Proteinuria & Nephrotic Syndrome

Renal Handling of Proteins

- **Protein normally present in urine:** small quantities
- **Mechanisms limiting proteinuria:**
  - Glomerular restriction of protein filtration
  - Tubular reabsorption of filtered proteins

Glomerular Restriction

- **Glomerular capillaries:** efficient sieving filters
  - **Free water: 150–180 L/day**
  - Freely filtered solutes: **<10,000 Daltons**
  - Macromolecules ≥ albumin restricted (**cut-off 1.5 nm**)
- **Filtration barrier components:**
  - Endothelial fenestrae (**1000 Å**)
  - Basement membrane: traps molecules of **~100,000 MW**
  - Negatively charged epithelial cells with foot processes

Tubular Reabsorption

- **Albumin:**
  - **500–1000 mg/day** filtered
  - **~30 mg/day** excreted in urine
- **Low-molecular-weight proteins:**
  - Freely filtered and reabsorbed
  - Degraded by tubules
  - Examples: lysozyme, insulin, β2-microglobulin, GH, PTH

Normal Urinary Protein Excretion

- **Adults: <150 mg/day**
- **Children: <140 mg/m²/day**
- **Composition:**
  - Tamm–Horsfall protein: **70 mg**
  - Blood group substances: **35 mg**
  - Albumin: **<30 mg**
  - Immunoglobulins: **6 mg**
  - Mucopolysaccharides: **16 mg**

Proteinuria

- **Definition:** urinary protein excretion **>150 mg/day**
- ### Grades
  - **Microalbuminuria: 30–300 mg/day**
  - **Mild proteinuria: <1000 mg/day**
  - **Moderate proteinuria: 1000–2000 mg/day**
  - **Heavy proteinuria: >2000 mg/day**
  - **Nephrotic range: >3500 mg/day**
- ### Proteinuria vs Albuminuria
  - **Proteinuria:**
    - Excretion of all proteins **>150 mg/day**
  - **Albuminuria:**
    - Albumin excretion **>30 mg/day**
    - Major fraction in:
      - Glomerular disease
      - Diabetic nephropathy
      - Hypertensive nephropathy

Microalbuminuria

- **Definition:**
  - Albumin excretion **>30 mg/day** but **<300 mg/day**
- **Clinical use:**
  - Early marker of diabetic nephropathy
- **Measurement:**
  - RIA
  - ELISA
  - Special dipstick
- **Albuminuria grading:**
  - **A1: <30 mg/day**
  - **A2: 30–300 mg/day**
  - **A3: >300 mg/day**

Causes of Proteinuria

- ### Renal Causes
  - Glomerulonephritis
  - Drugs (gold, penicillamine)
  - Diabetes mellitus
  - Amyloidosis
  - Malignancy (myeloma)
  - SLE
  - Infection

Non-Renal Causes

- Fever
- Severe exercise
- Severe hypertension
- Burns
- Heart failure
- Orthostatic proteinuria

Transient Proteinuria

- Cold exposure
- Vigorous exercise
- Febrile illness
- Abdominal surgery
- Heart failure

Nephrotic Syndrome

Definition

- **Heavy proteinuria: >3.5 g/1.73 m²/day**
- **Massive edema**
- **Hypoalbuminemia**
- **Hyperlipidemia**

Causes

- **Primary glomerular disease:**
  - Minimal change nephritis
  - FSGS
  - Membranous GN
  - Proliferative GN
- **Secondary causes:**
  - Infection (HBV, HCV, malaria, schistosoma)
  - Drugs (NSAIDs, gold)
  - Metabolic (diabetes, amyloidosis)
  - Autoimmune (SLE, vasculitis)
  - Malignancy
  - Congenital causes

Pathogenesis

- **Proteinuria → Hypoalbuminemia**
- **Hypoalbuminemia:**
  - ↓ plasma oncotic pressure
  - ↓ effective circulating volume
- **Edema formation:**
  - Sodium and water retention
  - ↑ aldosterone and ADH
- **Hyperlipidemia:**
  - ↑ cholesterol, LDL, VLDL, triglycerides
  - ↓ HDL

Clinical Features

- **Edema:**
  - Soft pitting
  - Periorbital morning swelling
  - Ankle edema evening
  - Generalized anasarca
- **Fluid retention manifestations:**
  - Weight gain
  - Raised JVP
  - Pulmonary crepitations
- **Others:**
  - Pallor
  - Features of underlying cause

Complications

- **Infections:**
  - URTI
  - UTI
  - Skin infections
  - Peritonitis
- **Thromboembolism:**
  - DVT
  - Renal vein thrombosis
  - Pulmonary embolism
- **Others:**
  - Hypertension
  - AKI
  - Anemia
  - Vitamin D deficiency
  - Hypothyroidism
  - Premature atherosclerosis
  - Hypovolemia

Investigations

Laboratory

- Urinalysis: proteinuria, RBCs, casts
- Quantitative urinary protein
- Renal function tests: urea, creatinine, eGFR

Kidney Biopsy

- Establish type of glomerular disease
- Guide treatment decisions

Treatment

General Measures

- Treat underlying cause
- Treat infections with antibiotics
- Salt restriction
- Adequate calories and vitamins

Diet

- Protein intake: **1 g/kg/day + urinary losses**

Diuretics

- Loop diuretics (furosemide **20–60 mg/day**)
- Severe cases: up to **120 mg IV**
- Metolazone for resistant edema

Albumin Infusion

- Indications:
  - Severe resistant edema
  - Before surgery or biopsy

Blood Pressure Control

- **Target: 125/75 mmHg** if proteinuria **>1 g/day**
- ACE inhibitors or ARBs

Corticosteroids

- Best response: minimal change disease
- **Prednisolone:**
  - **60 mg/day** (max **80 mg/day**) for **8–12 weeks**
  - Gradual taper
- Severe cases:
  - IV methylprednisolone **10–15 mg/kg**

Immunosuppressive Drugs

- Cyclosporine
- Azathioprine
- Cyclophosphamide
- MMF