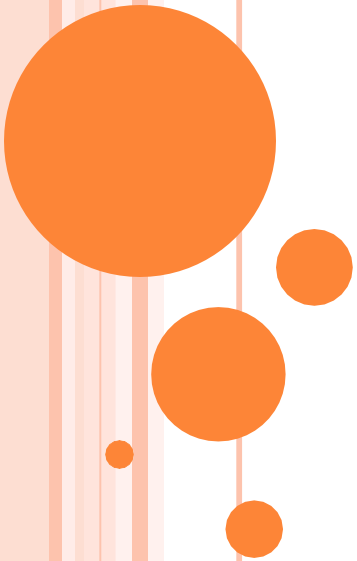
Nephrotic Syndrome



Definition

- Urinary protein excretion **> 3.5** g/day/1.73 m^2 of body-surface area

- Syndrome of –

  heavy urinary protein loss
  hypoalbuminaemia
  oedema

Causes of NS

- **NS with bland urinary sediment**

  Primary

  Minimal change

  FSGS

  Membranous

  Secondary

  Amyloidosis

  Diabetic Nephropathy

Causes of NS

- **NS with active urinary sediment**

  Primary

  Mesangio-capillary GN

  Mesangial proliferative GN

  Secondary

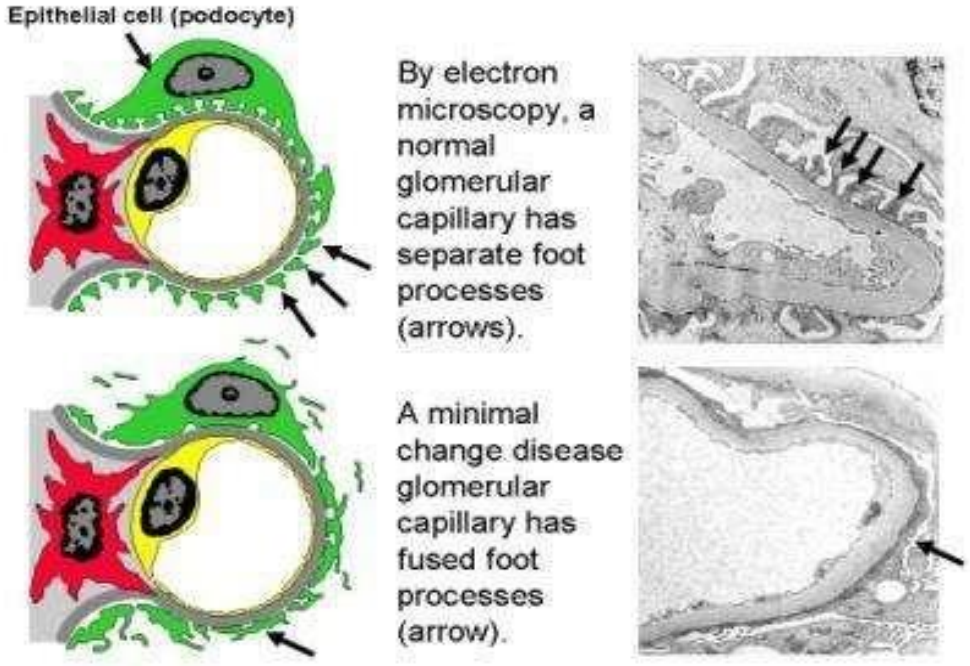
  SLE

  HSP

Minimal Change Nephropathy

- LM → normal glomeruli
- EM → fusion of foot processes of epithelial cells

  Is a non-specific change
- Highly selective proteinuria - albumin



Minimal Change Nephropathy

- Most common in children

  Males > Females

- Causes 20-25% of adult NS

- Usually does NOT lead to CKD

Focal Segmental Glomerulosclerosis (FSGS)

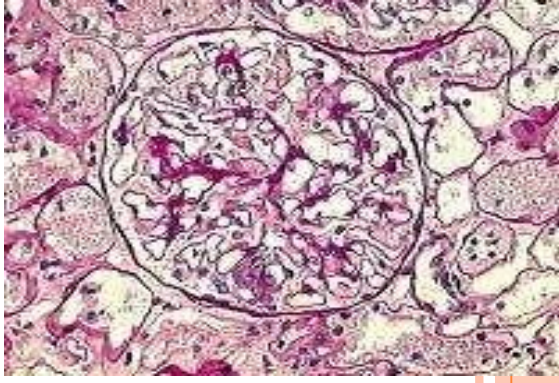
- Aetiology unknown
- LM – segmental → global glomerulosclerosis

  Deep glomeruli at cortico-medullary junction affected first – missed on renal biopsy
- IF – C3 & IgM deposition
- Non-selective proteinuria

Focal Segmental Glomerulosclerosis

- Present as proteinuria or frank NS
- Affect all ages
- 50% progress to ESKD within 10 years
- Recurs in transplanted kidney

Membranous GN



- Capillary BM thickened by immune complex deposition

- **Associations –** SLE
  GI, lung & breast CA
  Lymphoma
  Penicillamine, NSAIDs
  HBV, HCV

- Mainly in adult males

Membranous GN

- 1/3 develop ESKD in 10-20 years
- 1/3 remit spontaneously

- Good prognosis in -
  - females
  - younger age
  - asymptomatic modest proteinuria

- Poor prognosis → may benefit from steroids & immuno-suppressants

History in NS

- Diabetes
- Exposure to drugs/allergen
- Personal/family history of atopy (Minimal change)
- Family history of renal disease
- Frothy urine

Examination in NS

- Oedema → periorbital
  sacral
  leg
  ascitis

  Pleural effusions

  Pericardial effusion

  (NO pulm oedema or ↑JVP)

- Features of underlying disease –

  butterfly rash → SLE

  Neuropathy & Retinopathy → DM

Differential Diagnosis of Oedema

- Primary cardiac failure

  ↑ JVP, no peri-orbital oedema

- Inadequate protein intake

  - Protein-energy malnutrition

- Failure of protein production

  - Liver disease

- Excessive protein loss

  - Protein-losing enteropathy, Burns

- Pregnancy

Basic Investigations in NS

- 24-hour urinary protein >3.5 g/day
- s.albumin <30g/L
- ↑ LDL
  ↑ TG in 50%
  normal HDL
- BU & s.creatinine - may be elevated
- Creatinine clearance - may be reduced

Investigations to Determine Cause I

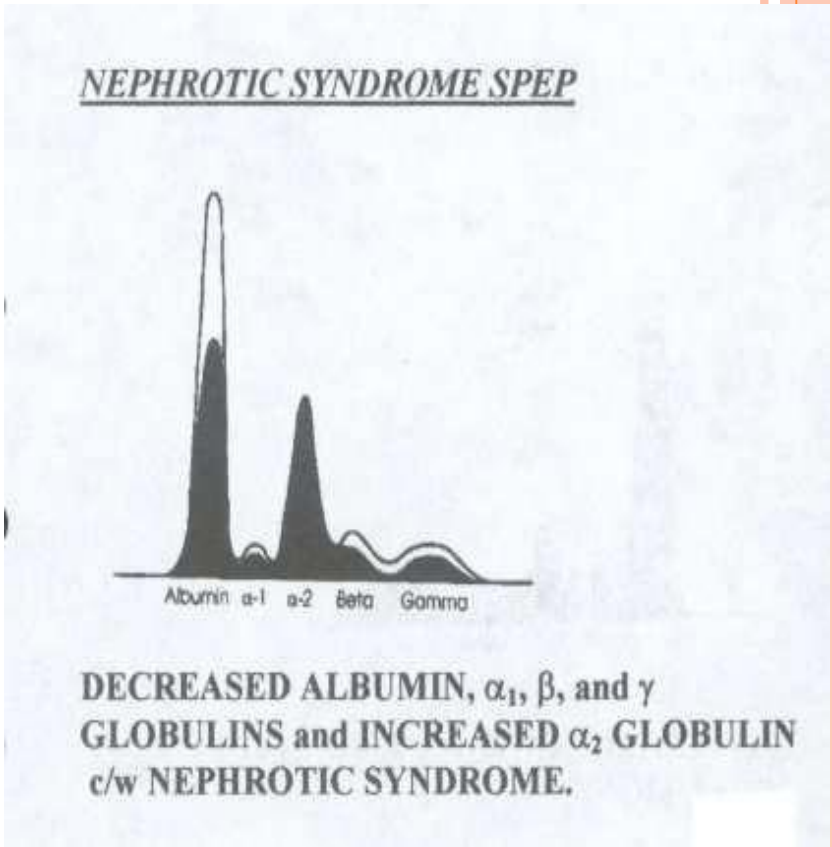
- Urine microscopy
- ANA → *SLE (dsDNA/ENA)*
- Screening for HBsAg & HCV Ab
- Fasting blood sugar → DM

Investigations to Determine Cause II

- Serum Electrophoresis →

  ↓ albumin, ↑ in α2 globulin in NS

  (monoclonal paraprotein band with immune paresis in Myeloma)



Renal Biopsy

- Indicated in -

  doubts about presence of minimal change NS

  other GN

- **NOT** indicated in –

  Young children

  DM → long standing, insulin dependant, with retinopathy and/or neuropathy

  Drug induced → stop drug first

Renal Biopsy - Technique

Practical box 11.3

Transcutaneous renal biopsy

Before biopsy

1. A coagulation screen is performed. It must be normal.
2. The serum is grouped and saved for crossmatching.
3. The patient is given a full explanation of what is involved.

During biopsy

1. The patient lies prone with a hard pillow under the abdomen.
2. The kidney is localized by ultrasound.
3. Local anaesthetic is injected along the biopsy track.
4. The patient holds a breath when the biopsy is performed.

After biopsy

1. A pressure dressing is applied to the biopsy site and the patient rests in bed for 24 hours.
2. The fluid intake is maximized to prevent clot colic.
3. The pulse and blood pressure are checked regularly.
4. The patient is advised to avoid heavy lifting or gardening for 2 weeks.

Treatment to Reduce Oedema

- **Reduce dietary sodium**
  (appx 3 g of sodium chloride per day)
- **Thiazides**
- **Frusemide +/- Amiloride**
  may need IV
  oral may not be absorbed well
- **Albumin infusion**
  in resistant oedema
  transient effect
  expensive

Treatment to Reduce Proteinuria

- ACE Inhibitors
- Normal protein diet

Management of Minimal Change Nephropathy

- **Aim** → reverse abnormal urinary protein leak

- High dose steroids

  >95% of children respond

  adults respond less well – will need longer courses

- May need Cyclophosphamide or Ciclosporin

- Spontaneous remissions in some
- If remission lasts >4 years relapse is rare

Management of FSGS

- Prednisolone

  mostly poor response

- Ciclosporin

Management of Membranous NS

- Steroids ineffective
- Cyclophosphamide & Chlorambucil reserved for severe cases

Complications of NS

- Venous thrombosis
- Sepsis
- Oliguric renal failure
- Hyperlipidaemia

Venous Thrombosis

- Renal vein thrombosis
  - frequent in Membranous GN
  - affects 20- 30% - only 10% have symptoms
  - flank pain & gross haematuria
  - increased renal size
  - loss of renal function
- Pulmonary embolism
- Deep venous thrombosis
- Arterial thrombosis less common

Management of Venous Thrombosis

- Due to – Hypovolaemia
  Hyper-coagulable state
- Avoid prolonged bed rest
- Long term prophylactic anti-coagulation

Management of Sepsis in NS

- Can cause death
- Increased susceptibility due to loss of IgG in urine
- Give Pneumococcal vaccine prophylactically
- Early detection & aggressive treatment better than long-term antibiotic prophylaxis

Management of Hyperlipidaemia

- May increase MI & PVD risk
- Treated with statins

Summary

- NS = urinary protein loss > 3.5 g/d, hypoalbuminaemia & oedema
- Commonest cause worldwide is Diabetic Nephropathy
- Primary GN causing NS are Minimal Change *(children)*, Membranous & FSGS *(adults)*
- Renal biopsy is indicated ***only if*** there are doubts about presence of minimal change nephropathy or if other types of GN are suspected

Summary

- General treatment - restriction of dietary sodium, high dose loop diuretics & ACE inhibitors
- Initial specific therapy is high dose steroids

  If poorly responsive → cyclophosphamide
- NS may be complicated by venous thrombosis, sepsis, oliguric renal failure & hyperlipidaemia