Nephrotic Syndrome: Causes, Symptoms and Treatment in Pediatrics

Nephrotic Syndrome is a **clinical syndrome** characterized by **excessive protein loss in the urine** due to increased permeability of the glomerular filtration barrier.

It is **not a single disease** , but a **manifestation of various glomerular disorders** affecting the kidney's filtering unit (the glomerulus).

? Core Diagnostic Characteristics (Classic Tetrad)

Feature	Description
Proteinuria	**>3.5 g/day** in adults or **>40 mg/m²/hour** in children
Hypoalbuminemia	Serum albumin **<2.5–3.0 g/dL**
Edema	Generalized, pitting edema due to ? plasma oncotic pressure
Hyperlipidemia	? serum cholesterol, triglycerides; also may see **lipiduria** (fatty casts, oval fat bodies in urine)

Mnemonic: "P-H-E-M"

Letter	Meaning
P	**Proteinuria** (>3.5 g/day)
H	**Hypoalbuminemia**
E	**Edema** (especially periorbital, pedal)
M	**Hyperlipidemia** (with lipiduria)

Why Is Nephrotic Syndrome Important?

Though relatively rare, nephrotic syndrome is clinically significant because:

- It is a **major cause of pediatric and adult referrals** to higher-level care.
- Often **chronic** and prone to **frequent relapses** .
- Has a **complex evaluation and management pathway** .
- It is not a disease itself, but a **syndrome resulting from various glomerular diseases** .

? Core Diagnostic Features (Mnemonic: P-HEM)

1. **Proteinuria** >3.5 g/day
2. **Hypoalbuminemia**
3. **Edema** (generalized, pitting)
4. **Hyperlipidemia** (? triglycerides, ? cholesterol)

? *Pathognomonic* : Massive proteinuria is the hallmark and the initiating feature.

? Pathophysiology

The glomerulus acts as a **charge- and size-selective barrier** :

- **Fenestrated endothelium**
- **Glomerular basement membrane (GBM)**
- **Podocyte slit diaphragms**

In nephrotic syndrome:

- Damage to the GBM and podocytes increases permeability ? **protein loss** in urine.
- Loss of **negative charge selectivity** (e.g., due to decreased heparan sulfate) allows albumin and other proteins to pass.

? **Key Molecular Players:**

- **Albumin** : Main protein lost; smallest major plasma protein.
- **Savin factor** (FSGS): Circulating permeability factor increasing GBM permeability.

? Consequences of Proteinuria

Effect	Mechanism	Clinical Impact
? Oncotic Pressure	Loss of albumin	Edema, hypovolemia
RAAS Activation	? Renal perfusion	Sodium/water retention
? IgG, factor B	Urinary loss	Immunosuppression, ? infection risk
? Transferrin, Vitamin D–binding protein	Urinary loss	Iron-deficiency anemia, hypocalcemia
? Antithrombin III	Urinary loss	**Hypercoagulability** , risk of thromboembolism
? Hepatic Lipogenesis	Compensatory	**Hyperlipidemia, lipuria**

? Etiology and Classification

? Primary (Idiopathic) Nephrotic Syndrome

- **Minimal Change Disease (MCD)** – most common in children
- **Focal Segmental Glomerulosclerosis (FSGS)**
- **Membranous Nephropathy** – common in adults
- **Hereditary Nephropathies** – e.g., Alport syndrome

? Secondary Nephrotic Syndrome

- **Diabetes Mellitus** (most common cause in adults)

- **Systemic Lupus Erythematosus**
- **Infections** : Hep B, Hep C, HIV
- **Malignancies** : Hodgkin lymphoma
- **Drugs** : NSAIDs, gold, penicillamine, mercury
- **Preeclampsia**
- **Amyloidosis and multiple myeloma**

? Complications

1. **Hypovolemia**
2. **Acute kidney injury (AKI)**
3. **Infections** : Peritonitis, sepsis
4. **Thromboembolism** : Renal vein thrombosis, DVT
5. **Malnutrition/protein deficiency**
6. **Dyslipidemia**
7. **Growth retardation in children**

? Signs and Symptoms

- **Pitting edema** : Starting periorbitally ? generalized
- **Ascites and pleural effusion**
- **Foamy urine** (due to proteinuria)
- **Features of complications** :
    - Hypotension, oliguria (hypovolemia)
    - Fever (infection)
    - Flank pain (renal vein thrombosis)

? Diagnostic Workup

Urine Studies

- **Urinalysis** : Proteinuria (>3+), lipiduria (fatty casts)
- **24-hr Urine Protein** or **Spot protein/creatinine ratio**
- **Urine microscopy** : Oval fat bodies ("Maltese cross" under polarized light)

Blood Tests

- **Serum albumin** : <2.5 g/dL
- **Serum creatinine, urea** : Check renal function
- **Lipid profile** : ? total cholesterol, ? triglycerides
- **Electrolytes** : Possible hyponatremia, hypocalcemia

Immunological/Serological Tests

- ANA, anti-dsDNA (SLE)
- Hepatitis B/C serologies
- HIV testing
- Serum protein electrophoresis (amyloidosis)

Imaging

- **Renal ultrasound** : Kidney size and echogenicity
- **Renal biopsy** : Indicated in adults, atypical cases, or steroid resistance

?? Management

General Measures

- **Low salt diet**
- **Normal protein intake** (excess worsens proteinuria)
- **Fluid restriction** if edema severe
- **Daily weight and urine output monitoring**

1. Edema Management

- **Salt restriction**
- **Diuretics** :
  - **Furosemide** (1–2 mg/kg/day)
  - **Spironolactone** : Prevents hypokalemia
  - Avoid in **hypovolemic** patients
- **Albumin infusion + diuretic** : If hypovolemia with edema

2. Immunosuppressive Therapy

- **First-line** : Prednisone 60 mg/m²/day for 4–6 weeks, then taper
- **Steroid-resistant cases** :
  - **Cyclophosphamide**
  - **Calcineurin inhibitors** : Cyclosporine, Tacrolimus
  - **Rituximab** in refractory cases

3. Proteinuria Reduction

- **ACE inhibitors** : Captopril, Enalapril
- **ARBs** : Losartan, Valsartan
- These agents also **reduce intraglomerular pressure** and progression of kidney disease.

4. Infection Prophylaxis and Treatment

- **Penicillin V** : Prophylaxis for patients with ascites or recurrent infections
- Empirical antibiotics: 3rd generation cephalosporins + antistaphylococcal coverage

5. Thrombosis Prevention

- Encourage **early ambulation**
- Consider anticoagulation in high-risk patients

6. Hypertension

- **Nifedipine or Hydralazine** for short-term control
- **Atenolol** if needed

7. Psychosocial Support

- Chronic disease in children can affect **mental health, growth, and school performance**. Provide appropriate counseling and support.

? Differential Diagnoses

- **Acute glomerulonephritis**
- **Acute/chronic kidney disease**
- **Kwashiorkor**
- **Congestive heart failure**
- **Liver cirrhosis (hypoalbuminemia)**
- **Protein-losing enteropathy**

? High-Yield Notes

- **Minimal Change Disease** is the most common cause in children—typically responds well to steroids.
- **FSGS** is the most common cause in adults with poor steroid response.
- **Renal vein thrombosis** is a classic complication of nephrotic syndrome.
- Avoid nephrotoxic drugs (e.g., NSAIDs, aminoglycosides).
- Use **biopsy** to differentiate cause in adults or steroid non-responders.