

**Final
Diagnosis**

- **Nonischemic cardiomyopathy**
- **Hypoalbuminemia**
- **Multifactorial Generalized Edema**
- **Atypical CLL/SLL**

Principal Causes of Generalized Edema: History, Physical Examination, and Laboratory Findings

Organ System	History	Physical Examination	Laboratory Findings
Cardiac	<u>Dyspnea with exertion prominent</u> —often associated with orthopnea—or paroxysmal nocturnal dyspnea	Elevated jugular venous pressure, ventricular (S ₃) gallop; occasionally with displaced or dyskinetic apical pulse; peripheral cyanosis, cool extremities, small pulse pressure when severe	Elevated urea nitrogen-to-creatinine ratio common; serum sodium often diminished; elevated natriuretic peptides
Hepatic	Dyspnea uncommon, except if associated with significant degree of ascites; most often a history of ethanol abuse	Frequently associated with ascites; jugular venous pressure normal or low; blood pressure lower than in renal or cardiac disease; one or more additional signs of chronic liver disease (jaundice, palmar erythema, Dupuytren's contracture, spider angiomas, male gynecomastia; asterix and other signs of encephalopathy) may be present	If severe, <u>reductions in serum albumin</u> , cholesterol, other hepatic proteins (transferrin, fibrinogen); liver enzymes elevated, depending on the cause and acuity of liver injury; tendency toward hypokalemia, respiratory alkalosis; macrocytosis from folate deficiency
Renal (CRF)	Usually chronic: may be associated with uremic signs and symptoms, including decreased appetite, altered (metallic or fishy) taste, altered sleep pattern, difficulty concentrating, restless legs, or myoclonus; dyspnea can be present, but generally less prominent than in heart failure	Elevated blood pressure; hypertensive retinopathy; nitrogenous fetor; pericardial friction rub in advanced cases with uremia	Elevation of serum creatinine and cystatin C; albuminuria; hyperkalemia, metabolic acidosis, hyperphosphatemia, hypocalcemia, anemia (usually normocytic)
Renal (NS)	Childhood diabetes mellitus; plasma cell dyscrasias	Periorbital edema; hypertension	Proteinuria (≥ 3.5 g/d); <u>hypoalbuminemia</u> ; hypercholesterolemia; microscopic hematuria

Braunwald E, Loscalzo J. Edema. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. eds. Harrison's Principles of Internal Medicine, 20e. McGraw Hill; 2018.

Table 2. Initial Clinical Diagnoses for 45 Patients with Bilateral Leg Edema*

Diagnosis	Number (%)
Congestive heart failure	8 (18)
Venous insufficiency	33 (71)
Nephrotic syndrome	6 (13)
Lymphedema	1 (2)
Pulmonary hypertension	1 (2)
Cor pulmonale	1 (2)
Hypoalbuminemia	1 (2)
Use of nonsteroidal anti-inflammatory drug	1 (2)
Use of corticosteroids	1 (2)
Sleep apnea	1 (2)
Obesity	1 (2)
Uncertain	3 (7)

* Patients could have more than one diagnosis.

Blankfield RP, Finkelhor RS, Alexander JJ, Flocke SA, Maiocco J, Goodwin M, Zyzanski SJ. Etiology and diagnosis of bilateral leg edema in primary care. *Am J Med.* 1998 Sep;105(3):192-7. doi: 10.1016/s0002-9343(98)00235-6. PMID: 9753021.

Table 3. Final Diagnoses for 45 Patients with Bilateral Leg Edema after Laboratory Investigation

Diagnosis*	Number (%)
Cardiac diagnosis	
Left ventricular systolic dysfunction	8 (18)
Right ventricular systolic dysfunction	1 (2)
Diastolic dysfunction	4 (9)
Mitral regurgitation	1 (2)
Aortic stenosis	1 (2)
Atrial septal defect	1 (2)
Atrial fibrillation	2 (4)
Pulmonary diagnosis [†]	
Pulmonary hypertension (>40 mm Hg)	9 (20)
Borderline pulmonary hypertension (31–40 mm Hg)	10 (22)
Venous insufficiency	10 (22)
Nephrotic syndrome	1 (2)
Transient renal disease	1 (2)
Proteinuria (>1 g but <3 g per day)	6 (13)
Hypoalbuminemia	1 (2)
Lymphedema	1 (2)
Stenosis of inferior vena cava	1 (2)
Use of nonsteroidal anti-inflammatory drug (definite)	1 (2)
Use of corticosteroid or nonsteroidal anti-inflammatory drug (probable cause)	6 (13)
Idiopathic (none of the above)	12 (27)

* Patients could have more than one diagnosis.

[†] Nine of these patients also had cardiac diagnoses.

- 7/8 patients initially diagnosed with heart failure subsequently proven with echo, strong association between initial and final diagnosis ($P < 0.01$).
- 77% of patients initially diagnosed with venous insufficiency, only 22% proven to have diagnosis on doppler ultrasound.

Takeaway: Edema is a challenging presentation to diagnose, and an extensive workup is often required to evaluate all etiologies.