• Nephrotic syndrome affects 1-3 per 100,000 children <16 yr of age.

• NS is the clinical manifestation of glomerular diseases associated with heavy proteinuria. (nephrotic-range).

• **Nephrotic range proteinuria is defined as proteinuria >3.5 g/24 hr or a urine protein : creatinine ratio >2.**
NS is characterized by:

- Heavy Proteinuria
- Hypoalbuminemia
- Hyperlipidemia
- Edema
CLINICAL CONSEQUENCES OF NEPHROTIC SYNDROME

Sorry I keep spilling all of this protein. I hope that doesn’t cause any other problems.
Proteinuria & Hypoalbuminemia is due to increase permeability of the glomerular capillary wall. → Edema and decreases plasma oncotic pressure → transudation of fluid from the intravascular compartment to the interstitial space → The reduction in intravascular volume → decreases renal perfusion pressure → activation of renin-angiotensin-aldosterone system & atrial natriuretic factor → increase reabsorption of sodium & water.

(However, this theory does not apply to all pts with NS).
• Hyperlipidemia is due to hepatic lipoprotein synthesis (stimulated by hypoalbuminemia) combined with decrease lipid catabolism due to urinary loss of lipoprotein lipase.
NS can be divided into:

1- Idiopathic (most common 90%).

2- Secondary to other diseases or syndromes.

3- Congenital.
Idiopathic NS

• It is divided into the following pathological types:

1. Minimal Change NS (85%) characterized by effacement "fusion" of the epithelial cell foot processes.

2. Focal Segmental Glomerulosclerosis; characterized by mesangial proliferation and segmental scarring.

3. Membranous Nephropathy; characterized by thickening of basement membrane with subepithelial deposits.

4. Other types include: Mesangial Proliferation & Membranoproliferative Glomerulonephritis (type 1 & 2).
CLINICAL MANIFESTATIONS

• Age: usually occur between 2-6 yr. (MCNS), whereas FSGS is tend to occur in older children.

• The initial episode and subsequent relapses may follow minor infections or sometimes insect bite.

• Children usually present with mild periorbital & lower extremities edema. Then edema becomes generalized with development of ascites, pleural effusions, and genital edema.

• Other symptoms include: irritability, anorexia, abdominal pain & diarrhea.
D.DX:

I. Glomerulonephritis,
II. Protein-losing enteropathy.
III. Protein malnutrition (kwashiorker)
IV. Hepatic failure.
V. Congestive HF.
**INVx:**

- GUE for Proteinuria (3+ or 4+) or (> 40 mg/m²/hr) or (>150 mg/kg/hr).

- Urinary protein/creatinine ratio >2. (1st voiding at morning)

- Serum Albumin <2.5 g/dL.

- Serum Cholesterol & Triglyceride (cholesterol >200 mg/dL).

- Serum Urea & Creatinine, C3 & C4 are typically normal.
• Renal Biopsy is not routinely indicated unless:

1. Age <1 yr or >8 yr.
2. Family hx of renal disease.
3. Extrarenal findings " (arthritis, rash, anemia).
4. Hypertension.
5. Hematuria.
6. Pulmonary edema.
7. Renal insufficiency.
8. Hypocomplementemia.
9. Resistance to steroid Rx.
Corticosteroids are the cornerstone in Rx of NS.

- Prednisone orally, 60 mg/m²/day (max. 80) as single dose in morning. For 4-6 wk. Then 40 mg/m² EOD for at least 4 wk, then tapered & stopped over the next 1-2 mo. (total 3-4 mo).

- The response (ve or trace proteinuria for 3 consecutive days) to steroid usually occur within 2-4 wk of daily steroid Rx.

- Children with 1st episode with mild to moderate edema can be managed as outpatient by the following (in addition to prednisone):
  1. Salt intake "No added salt".
  2. Diuretics orally with caution due to the risk of thromboembolism.
Children with severe edema, should be hospitalized & managed by the following (in addition to prednisone):

1. Fluid restriction (in addition to Na restriction) may be necessary if the child is hyponatremic.
2. Swollen scrotum may be elevated.
3. Diuretics e.g. furosemide orally or IV, 1-2 mg/kg/dose.
4. If the above measures are not effective, give 25% albumin IV (0.5-1 g/kg/dose) slowly followed by furosemide.
• Relapse in NS: Many children with NS will experience at least 1 relapse.

• patients who are frequent relapsers, steroid dependent or resistant or children suffer from severe SE of corticosteroids are candidate for alternative agents such as Cyclophosphamide, Cyclosporine..etc.

• ACE inhibitors & Angiotensin II blockers may be helpful as adjunct Rx to decrease proteinuria in steroid-resistant patients.
**Complications:**

1. **Infection**: It is the major Cx of NS. Spontaneous bacterial peritonitis is the most frequent infection, although sepsis, pneumonia, cellulitis, and UTI may also occur.

   *S. pneumoniae* is the most common organism as well as other Gram -ve bacteria e.g. *E. coli*.

**Notes:**

- Corticosteroid Rx usually mask fever and other signs of inflammation, thus it need high index of suspicion for infection combined with aggressive Rx after Dx.

- Vaccinations, especially "polyvalent" pneumococcal, varicella & influenza vaccines can be given during remission or low dose alternate day steroids.
2. Thromboembolism: it is uncommon Cx due to high prothrombotic factors (fibrinogen level, thrombocytosis, hemoconcentration, relative immobilization) and low fibrinolytic factors (urinary losses of antithrombin III, proteins C and S), thus overaggressive diuresis should be avoided. Anti-coagulation Px is not recommended unless there is previous thromboembolic event.

3. Hyperlipidemia; CVS events e.g. MI is rare in children.

4. Psychological effects; patient with NS should not be considered as an “ill”.
Secondary Nephrotic Syndrome:

1. **Glomerular diseases** may have a nephrotic component e.g. Membranous nephropathy; Membranoproliferative GN, Postinfectious GN, SLE, and HSP.

2. **Infections & infestation** e.g. HBV, HCV, HIV, Malaria and Schistosomiasis.

3. **Drugs** e.g. NSAIs, Penicillamine, Captopril, Phenytoin, Gold & Lithium.

4. **Malignancy** e.g. Lymphoma & Leukemia (but mainly in adults).

5. ** Syndromes** that may be associated with NS include: Alport syndrome, Hurler syndrome, Alagille syndrome, Glycogen storage disease .... etc
Congenital Nephrotic Syndrome:

Appears at birth or within the 1st 3 mo. of life.

Causes of congenital NS include:-

- **Finnish-Type NS**: It is the most common cause of congenital NS, inherited as AR. It is manifested in utero as fetal hydrops, large placenta high a fetoprotein; prematurity, respiratory distress, hypothyroidism and separation of cranial sutures.

- The disease is persistent edema and progressive renal failure with death by age of 5 yrs.

- Rx. Aggressive nutrition, ACE inhibitor, IV albumin, IVIG, unilateral (or bilateral) nephrectomy, chronic dialysis, and kidney transplantation; whereas corticosteroids & immunosuppressives are of no value in Finnish-type NS.

- **Congenital Infections** e.g. TORCHS can cause congenital NS
THANK YOU