

NEPHROTIC SYNDROME

NS is characterized by **heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia.**

NS can be divided into; **Idiopathic** (most common), **Secondary** to other diseases or syndromes, and **Congenital.**

Idiopathic Nephrotic Syndrome

INS is divided into the following pathological types:- 1. **Minimal Change NS**; 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). [⊗] **Comparison between: MCNS FSGS MN**

⊗ *Frequency:* 75% 10% 5% ⊗ *Nephrotic synd:* 100% 90% 80% ⊗ *Asymp proteinuria:* 0% 10% 20% ⊗ *Hypertension:* 10% 20% ?

⊗ *Hematuria:* ≈15% ≈70% 60% ⊗ *Response to steroid:* >90% 20% 50%

⊗ *Progression to ESRD:* No Usually Occasionally **Path.** ⊗ **Proteinuria & Hypoalbuminemia** is due to ↑ permeability of the

glomerular capillary wall. ⊗ **Edema** is due to hypoalbuminemia which → ↓ plasma oncotic pressure and 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 & antidiuretic hormone → ↑ reabsorption of sodium & water. However, this theory does not apply to all patients with NS.

☐ **Hyperlipidemia** is due to hepatic lipoprotein synthesis (stimulated by hypoalbuminemia) combined with ↓ lipid catabolism due to urinary loss

of lipoprotein lipase. **C.M.** NS usually occur between **2-6 yr**. MCNS tend to occur in young children, 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.** Glomerulonephritis, Protein-losing enteropathy, Protein malnutrition (kwashiorker), Hepatic failure, and Congestive HF. **Inv.** ☐ Urine should be examined for **Proteinuria** (3+, 4+, or > 3.5 g/24 hr) and **protein/creatinine** ratio (>2). **Note:** *Only the 1st voiding of urine at morning should be examined to exclude orthostatic proteinuria.* ☐ Serum **Albumin <2.5 g/dL**.

☐ Serum **Cholesterol** (>200 mg/dL) & **Triglyceride** are elevated. ☐ Serum **Urea & Creatinine**, as well as **C3 & C4 are typically normal**. ☐ **Renal Biopsy is not routinely indicated unless** there is suspicion of diseases other than MCNS e.g. Age <1 yr or >12 yr, Family hx of renal disease, Extrarenal findings (arthritis, rash, anemia), hypertension, Hematuria, Pulmonary edema, Renal insufficiency, Hypo-

complementemia, or Resistance to steroid Rx. **Rx. Corticosteroids** are the cornerstone in Rx of NS; but **rule out TB**

infection before starting immunosuppressive Rx. ☐ **Prednisone orally**, 60 mg/m²/day or 2 mg/kg/day (max. 60) as **single** dose in morning for **4-6 wk** (≈ 1 mo).

Then the dose should be tapered to 40 mg/m² or 1.5 mg/kg **every other day** for a period ranging from 8 wk to 5 mo, with tapering of the dose. The **response** to steroid usually occurs within **5 wk** of daily steroid Rx

which manifested as **-ve** (or trace) **proteinuria for 3 consecutive days**.

☞ 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. **Oral Diuretics**; but should be used 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 sodium restriction) may be necessary if the child is hyponatremic. Swollen scrotum may be elevated. 2.

Diuretics e.g. furosemide orally or IV, 1-2 mg/kg/dose. 3. 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

with the same features (i.e. 3+ or 4+ proteinuria with edema), especially when there is short initial course of steroid. ☞ **Frequent Relapsers**; relapse ≥ 4 in 1 yr.

☞ **Steroid Dependent**; relapse whereas on alternate-day or within 1 mo

of stopping steroid Rx. ☞ **Steroid Resistant**; failure to respond to daily prednisone Rx within 8 wk.

Rx of relapse is by the same dose of prednisone until remission, the

regimen is then switched to alternate-day therapy for varies depending on the frequency of relapses of the individual child; whereas patients

who are **frequent relapsers, steroid dependent, or resistant** are candidate for alternative agents, especially if the child suffers severe SE of corticosteroids. These agents include:- ☞ **Cyclophosphamide**; 2 mg/kg/day as a single oral dose for a total duration 8-12 wk. It usually given with alternate-day prednisone Rx. SE; Neutropenia, thus it should be withheld if WBC count <5,000/mm³.

☞ **Other immunosuppressant agents** include: Cyclosporine, Tacrolimus, Mycophenolate, Levamisole (antihelmenthic!), & Rituximab.

☞ **ACE inhibitors & Angiotensin II blockers** may be helpful as adjunct Rx to ↓ proteinuria in steroid-resistant patients.

Cx.

☒ **Infection**; it is the major Cx of NS, it is mainly due to immune deficiency

which caused by many factors. **Spontaneous bacterial peritonitis** is

the most frequent type of infection, although sepsis, pneumonia, cellulitis, and UTI may also occur. **S. pneumoniae** is the most common organism causing peritonitis as well as other Gram -ve bacteria e.g. *E.*

coli.

Note: *Corticosteroids 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. ☒ **Thromboembolism**; it is **uncommon** Cx due to ↑ prothrombotic factors (↑ fibrinogen level, thrombocytosis, hemoconcentration, relative

immobilization) and ↓ fibrinolytic factors (urinary losses of antithrombin III, proteins C and S), thus overaggressive diuresis should be avoided and use of indwelling catheters is limited. However, anti-

coagulation Px is **not** recommended unless there is previous

thromboembolic event. ☒ **Hyperlipidemia**; CVS events e.g. MI is **rare** in children. ☒

Psychological effects; patient with NS should be considered as **normal**

rather than "ill person", especially during **remission**.

☒ **SE of Corticosteroids**; see under Rx of asthma