Definitions:

- **In children NS is applied to any condition with a triad of:**
  - Heavy proteinuria (UACR ratio >200 mg/mmol or 24hr urinary protein> 1g/m2/day)
  - Hypoalbuminemia (<25 gm/L)
  - Generalised edema
  - Hypercholesterolemia

- **Congenital NS**
  - Is NS with onset during the first 3 months of life

- **Infantile NS**
  - Is NS with onset between 3 to 12 months of age
**Idiopathic NS**

Is NS with absence of other glomerular pathology mediated by:

- Systemic disease (e.g. SLE),
- Structural glom. changes (e.g. Alports syndrome),
- Vasculitis,
- Immune complex deposition (e.g. post-infectious GN)
idiopathic NS is the common cause of NS in children
There are three distinct histological variants of primary idiopathic nephrotic syndrome:
- 1. Minimal-change nephrotic syndrome (MCNS)
- 2. Focal segmental glomerulosclerosis (FSGS)
Minimal Change Disease
MCD
Commonest glomerular disease of children.
cause 80% of nephrotic syndrome in children.
Middle age of presentation is 2-3 yrs.
Common in boys
Over 90% will respond for steroid therapy.
60% of those who respond for steroid will subsequently develop a relapsing course.
80% will enter in long term remission during childhood.
Low risk of developing CKD.
Mortality rate is 1-7% due to sepsis and vascular thrombosis.
Histology:
- Light microscopy & Immunofluorescence
  - NO abnormalities
- Electron microscopy
- Podocyte foot process effacement
clinical features:

- Common age: 12 months - 12 years
- Boys more than girls
- Oedema: face, legs, abdomen, sacral oedema, scrotal oedema
- Blood pressure (normal / low)
Investigation:

- Urine:
  - protienuria
  - heamaturia (rare)
- 24hr urine collection > 1g/m2/day
- Albumin/creatinine ratio:
  - >2mg/mg
  - >200mg/mmol
- Urea creatinine: usually normal but can be high
- Viral screening
- Renal biopsy
Complication:

- infection:
  - pneumococcal peritonitis, pneumonia, cellulitis, empyema, bone and joint infections. (why??)

- Thromboembolic Complications:
  - Loss of antithrombin 3, protein S and C in the urine
  - ↑ production of procoagulant factors by the liver
  - immobility
  - steroid therapy
  - Hypovolemia
  - Drug toxicity
Management:

- A well balanced and healthy diet containing the recommended dietary reference value for protein with a "no added salt" regimen.
- Management of oedema.
- Induce remission with steroids.
Steroid Therapy
Definitions:

- **Urinary remission:** urine Albustix negative or trace for 3 consecutive days
- **Steroid sensitive NS (SSNS):** Achievement of remission within 4-6 weeks of daily prednisolone at a dose of 60 mg/m²
- **Relapse:** urine Albustix ≥++ for 3 consecutive days
Frequently relapsing NS:
≥2 relapses after the first 6 month or ≥4 within any 12 months

Steroid dependent NS:
Relapse while on steroid therapy or within 14 days of stopping steroid therapy

Steroid resistant NS (SRNS):
failure to achieve remission within 4 weeks of daily prednisolone at a dose of 60 mg/m²
Treatment of initial episode:

- Steroid therapy (prednisone or prednisolone)* be given for at least 12 weeks. (1B)

- Oral prednisone be given as a single daily dose (1B) starting at 60 mg/m2/d or 2 mg/kg/d to a max. 60 mg/d. (1D)

- Daily oral prednisone be given for 4–6 weeks (1C) followed by alternate-day as a single daily dose starting at 40 mg/m2 or 1.5 mg/kg (max. 40 mg on alternate days) (1D) and continued for 2–5 months with tapering of the dose. (1B)
Treatment of infrequent relapsing SSNS:

- Infrequent relapses of SSNS in children be treated with:
  - A single-daily dose of prednisone 60 mg/m$^2$ or 2 mg/kg (max. of 60 mg/d) until complete remission for at least 3 days. (2D)

- After achieving complete remission, children be given:
  - Prednisone as a single dose on alternate days (40 mg/m$^2$/dose or 1.5 mg/kg/dose: max. 40 mg on alternate days) for at least 4 weeks. (2C)
Treatmet of frequently relapsing (FR) and steroid dependent (SD) SSNS:

- Relapses in FR or SD SSNS be treated with daily prednisone until remission for at least 3 days, followed by alternate-day prednisone for at least 3 months. (2C)

- Prednisone be given on alter. days in the lowest dose to maintain remission without major adverse effects in children with FR and SD SSNS. (2D)
Treatment of FR and SD SSNS with steroid-sparing agents:

- Steroid-sparing agents be prescribed for children with FR SSNS and SD SSNS, who develop steroid-related adverse effects. (1B)

- Alkylating agents, cyclophosphamide or chlorambucil, be given as steroid-sparing agents for FR SSNS. (1B)
Steroid resistance NS (SRNS)

- **Primary SRNS** is defined as
  - failure to respond to daily prednisolone (60 mg/m²) for 4 weeks or
  - failure to respond after 8 weeks (4 weeks of daily prednisolone (60 mg/m²) followed by 40 mg/m² every other day for 4 weeks)

- **Types** are: FSGS, MCD, diffuse mesangial proliferation, MPGN, membranous GN, congenital and infantile NS

- **Secondary SRNS** defined as SRNS who was previously SSNS
Evaluation of children with SRNS:

- A minimum of 8 weeks treatment with corticosteroids to define steroid resistance. (2D)

The following are required to evaluate the child with SRNS (Not Graded):

- A diagnostic kidney biopsy;
- Evaluation of kidney function by GFR or eGFR;
- Quantitation of urine protein excretion.
Summary of recommendation

Treatment for SRNS:

- CNI be used as initial therapy for children with SRNS. (1B)
- CNI therapy be continued for a minimum of 6 months and then stopped if a partial or complete remission of proteinuria is not achieved. (2C)
- CNIs be continued for a minimum of 12 months when at least a partial remission is achieved by 6 months. (2C)
- Low-dose steroid therapy be combined with CNI therapy. (2D)
- Treatment with ACE-I or ARBs for children with SRNS. (1B)
In children who fail to achieve complete or partial remission with CNI therapy consider:

- mycophenolate mofetil (2D),
- high-dose corticosteroids (2D),
- or a combination of these agents (2D)

Cyclophosphamide not be given to children with SRNS. (2B)

In patients with a relapse after complete remission, restart therapy using any one of the following options: (2C)

- Oral corticosteroids (2D);
- Return to previous successful immunosuppressive agent (2D);
- An alternative immunosupp. agent to reduce toxicity (2D).
Side effects of steroid therapy:

- Cushingoid facies
- obesity, striae
- hirsutism
- hypertension
- impaired glucose tolerance
- posterior subcapsular cataracts
- emotional problems and growth retardation.
Prognosis of NS:

- The majority of steroid-sensitive NS have repeated relapses

  - which become infrequent
  - or cease as the child grows older

- Steroid-resistant cases have poor prognosis with progressive renal failure leading to ESRD
THANK YOU