Edema Evaluation: Generalized vs Localized, Nephrotic vs Cardiac vs Hepatic

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Definition & Pathophysiology: Starling Forces

Edema = Abnormal accumulation of fluid in interstitial space (outside cells, outside intravascular)

Starling Equation Governs Fluid Movement

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Net Filtration Force = (Pc − Pi) − (πc − πi)
                     = Hydrostatic gradient − Oncotic gradient
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Where: - **Pc** = Capillary hydrostatic pressure (pushes fluid OUT) - **Pi** = Interstitial hydrostatic pressure (pushes fluid IN) — usually ~0, less important - **πc** = Capillary oncotic pressure (pulls fluid IN) — mainly from albumin - **πi** = Interstitial oncotic pressure (pulls fluid OUT)

For edema to develop, ONE of these must occur: 1. ↑ **Capillary hydrostatic pressure (Pc ↑)** — venous obstruction, right-sided HF 2. ↓ **Capillary oncotic pressure (πc ↓)** — hypoalbuminemia (nephrotic syndrome, cirrhosis, malnutrition) 3. ↑ **Interstitial oncotic pressure (πi ↑)** — increased protein leak to interstitium (inflammation, capillary leak) 4. ↓ **Lymphatic drainage** — obstruction, malignancy, infection

> [!tip] **Quick decision tree:** - Edema present + LOW albumin → nephrotic syndrome or liver disease (usually) - Edema present + NORMAL albumin → cardiac/renal sodium retention or lymphatic obstruction (usually)

Generalized Edema (Whole Body)

Nephrotic Syndrome (~1.5% prevalence in general population)

Definition: Proteinuria >3.5 g/day + hypoalbuminemia + hyperlipidemia + edema

Primary causes (60%): - FSGS (focal segmental glomerulosclerosis) — 40% - Membranous nephropathy — 20% - Minimal change disease — 15% - IgA nephropathy — 10% - Other GN — 15%

Secondary causes (40%): - Diabetes mellitus (~50% of secondary) - SLE (~10%) - Infection (HIV, HCV, syphilis) — 5–10% - Malignancy (solid tumors, hematologic) — 10% - Amyloidosis, light chain disease — 5–10% - Drugs (NSAIDs, INH, heroin) — 5% - Allergic (pollen, insect venom) — rare

Pathophysiology: - **Heavy proteinuria** (>3.5 g/day) → protein loss exceeds synthesis - ↓ **Plasma oncotic pressure** (πc ↓ from low albumin) - **Edema results** from Starling force imbalance - **Secondary effects:** - Hepatic compensatory albumin synthesis ↑ (but overwhelmed) - Liver synthesizes more apoB → ↑ cholesterol, ↑ LDL (nephrotic hyperlipidemia) - Proteinuria includes iron-binding proteins → iron loss → anemia - Loss of anticoagulant proteins (antithrombin III, protein S) → thrombosis risk ↑↑

Clinical Features: - **Edema (pitting, symmetric):** Periorbital (morning worst), lower extremities - **Weight gain:** Often 5–15 lbs overnight from fluid retention - **Foamy urine:** Proteinuria visible as foam - **Lipiduria:** "Oval fat bodies" on UA (lipid-laden tubular cells; pathognomonic if present)

Labs: - **Albumin <2.5 g/dL** (marked hypoalbuminemia) - **Proteinuria 3.5–15 g/day** (can range) - **Cholesterol >300 mg/dL** (nephrotic hyperlipidemia) - **Complement:** Variable (normal in FSGS; ↓C3 in PSGN/ANCA)

Complications: - **Infection:** ↓ Immunoglobulin loss; asplenic-like state (S. pneumoniae risk ↑) - **Thrombosis:** VTE, PE, renal vein thrombosis (RVT) — hypercoagulable from loss of anticoagulants + ↑ fibrinogen - **Hypertension:** From fluid retention - **AKI:** From volume depletion if diuretics too aggressive, or renal artery stenosis (if membranous on anticoagulation)

Management: 1. **Identify cause:** Serologies, imaging (kidney biopsy if diagnosis uncertain) 2. **Reduce proteinuria:** - ACE-I/ARB first-line (reduce intraglomerular pressure) - SGLT2 inhibitor (emerging; dapagliflozin reduces nephrotic proteinuria) - Finerenone (if CKD + proteinuria) 3. **Edema control:** - **Sodium restriction:** <2 g/day (reduces volume retention) - **Diuretics:** Furosemide (high-dose often needed; large proteinuria impairs diuretic secretion in tubules) - Caution: Overly aggressive diuresis → AKI (RVT risk if membranous) 4. **Monitor & prevent complications:** - Anticoagulation if RVT risk (SQ LMWH or warfarin if membranous) - Statin for nephrotic lipids - Pneumococcal vaccine + prophylaxis (splenectomy-like protection)

Congestive Heart Failure (CHF) / Acute Decompensated Heart Failure (ADHF)

Mechanism: Right-sided HF → venous congestion → ↑ Pc (hydrostatic pressure ↑)

Pathophysiology: - **Impaired ventricular emptying** → ↑ LV diastolic pressure → ↑ LA pressure → ↑ pulmonary vein pressure → ↑ capillary Pc - **Backward flow** → systemic venous congestion → hepatomegaly → ↑ JVP - **Neurohormonal activation:** RAAS ↑, SNS ↑ → Na retention → ↑ preload (further worsens HF)

Clinical Features: - **Peripheral edema:** Bilateral, gravity-dependent (worse in ankles/legs standing; sacral if bedbound) - **Orthopnea, PND:** Pulmonary edema from ↑ pulmonary capillary pressure - **Elevated JVP:** Hepatic venous congestion - **Hepatomegaly:** RV pressure transmits to liver - **Weight gain:** Acute (overnight gains 2–5 lbs = fluid) - **Third heart sound (S3 gallop):** Ventricular dysfunction - **Bibasilar crackles:** Pulmonary edema

Labs: - **BNP or NT-proBNP ↑:** (Natriuretic peptides from ventricular stretch) - **Echocardiogram:** Reduced ejection fraction (EF <40% = HF with reduced EF, HFrEF) or normal EF (HF with preserved EF, HFpEF) - **Albumin normal** (no massive protein loss like nephrotic) - **Troponin elevation:** If acute MI precipitated HF

Management: 1. **Acute:** - IV diuretics (furosemide) for fluid overload, pulmonary edema - Vasodilators (nitroglycerin, nitroprusside) to reduce afterload - Inotropes (dobutamine, milrinone) if shock - Oxygen/intubation if respiratory failure

2. **Chronic:**
    - ACE-I/ARB (GDMT cornerstone; reduce afterload, neurohormonal axis)
    - Beta-blocers (carvedilol, metoprolol) — slow HR, reduce contractility demand
    - Aldosterone antagonist (spironolactone) — RAAS inhibition
    - SGLT2 inhibitors (dapagliflozin, empagliflozin) — proven HF benefit
    - Diuretics (furosemide, torsemide) for volume management

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Liver Cirrhosis (Hepatic Edema)

Mechanism: Complex; multiple Starling force abnormalities

Pathophysiology: 1. **Portal hypertension** (fibrosis/cirrhosis obstructs flow) → ↑ splanchnic capillary pressure (↑ Pc) 2. **Decreased albumin synthesis** (hepatocytes damaged) → ↓ πc 3. **Splanchnic vasodilation** (nitric oxide, other vasodilators ↑) → underfilling of systemic circulation → RAAS activation → Na retention

Clinical Features: - **Peripheral edema:** Often symmetric; worse in evening/lower extremities - **Ascites:** Abdominal fluid; tense, bulging abdomen; fluid wave positive - **Spider angiomas, palmar erythema:** Hyperestrogenism (liver can't metabolize estrogen) - **Jaundice:** Bilirubin ↑ - **Hepatomegaly:** Cirrhotic liver may be shrunken (late cirrhosis) - **Splenomegaly:** Portal hypertension - **Encephalopathy:** Ammonia ↑ (liver dysfunction)

Labs: - **Albumin LOW** (<2.5 g/dL) - **Bilirubin** ↑ (>2 mg/dL) - **INR** ↑ (coagulopathy from ↓ clotting factors) - **Platelets** ↓ (splenomegaly from portal HTN) - **AST/ALT mildly** ↑ (or may be normal if burnt-out cirrhosis)

Management: 1. **Address underlying liver disease:** Abstain from alcohol, DAA for HCV, immunosuppression for autoimmune, etc. 2. **Sodium restriction:** <1.5–2 g/day (critical; Na retention is major problem) 3. **Diuretics:** Spironolactone (target low-dose; avoid ototoxicity) + furosemide (if needed for ascites) 4. **Paracentesis:** Therapeutic if tense ascites; improves breathing, comfort 5. **TIPS:** Transjugular intrahepatic portosystemic shunt (if refractory ascites; invasive; reserved for specific indications) 6. **Liver transplant:** Definitive; consider if decompensated despite medical management

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Localized Edema (One Limb)

Venous Insufficiency / Deep Vein Thrombosis (DVT)

Mechanism: ↑ Pc from venous obstruction/incompetence

Venous insufficiency (Chronic): - Valvular insufficiency → retrograde flow → venous HTN in lower extremity - **Edema:** Unilateral (usually one leg worse); warm, non-pitting initially; may pit if severe - **Associated:** Varicose veins, skin changes (hyperpigmentation, ulceration)

DVT (Acute): - Thrombosis blocks venous return → ↑ capillary pressure - **Edema:** Sudden, unilateral (swollen >2 cm circumference vs other leg); calf pain, warmth - **Risk:** Immobilization, cancer, hypercoagulable state, surgery - **Diagnosis:** Duplex ultrasound (gold standard) - **Treatment:** Anticoagulation (LMWH, DOACs, warfarin)

Lymphedema

Mechanism: ↓ Lymphatic drainage → fluid accumulates in interstitium

Causes: - **Primary:** Congenital hypoplasia/hyperplasia of lymph vessels (rare) - **Secondary:** Lymph node removal (cancer surgery), radiation, infection (cellulitis worsens)

Clinical Features: - **Non-pitting edema** (firm, woody; doesn't leave impression) - **Bilateral in primary;** unilateral in secondary - **Onset:** Gradual; may not appear for years post-surgery

Management: - Compression stockings (not much helps; supportive) - Lymphatic massage, elevation - Limb protection (avoid infection, trauma)

Diagnostic Approach: Edema Workup

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EDEMA IDENTIFIED
    |
    ├─ HISTORY & EXAM
    |   ├─ Pitting vs non-pitting?
    |   ├─ Bilateral (generalized) vs unilateral (localized)?
    |   ├─ Onset (acute vs chronic)?
    |   ├─ Associated symptoms (SOB, orthopnea? abdominal distension?)
   |   └─ Past medical history (HF, kidney disease, liver disease, malignancy, thrombosis)
    |
    ├─ PHYSICAL EXAM
    |   ├─ JVP (elevated? → cardiac/venous congestion)
    |   ├─ Heart sounds (S3 gallop? → HF)
    |   ├─ Lung auscultation (crackles? → pulmonary edema, HF)
    |   ├─ Hepatomegaly, ascites? (→ liver disease or RV HF)
    |   ├─ Calf tenderness, warmth? (→ DVT)
    |   └─ Skin changes (hyperpigmentation, ulceration? → venous insufficiency)
    |
    ├─ LABS
    |   ├─ Albumin (↓ → nephrotic, liver disease)
    |   ├─ Urinalysis (proteinuria >3.5? → nephrotic)
    |   ├─ Cr, BUN (elevated? → kidney disease, poor perfusion)
    |   ├─ LFTs (↑ bilirubin? → liver disease)
    |   ├─ BNP/NT-proBNP (↑ → HF)
    |   └─ CBC (↓ platelets? → liver disease, splenomegaly)
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│
├─ IMAGING
│  ├─ CXR (pulmonary edema? cardiomegaly? → HF)
│  ├─ Echocardiogram (EF? systolic function? → HF assessment)
│  ├─ Duplex ultrasound (if unilateral; rule out DVT)
│  ├─ Abdominal ultrasound (cirrhosis findings? ascites? → liver disease)
│  └─ Kidney biopsy if nephrotic + unclear etiology
│
└─ CLASSIFY & TREAT
   ├─ Nephrotic: ACE-I/ARB + diuretics + Na restriction
   ├─ Cardiac: GDMT (ACE-I, beta-blocker, aldosterone antagonist, SGLT2i)
 ├─ Hepatic: Na restriction + diuretics (spironolactone) + address liver disease
   ├─ Venous: Compression stockings, elevation; anticoagulation if DVT
   └─ Lymphatic: Compression garments, massage, elevation
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Board-Style Pearls

[!tip] 1. **Nephrotic edema + proteinuria >3.5** → Start ACE-I/ARB immediately (reduce proteinuria + GFR protection) 2. **Pulmonary edema + ↓ EF** → HF; use IV diuretics + vasodilators 3. **Ascites + ↓ albumin + ↑ bilirubin** → Cirrhosis; Na restrict, avoid NSAIDs (acute kidney injury risk) 4. **Unilateral leg edema + calf pain** → DVT until proven otherwise; duplex 5. **Non-pitting edema in leg** → Lymphedema; compression stockings main therapy

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Related Resources

- Detailed Edema Differential
- Starling Forces & Pathophysiology
- CKD & Nephrotic Syndrome
- Advanced Kidney Disease Management

Self-Test Questions

1. **62F with bilateral ankle edema, proteinuria 5 g/day, albumin 2.0, Cr 1.8, BP 155/92**
   - Diagnosis: Nephrotic syndrome (proteinuria >3.5 + hypoalbuminemia + edema)
   - Management: ACE-I (e.g., lisinopril 10 mg), diuretics (furosemide 40 mg), Na restrict <2 g
   - Monitor: Proteinuria reduction; BP target <120; check for RVT if membranous
2. **48M with SOB on exertion, orthopnea, ankle edema, S3 gallop, JVP elevated, EF 28%**
   - Diagnosis: HFrEF with acute decompensation (pulmonary congestion)
   - Immediate: IV furosemide, oxygen, consider vasodilators
   - Chronic: ACE-I, beta-blocker, aldosterone antagonist, SGLT2i; diuretics as needed

3. **72M with ascites, jaundice, spider angiomas, albumin 1.8, INR 2.2, platelets 80K**
    - Diagnosis: Cirrhosis (liver disease; multi-organ signs of hepatic dysfunction)
    - Management: Sodium restrict <1.5 g; spironolactone (low-dose to minimize AKI); paracentesis if tense
    - Avoid: NSAIDs (↑ AKI, renal vasoconstriction), aggressive diuretics (↑ hepatorenal syndrome)

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References: KDIGO Nephrotic Syndrome Guidelines. 2022 AHA/ACC/HFSA HF Guideline. Liver Cirrhosis & Ascites Management (AASLD).