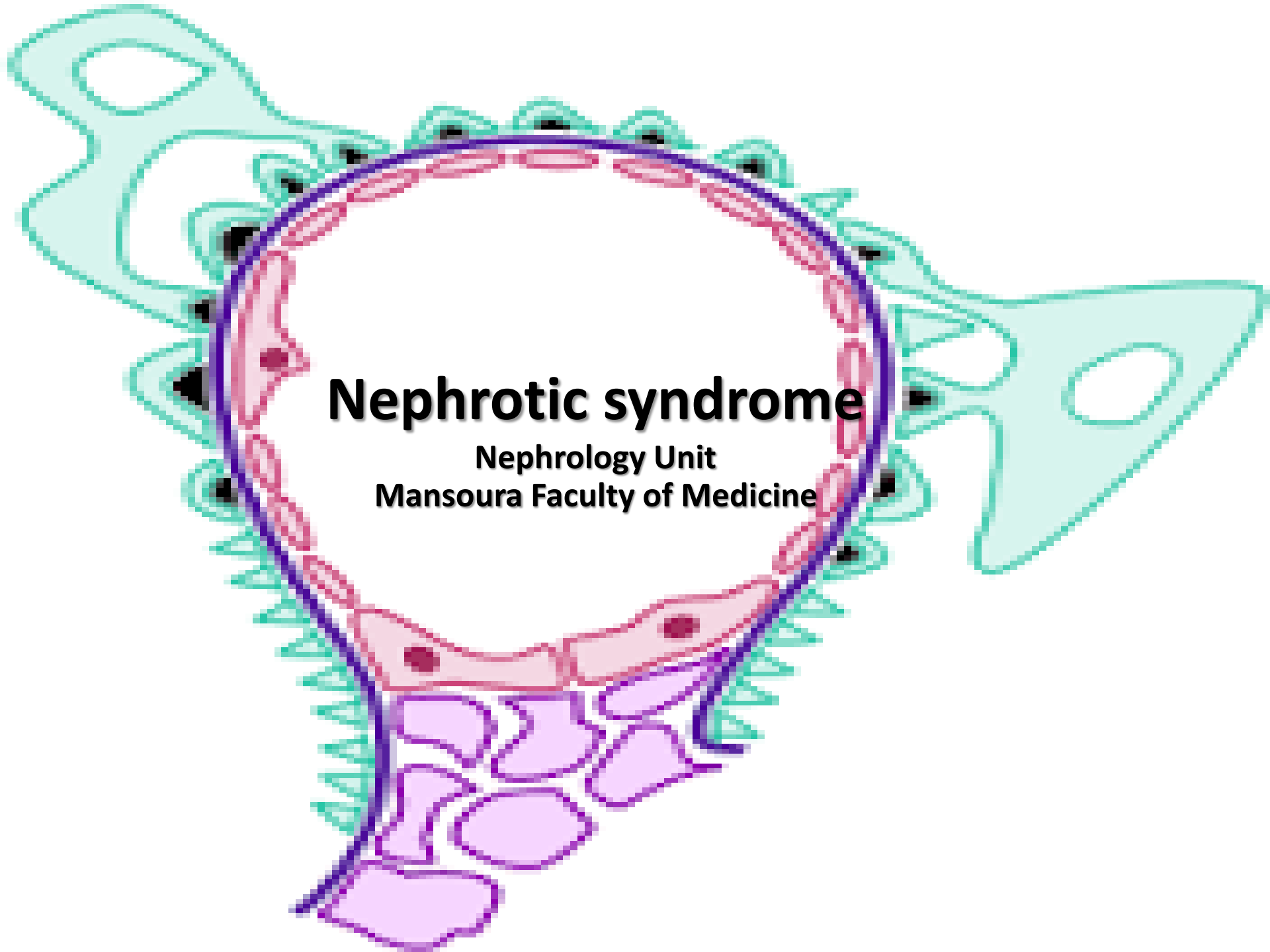


Nephrotic syndrome

Nephrology Unit
Mansoura Faculty of Medicine

Nephrotic Syndrome

A syndrome characterized by:

1. Heavy proteinuria (> 3.5 gm/1.73 m^2/d.)
2. Massive oedema.
3. Hypoalbminaemia.
4. Hyperlipidaemia.

Causes

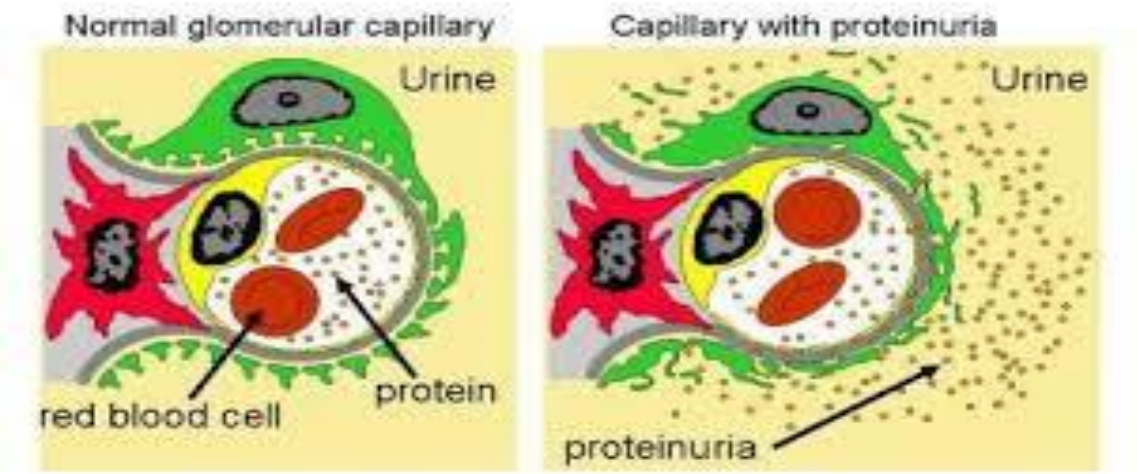
- **1ry glomerular disease (no identifiable cause)**

- **2ry NS due to any of the following:**
  - **Infection or post infection** (Schistosoma, Malaria, HCV, HBV,…etc.)
  - **Drugs:** gold, penicillamin, NSAIDs, …etc.
  - **Metabolic:** diabetes mellitus, amyloidosis, …etc.
  - **Collagen & Autoimmune disease:** SLE, Vasculitis, …etc.
  - **Malignancy:** Lymphoma, Multiple Myeloma, …etc.
  - **Congenital and familial conditions**

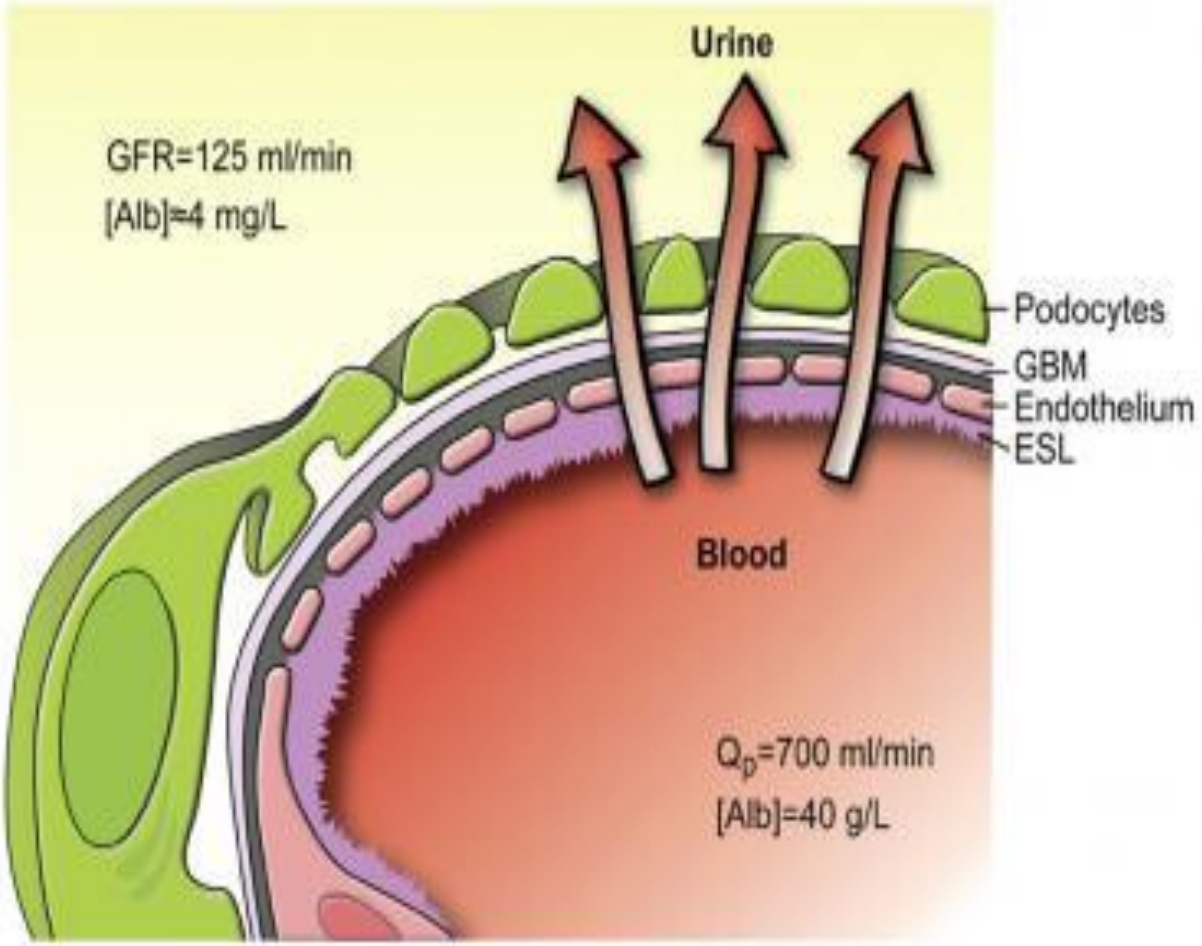
Pathology of Nephrotic Syndrome

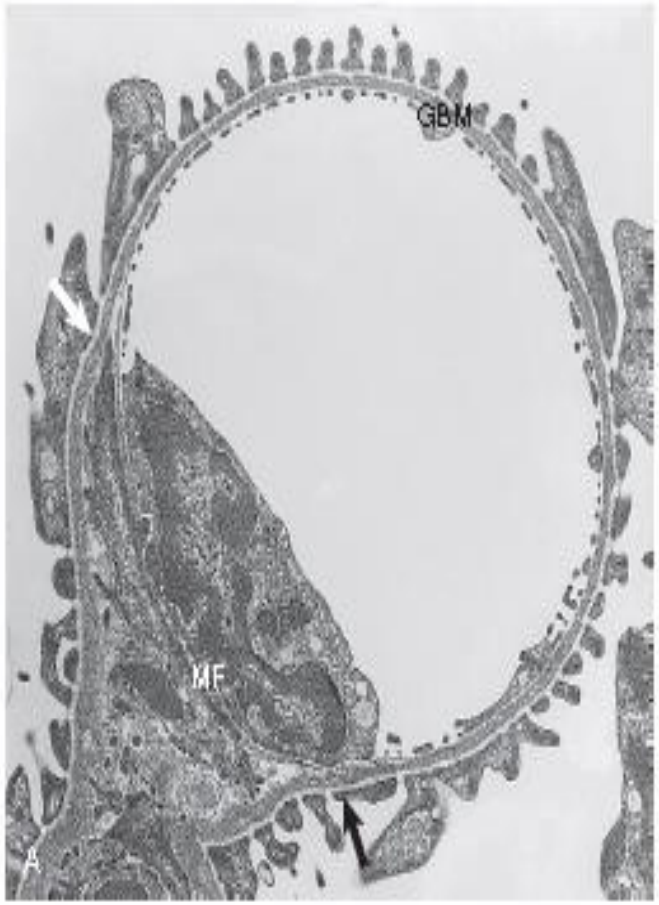
- Minimal change nephritis.
- Focal and segmental glomerulosclerosis.
- Membranous glomerulonephritis.
- Proliferative glomerulonephritis.
    - Mesangial proliferative.
    - Mesngiocapillary.
    - Crescentic GN.
    - IgA nephropathy.

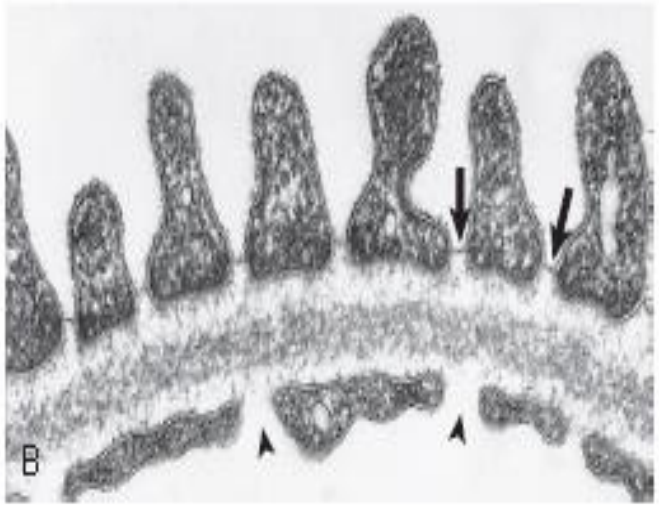
Pathogenesis



proteinuria



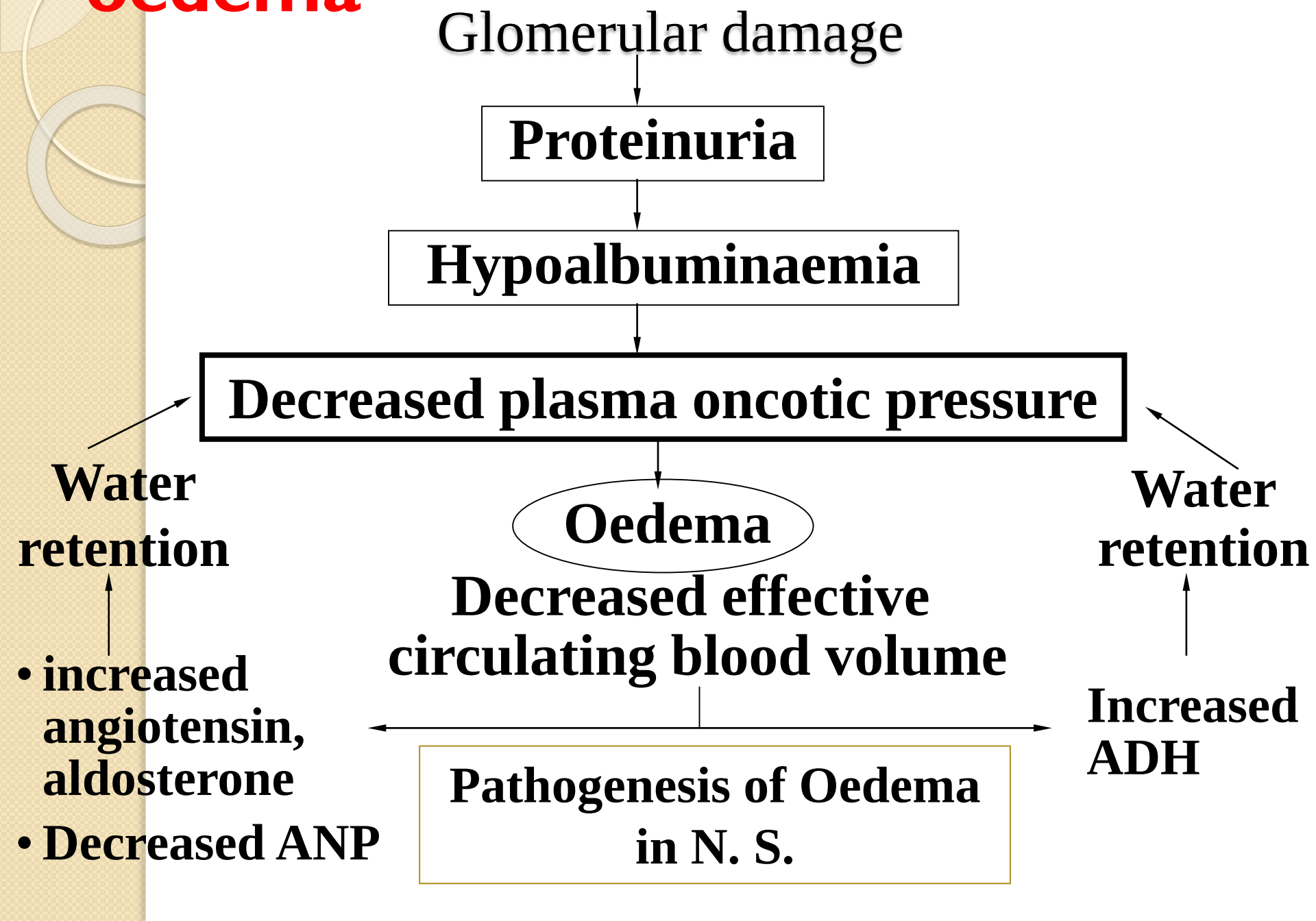




Hypoalbuminaemia

1. Albuminuria
2. The **decreased intake** (due to anorexia) and **decreased absorption**(due to oedema of the intestinal wall).
3. The increased concentration of albumin in the glomerular filtrate which is accompanied by **increase in its catabolism by the renal tubules.**
4. Sometimes **decreased** rate of hepatic **biosynthesis** of albumin.

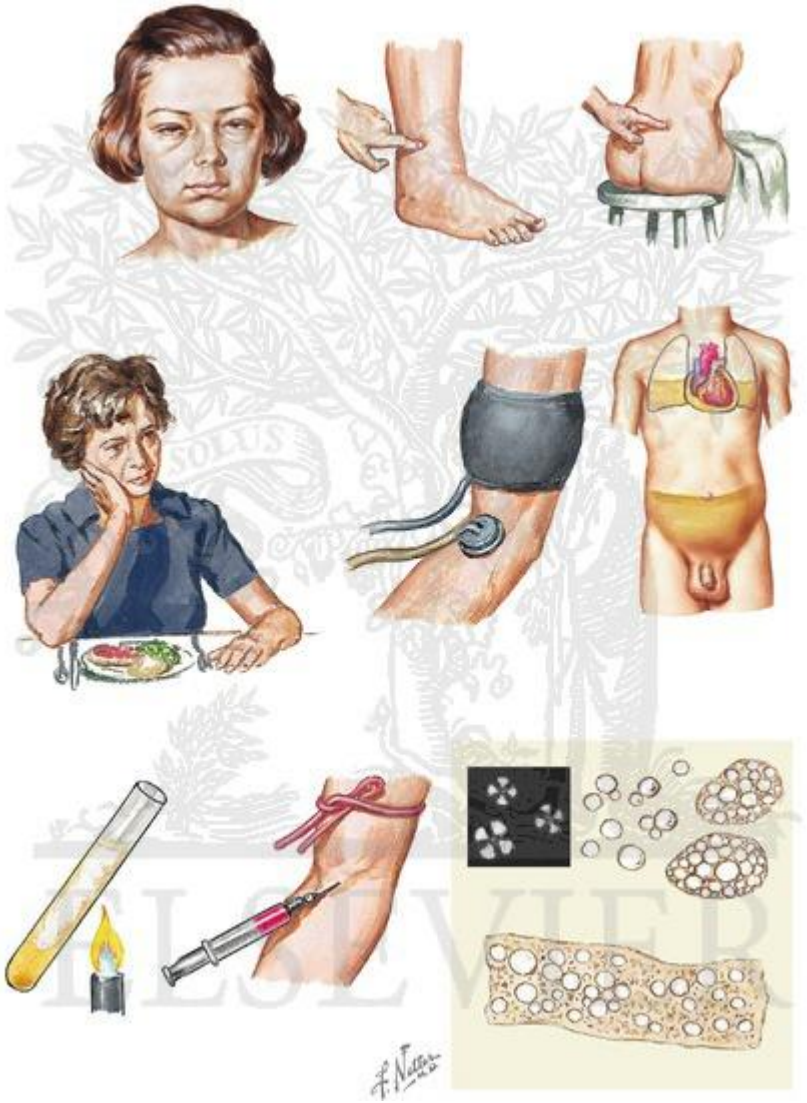
oedema


Glomerular damage
Proteinuria
Hypoalbuminaemia
Decreased plasma oncotic pressure
Water retention
Oedema
Water retention
Decreased effective circulating blood volume
• increased angiotensin, aldosterone
• Decreased ANP
Increased ADH
Pathogenesis of Oedema in N. S.

Hyperlipidemia in N. S.

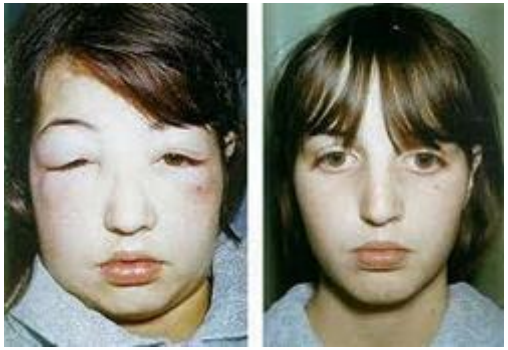
- ↑ Cholesterol, VLDL, LDL
- ↑triglycerids, ↓ HDL
  - ↑ Hepatic synthesis
  - ↓Catabolism due to inhibition of lipoptn lipase.

Clinical Features of N. S.



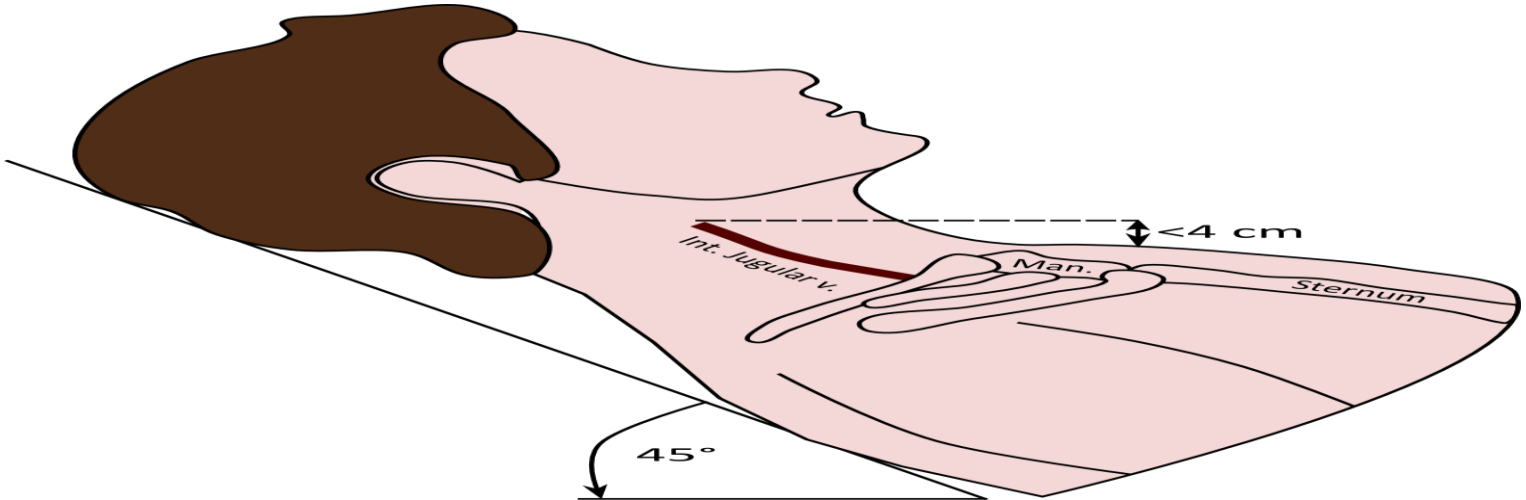
Oedema

- Soft pitting
- Swelling of the face in the morning & ankles in the evening
- Later it become persistent and there may be generalized anasarca



Manifestations of fluid retention

- Mental dullness, headache,convulsions.
- Lassitude, anorexia,malabsorption.
- Wt gain.
- Increase JVP, pul crepitations.



others

1. Pallor
2. Manifestations of the etiologic cause.
3. Manifestations of complications.

Complications of N. S

Complications of N. S.

Infection

- Especially upper respiratory, urinary, skin and peritoneal infections.

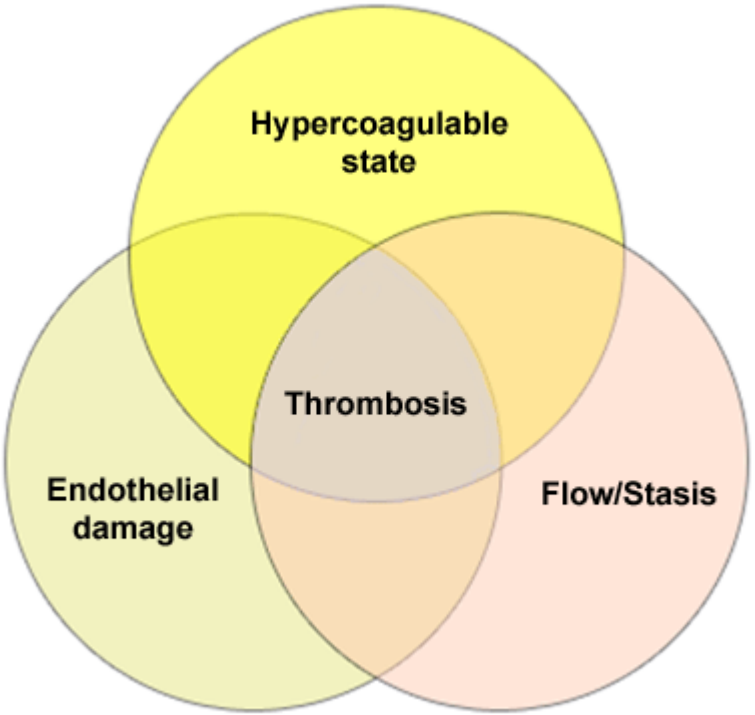
- Recurrent infection is due to nutritional deficiencies, urinary loss of immunoglobulins.

Complications of N. S.

Clotting episodes

- These manifest as a recurrent DVT, or renal vein thrombosis.

- It may be complicated by pulmonary embolism.



Clotting episodes causes

1. Increased concentration of coagulation factors resulting from an **increased hepatic synthesis** e.g. fibrinogen, factor III, and VIII.
2. **Urinary loss of antithrombin III** and protein C which normally act against intravascular clotting.
3. **Abnormal vascular endothelium**.
4. **Hypovolemic state**

Complications of N. S.

Premature atherosclerosis

- it is due to hyperlipidaemia

- This complication occurs mainly in cases with frequent relapses or cases resistant to treatment

Hypovolaemia

Which causes postural hypotension.

Complications of N. S.

Hypertension

- In nearly 50% of the cases, according to the etiologic and pathologic type of NS
  - Idiopathic minimal change NS cases are always normotensive while cases with mesangiocapillary GN whether idiopathic or secondary are always hypertensive.
- Corticosteroid ttt & pts developing CKD may be the cause of HTN

Complications of N. S.

Acute renal failure

- *this may be due to severe hypovolaemia (due to* the severe hypoalbuminaemia and use of big doses of diuretics), or due to acute interstitial nephritis (drug induced as large dose of furosemide).

Complications of N. S.

Bone disease

- Due to hypocalcemia (resulting from deficient intake and urinary loss of vitamin D binding globulin). It causes secondary hyperparathyroidism.

Anaemia

- Due to nutritional deficiencies and urinary loss of transferrin.

Complications of N. S.

Drug related complications:

1. **Diuretics** which may cause hypovolaemia, hypokalaemia, or hyponatraemia.
2. **Corticosteroids** that may cause diabetes mellitus, cataract, D.U., infections, and bone disease.
3. Other **Immunosuppressive drugs** as cyclophosphamide which may cause haemorrhagic cystitis, alopecia, infection and malignancy.

Investigations of NS

Laboratory Investigation

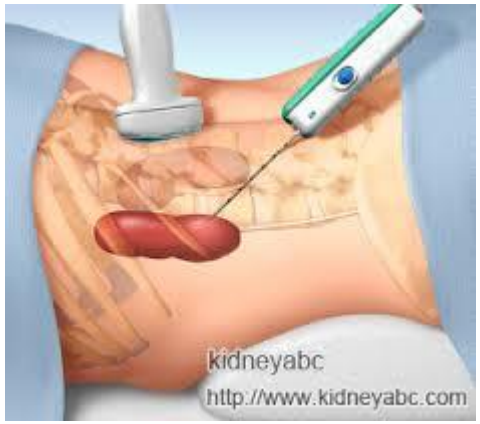
- **Urinalysis :** RBCs, RBCs cast, proteinuria.

- **Quantitative urinary protein.** Nephrotic range proteinuria (>3.5 gm/24h), subnephrotic range.

- **Renal function tests:** blood urea, creatinine, estimated GFR, creatinine clearance.

Kidney biopsy

- Renal biopsy is generally required to establish the type of glomerular disease and to guide treatment decisions



Investigation to diagnose the underlying causes:

- ANA (antinuclear antidoy) Anti-ds DNA positive in systemic lupus erythromatosis (SLE).
- C3, C4 (complement) may be consumed.
- ASOT (anti-streptolysin O titre) positive in post streptococcal GN.
- ANCA (antineutrophilic antibody) positive in Wagner granulomatosis.
- Antiglomerular basement membrane (AGBM) positive in Goodpasuture syndrome

Treatment of N. S.

Treatment of N. S.

- **Treatment of the cause** in secondary cases- for example- by proper control of blood sugar in D.M. and steroids and immunosuppressive drugs in SLE.

- **Treatment of complications** as infection by antibiotics

Treatment of N. S.

Diet

- Salt restricted supported with vitamins especially vitamin D and calcium.
- Protein content should equal the daily physiologic needs (1g/kg) plus the amount of daily urinary protein loss

  e.g. a 60kg patient who loses 10 gm daily should be given 70 gm protein containing diet.

Treatment of N. S.

Diuretics

- Mainly loop diuretics (e.g. Frusemide) initially can be given orally in variable doses (according to severity and response e.g. 20-60 mg/d.).
- In severe resistant cases doses up to 120 mg. I.V. may be given.
- Addition of metolazone (a thiazide diuretic) may have a potentiating effect for frusemide in diuretic resistant cases.

Treatment of N. S.

Salt poor albumin

- is expensive and when given is lost quickly in urine.
- So it is indicated only when there is
  - severe oedema resistant to large doses of diuretics
  - and if the nephrotic patient is to be subjected to surgery or invasive procedure (e.g. biopsy)..

Treatment of N. S.

Hypertension

- Blood pressure control is important for both renal and cardiovascular protection.
- For patients with proteinuria of more than 1 g/day, the target for blood pressure is 125/75 mm Hg unless contraindicated for clinical reasons
- ACEI and ARBs are cardioprotective and can reduce proteinuria and slow progression of renal disease in both diabetic and nondiabetic patients with chronic nephropathy

Treatment of N. S.

Corticosteroids

- are given when there is no response to previous lines of treatment.

- Minimal change glomerulonephritis gives the best response while mesangiocapillary glomerulonephritis is always steroid resistant.

Corticosteroids

- For patients with secondary GN, steroids are given if indicated for the causative disease as in SLE but not in D.M.

- The dose and duration of steroid treatment depends on the type of disease and response.

Corticosteroids

In primary (idiopathic) minimal change

- ***Prednisolone*** is given orally in a dose of 60 mg / day (max. 80mg/d) .

- This full dose is to be given for ***8-12*** **weeks** then tapered gradually over equal time period.

- In severe cases 1-3 doses of ***Methylprednisolone*** is given by ***I.V. infusion*** (10-15mg/kg) as induction, followed by oral prednisolone.

Immunosuppressive drug

- Cyclosporin is an immunosuppresive drug which is commonly added to steroids(e.g. steroid resistant and steroid dependant cases), and in patients with membranous nephropathy.
- Other commonly used immunosuppresive drugs includes Azathioprine,Cyclophosphamide,and MMF(Cell Cept).


Thank
You