PEDIATRIC NEPHROTIC SYNDROME

1. Proteinuria & The Urine Dipstick

- **Dipstick Readings:** Negative/Trace (150 mg/L) is normal. 1+ (300 mg/L), 2+ (1000 mg/L), 3+ (3000 mg/L), 4+ (20000 mg/L).
- **Diagnosis:** +1 (300 mg/L) or more in non-concentrated urine is considered positive. The **24-hr urine collection** is the gold standard for quantitation.

Diagnostic Cutoffs (MCQ Highly Tested)

- **Normal:** < 4 mg/m^2/hr (or 0.15 g/24 hr).
- **Abnormal:** 4 – 40 mg/m^2/hr.
- **Nephrotic Range:** > 40 mg/m^2/hr (or > 50 mg/kg in 24 hrs).
- **UPr/UCr Ratio:** Normal < 0.2 mg/mg. **Nephrotic > 2 mg/mg.**

Dipstick False Results

- **False Positives:** Gross hematuria, Antiseptic agents (chlorhexidine), Highly alkaline urine (pH > 7.0).
- **False Negatives:** Dilute urine, or when the predominant protein is **NOT** albumin.

MEMORY AID: THE NS TETRAD

Remember **P.A.L.E.** for Nephrotic Syndrome hallmarks:

- **P**roteinuria (Heavy: > 40 mg/m^2/hr)
- **A**lbumin is low (Hypoalbuminemia < 2.5 g/dL)
- **L**ipids are high (Hyperlipidemia)
- **E**dema

2. Causes of Proteinuria

- **Transient:** Fever, Exercise, Dehydration, Cold exposure, CHF, Seizure, Stress.
- **Orthostatic:** Postural proteinuria.
- **Tubular Diseases:** Cystinosis, Wilson disease, Lowe syndrome, Galactosemia, Heavy metal poisoning, ATN.
- **Glomerular Diseases:** FSGS, Membranous, MPGN, Lupus, IgA Nephropathy, HSP, Amyloidosis, Diabetic.

3. Etiology & Pathophysiology of Nephrotic Syndrome

Nephrotic syndrome is characterized by fusion (effacement) of podocyte foot processes due to mutations (e.g., NPHS1/nephrin, NPHS2/podocin).

- **Edema:** Glomerular permeability increases → Massive Proteinuria → Hypoalbuminemia → **Decreased plasma oncotic pressure** → Fluid transudation to interstitium.
- **Hyperlipidemia:** Hypoalbuminemia stimulates the liver to drastically increase generalized protein synthesis (including lipoproteins), while lipid catabolism diminishes.

Idiopathic (INS) vs. Secondary NS

Idiopathic NS (90% of cases)	Secondary NS (10% of cases)
Intrinsic to the kidney.	Related to systemic causes, mostly in kids **> 8 years old**.
1. **Minimal Change Disease (MCD) - 85%** 2. Focal Segmental Glomerulosclerosis (FSGS) - 10% 3. Mesangial Proliferation - 5%	- **Infections:** HBV, HCV, HIV, Malaria, Schistosomiasis. - **Drugs (MCD):** Ethosuximide, Lithium. - **Drugs (Membranous):** Captopril, Gold, NSAIDs, Penicillamine. - **Malignancies:** Hodgkin Lymphoma, Lung/GI cancers.

4. Minimal Change Disease (MCD) Profile

- **Demographics:** Appears ages 2-6 years. More common in males (2:1).
- **Presentation:** Initially periorbital/lower extremity edema, progressing to generalized edema (ascites, pleural effusions).
- **Clinical Rules:** 100% nephrotic, only 10-20% have hematuria, 10% HTN. **Does NOT progress to ESRD.** 90-95% respond beautifully to steroids.
- **Complement Levels:** C3 and C4 are **NORMAL**.

> **MCQ TRAP: WHEN TO BIOPSY**
>
> A renal biopsy is **NOT REQUIRED** for a classic MCD presentation. You ONLY biopsy if the presentation is **Atypical**:
>
> - Gross Hematuria or Hypertension
> - Renal insufficiency or **Hypocomplementemia (Low C3/C4)**
> - Age **< 1 year OR > 12 years**
> - Steroid Resistant (SRNS)

5. Pathology (Microscopy Buzzwords)

Disease	Light Microscopy (LM)	Immunofluorescence (IF)	Electron Microscopy (EM)
MCD (85%)	Normal (or minimal mesangial increase)	**Negative**	Effacement of foot processes
FSGS (10%)	Segmental scarring	**IgM and C3**	Segmental scarring + effacement
Mesangioproliferative (5%)	Diffuse mesangial cells/ matrix	IgM and/or IgA	Mesangial cells + effacement

6. Treatment & Steroid Definitions (High-Yield for Boards)

First-Line Treatment: Steroids (Prednisone 60 mg/m^2/day or 2 mg/kg/day, max 60mg) for 4-6 weeks, then taper to every other day (EOD) for 3 months. Restrict sodium during acute illness.

Terminology	Strict Clinical Definition
SSNS (Steroid Sensitive)	Urine trace or negative for protein for **3 consecutive days** within the first 28 days of treatment.
SRNS (Steroid Resistant)	Continues to have proteinuria (2+ or greater) after a **full 6 weeks** of proper steroid therapy. *(Note: ALL SRNS patients require a biopsy! Usually progresses to ESRD.)*
Relapse	3+ to 4+ proteinuria and edema for **> 3 days**.
Steroid Dependent (SDNS)	Relapse occurs **while on the taper** (alternate-day therapy) OR within **14 days of stopping** steroids.
Frequent Relapser (FRNS)	**4 or more** relapses in 12 months.

**Second-line therapies for SDNS, FRNS, and SRNS: Cyclophosphamide, Cyclosporin, Tacrolimus, MMF, Rituximab, ACEi/ARBs.*

7. Complications of Nephrotic Syndrome

1. Infections (Major Cause of Death)

- **Spontaneous Bacterial Peritonitis (SBP)** is the most frequent type.
- **Most common bug:** *Streptococcus pneumoniae* (Gram-negative E. coli can also cause it).

2. Thrombosis

- Increased risk of arterial and venous events (Renal vein, Pulmonary embolus, Sagittal sinus).

- Due to urinary loss of immunoglobulins and properdin factor B.
- **Vaccines:** Need polyvalent pneumococcal and yearly flu. Varicella vaccine given **ONLY in remission**.
- Due to **loss of Antithrombin III and Proteins C/S** in urine, plus high fibrinogen and thrombocytosis.
- **NO prophylactic anticoagulation** unless previous event occurred.

3. Drug Side Effects

- **Steroids:** Cushingoid, HTN, cataracts, growth failure.
- **Cyclophosphamide:** Neutropenia, disseminated varicella, hemorrhagic cystitis, alopecia, **sterility**.
- **Cyclosporin:** Hypertension, nephrotoxicity, **hirsutism, gingival hyperplasia**.