizing myofasciitis)	tender than that due to angioedema and more circumscribed than that due to DVT With necrotizing infections, severe pain, constitutional symptoms	Cultures Sometimes ultrasound to rule out DVT
Lymphatic obstruction		
Iatrogenic (eg, after lymph node dissection in cancer surgery or after radiation therapy)	Etiology usually apparent by history Initially pitting edema, with fibrosis developing later	Clinical evaluation
Congenital (rare)	Often onset in childhood, but for some types, only later onset May be familial	Sometimes lymphoscintigraphy
Lymphatic filariasis	History of being in an endemic area Usually focal edema, sometimes involving the genitals	Microscopic examination of blood smear

* Most patients with generalized edema require complete blood count (CBC), electrolytes, blood urea nitrogen (BUN), creatinine, liver tests, serum protein measurement, and urinalysis (to check for proteinuria).

† Decreased plasma oncotic pressure often triggers secondary sodium and water retention, leading to fluid overload.

DVT = deep venous thrombosis; NSAIDs = nonsteroidal anti-inflammatory drugs; PT = prothrombin time; PTT = partial thromboplastin time; S3 = third heart sound; S4 = fourth heart sound.

Evaluation of Edema

History

History of present illness should include location and duration of edema and presence and degree of pain or discomfort. Female patients should be asked whether they are pregnant and whether edema

seems related to menstrual periods. Having patients with chronic edema keep a log of weight gain or loss is valuable.

Review of systems should include symptoms of causative disorders, including dyspnea during exertion, orthopnea, and paroxysmal nocturnal dyspnea (heart failure); alcohol or hepatotoxin exposure, jaundice, and easy bruising (a liver disorder); malaise and anorexia (cancer or a liver or kidney disorder); and immobilization, extremity injury, or recent surgery (DVT).

Past medical history should include any disorders known to cause edema, including heart, liver, and kidney disorders and cancer (including any related surgery or radiation therapy). The history should also include predisposing conditions for these causes, including streptococcal infection, recent viral infection (eg, hepatitis), alcohol use disorder, and hypercoagulable disorders. Medication history should include specific questions about medications known to cause edema (see table Some Causes of Edema). Patients are asked about the amount of sodium used in cooking and at the table.

Physical examination

The area of edema is identified and examined for extent, warmth, erythema, and tenderness; symmetry or lack of it is noted. Presence and degree of pitting (visible and palpable depressions caused by pressure from the examiner's fingers on the edematous area, which displaces the interstitial fluid) are noted.

In the general examination, the skin is inspected for jaundice, bruising, and spider angiomas (suggesting a liver disorder).

Lungs are examined for dullness to percussion, reduced or exaggerated breath sounds, crackles, rhonchi, and a pleural friction rub.

The internal jugular vein height, waveform, and reflux are noted.

The heart is palpated for thrills, thrust, parasternal lift, and asynchronous abnormal systolic bulge. Auscultation for loud pulmonic component of second heart sound (P2), third (S3) or fourth (S4) heart sounds, murmurs, and pericardial rub or knock is done; all suggest cardiac origin.

The abdomen is inspected, palpated, and percussed for ascites, hepatomegaly, and splenomegaly to check for a liver disorder or heart failure. The kidneys are palpated, and the bladder is percussed. An abnormal abdominal mass, if present, should be palpated.

Red flags

Certain findings raise suspicion of a more serious etiology of edema:

- Sudden onset
- Significant pain
- Shortness of breath
- Fever
- History of a heart disorder or an abnormal cardiac examination

- Hemoptysis, dyspnea, or pleural friction rub
- Hepatomegaly, jaundice, ascites, splenomegaly, or hematemesis
- Unilateral leg swelling with tenderness

Interpretation of findings

Potential acute life threats, which typically manifest with sudden onset of focal edema, must be identified. Such a presentation suggests acute DVT, soft-tissue infection, or angioedema. Acute DVT may lead to pulmonary embolism (PE), which can be fatal. Soft-tissue infections range from minor to life threatening, depending on factors that include the infecting organism and the patient's health. Acute angioedema sometimes progresses to involve the airway, with serious consequences.

Dyspnea may occur with edema due to heart failure, DVT if PE has occurred, acute respiratory distress syndrome, or angioedema that involves the airways.

Generalized, slowly developing edema suggests a chronic heart, kidney, or liver disorder. Although these disorders can also be life threatening, complications tend to take much longer to develop.

These factors and other clinical features help suggest the cause (see table Some Causes of Edema).

Testing

For most patients with generalized edema, testing should include complete blood count (CBC), serum electrolytes, blood urea nitrogen (BUN), creatinine, liver tests, serum protein, and urinalysis (particularly noting the presence of protein and microscopic hematuria). Other tests should be done based on the suspected cause (see table Some Causes of Edema)—eg, brain natriuretic peptide (BNP) for suspected heart failure or D-dimer for suspected pulmonary embolism.

Point-of-care ultrasound (POCUS) can sometimes be useful to evaluate the following:

- Fluid and volume status (evaluating jugular venous pressure, inferior vena cava, B-lines, pleural effusions)
- Left ventricular ejection fraction
- Right ventricular abnormalities (eg, increased right ventricular pressure or size or impaired function) secondary to disorders such as pulmonary embolism or right ventricular failure

Patients with isolated lower-extremity swelling should usually have venous obstruction excluded by ultrasound.

Treatment of Edema

Specific causes are treated.

Patients with sodium retention often benefit from restriction of dietary sodium. Patients with heart failure should eliminate salt in cooking and at the table and avoid prepared foods with added salt.

Patients with advanced cirrhosis or nephrotic syndrome often require more severe sodium restriction (≤ 1 g/day). Potassium salts are often substituted for sodium salts to make sodium restriction tolerable; however, care should be taken, especially in patients receiving potassium-sparing diuretics, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin II receptor blockers (ARBs) and in those with a kidney disorder because potentially fatal hyperkalemia can result.

People with conditions involving sodium retention may also benefit from loop or thiazide diuretics. However, diuretics should not be given only to improve the appearance caused by edema. When diuretics are used, potassium wasting can be dangerous in some patients; potassium-sparing diuretics (eg, amiloride, triamterene, spironolactone, eplerenone) inhibit sodium reabsorption in the distal nephron and collecting duct. When used alone, they modestly increase sodium excretion. Both triamterene and amiloride have been combined with a thiazide to prevent potassium wasting. An ACE inhibitor–thiazide combination also reduces potassium wasting.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors (eg, canagliflozin, dapagliflozin, empagliflozin) lower serum glucose in patients with diabetes but also induce diuresis by increasing natriuresis and glycosuria without significantly affecting serum electrolytes (1, 2, 3, 4). They can be used in patients with heart failure or nephrotic syndrome with or without diabetes.

Treatment references

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4. Packer M, Anker SD, Butler J, et al: Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med* 383(15):1413–1424, 2020. doi: 10.1056/NEJMoa2022190

Geriatrics Essentials: Edema

In older adults, use of medications that treat causes of edema (particularly heart failure) requires special caution, such as the following:

- Starting doses low and evaluating patients thoroughly when the dose is changed
- Monitoring for orthostatic hypotension if diuretics, ACE inhibitors, angiotensin II receptor blockers, or beta-blockers are used
- Frequently testing for hypokalemia or hyperkalemia
- Not stopping calcium channel blockers because of pedal edema, which is benign

Logging daily weight helps immensely in monitoring clinical improvement or deterioration.

Key Points

- Edema may result from a generalized or local process and may occur anywhere in the body.
- Main causes of generalized edema are chronic heart, liver, and kidney disorders.
- Not all edema is serious; consequences depend mainly on the cause.
- Sudden onset should trigger prompt evaluation.