NEPHROTIC SYNDROME

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OBJECTIVES:

- Definition
- Etiology
- Pathogenesis
- Clinical fetures
- Investigations
- Treatment
- Complications

DEFINITION:

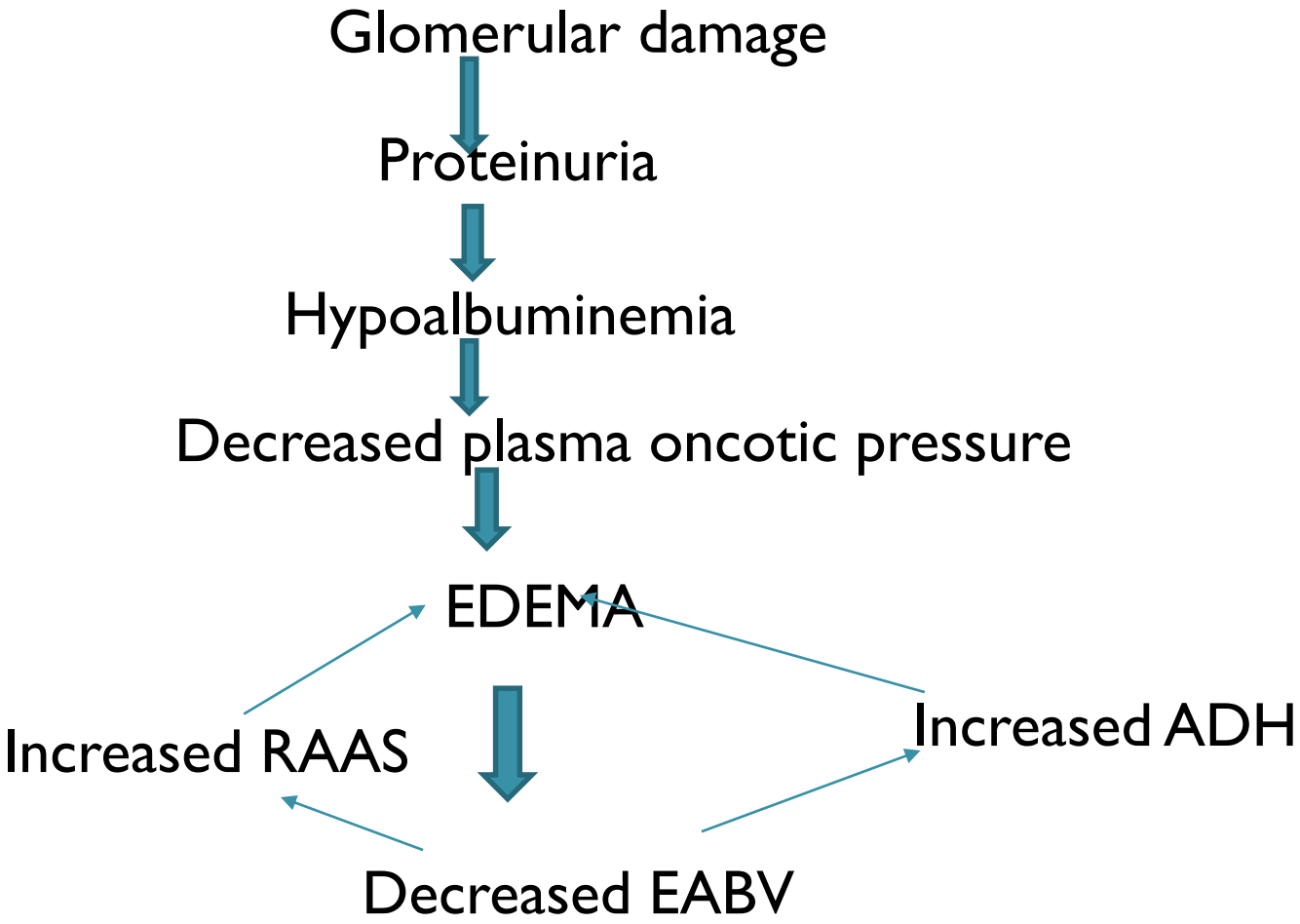
- **Heavy proteinuria** (more than 3.5gm/24h/1.73m2), hypoalbuminaemia, hyperlipidaemia and edema

ETIOLOGY:

- Primary:
- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous glomerulonephritis
- IgA Nephropathy
- Fibrillary-immunotactoid disease

ETIOLOGY:

- Secondary nephrotic syndrome:
- 1. Post infection .
- 2. Drug.
- 3. Metabolic.
- 4. Collagen and autoimmune disease.
- 5. Malignancy.
- 6. Renal vein thrombosis.
- 7. Congenital and familial conditions.


Glomerular damage
Proteinuria
Hypoalbuminemia
Decreased plasma oncotic pressure
EDEMA
Increased RAAS
Increased ADH
Decreased EABV

CLINICAL FEATURES:

- **Edema:**
- morning puffiness of the face.
- edema of lower limbs
- In severe cases, polyserositis.

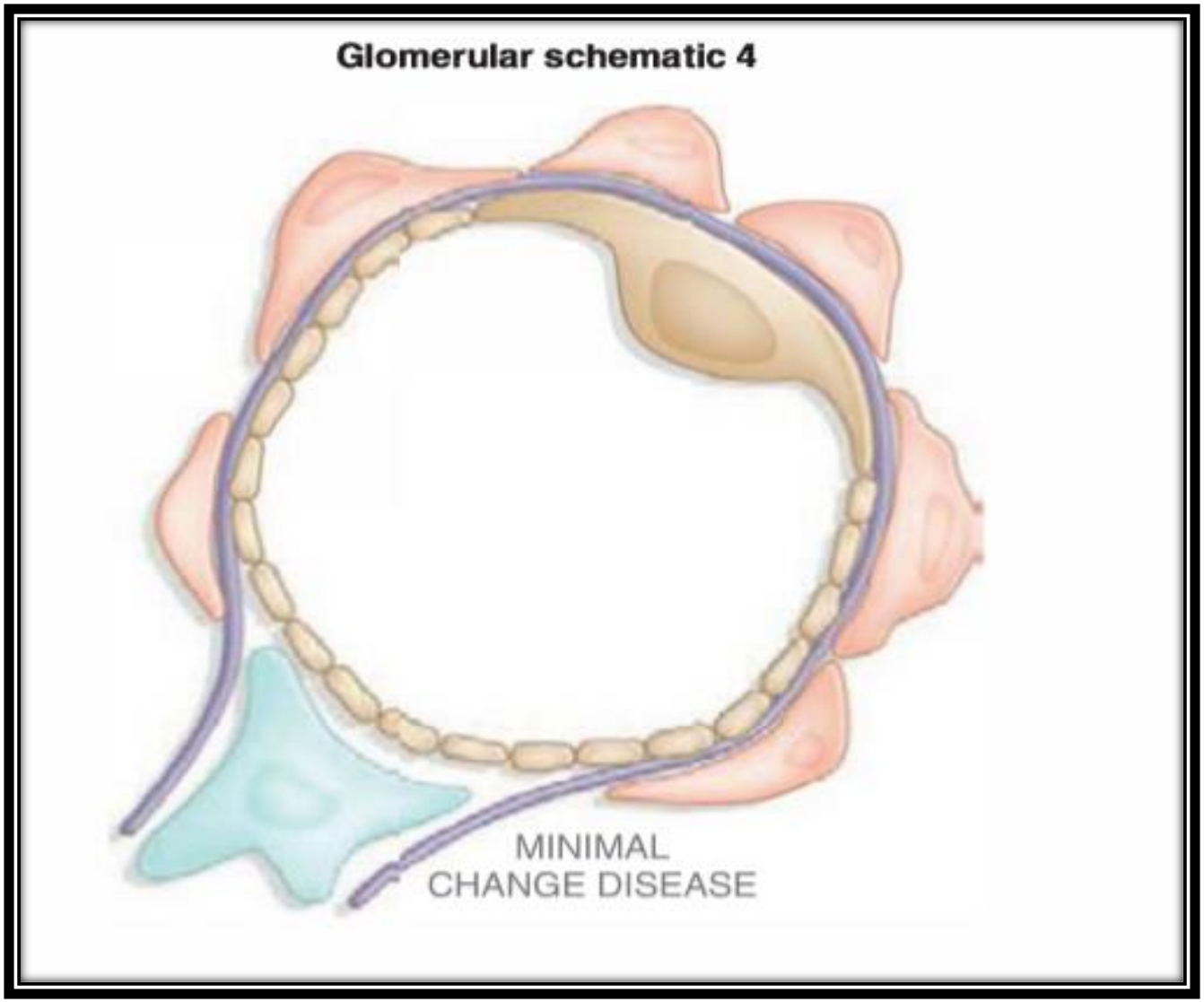
2. Hypertension: etiologic and pathologic type of nephrotic syndrome.

- Hypertension is either due to salt and water retention or it may be due to the excess secretion of renin.

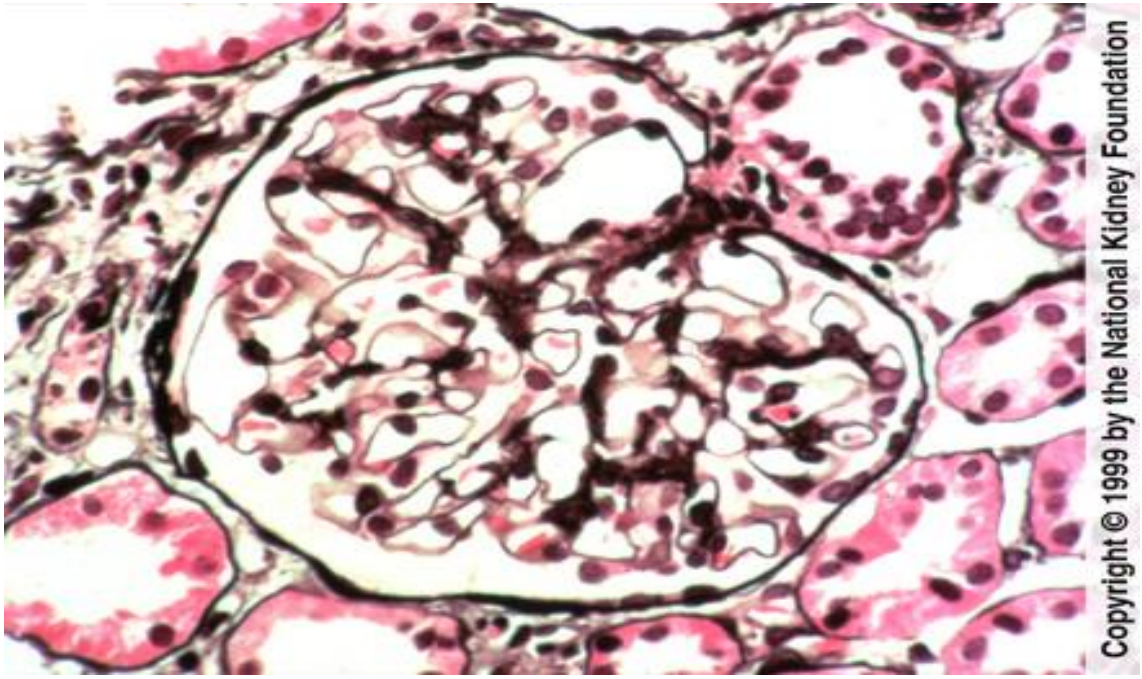
- **3. Other manifestations** of nephrotic syndrome include lassitude, anorexia, loss of appetite and pallor.
- 4. **Manifestations of the etiologic cause** in secondary cases as manifestations of diabetes in cases with diabetic nephropathy.

INVESTIGATIONS:

- **1.Urine analysis** :
- **2. Blood:**
- **3. Diagnosis of the cause in secondary**
- **4. Kidney biopsy**:

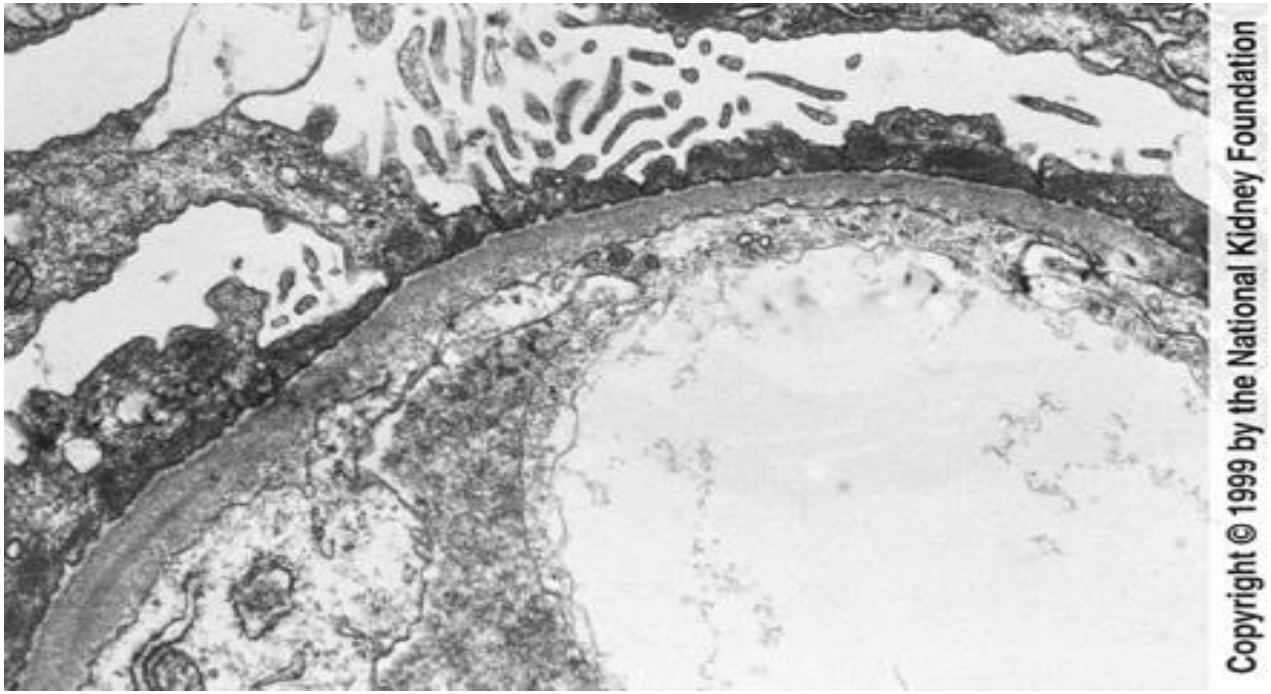

Glomerular schematic 4
MINIMAL
CHANGE DISEASE

Minimal change disease

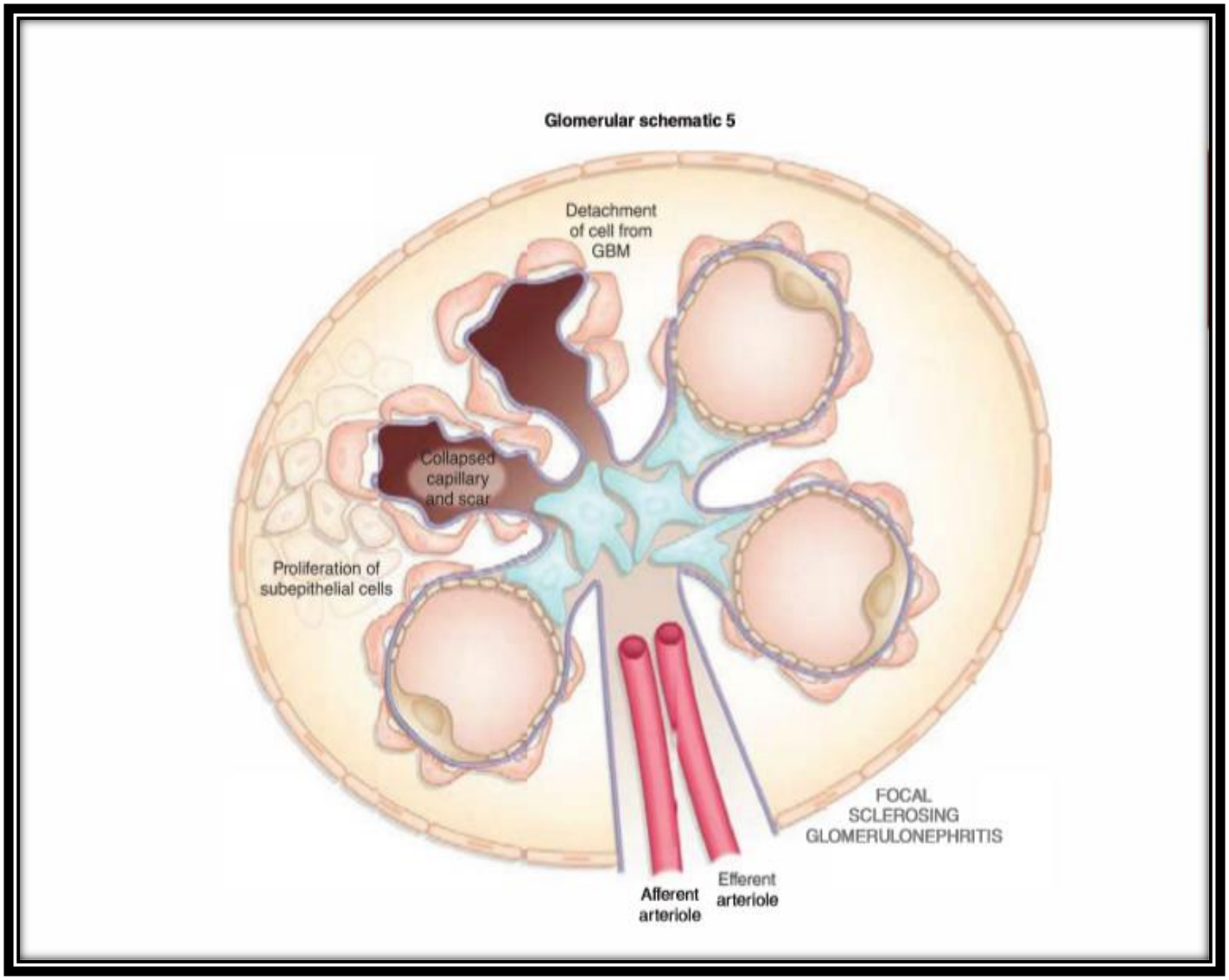


- The glomerular basement membrane is thin and delicate, and mesangial cellularity and matrix are within normal limits.

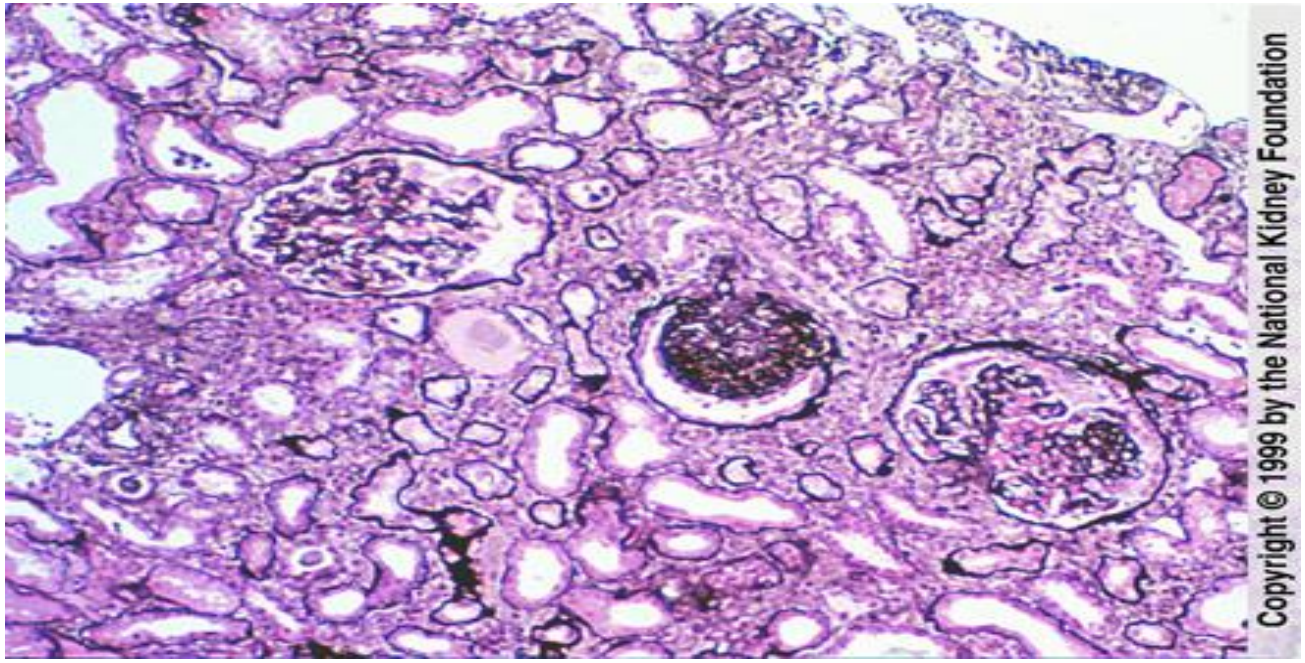
Electron microscopy - MCD



- The glomerular basement membrane is of normal thickness without deposits in this case of minimal change disease. The visceral epithelial cells show diffuse effacement of foot processes. An area of microvillous transformation is also present, representing the irregular epithelial-cell surface that occurs in proteinuric states. Foot-process effacement is generally quite extensive in minimal change disease, although the degree of foot-process effacement cannot be used to definitively distinguish minimal change disease from unsampled FSGS.

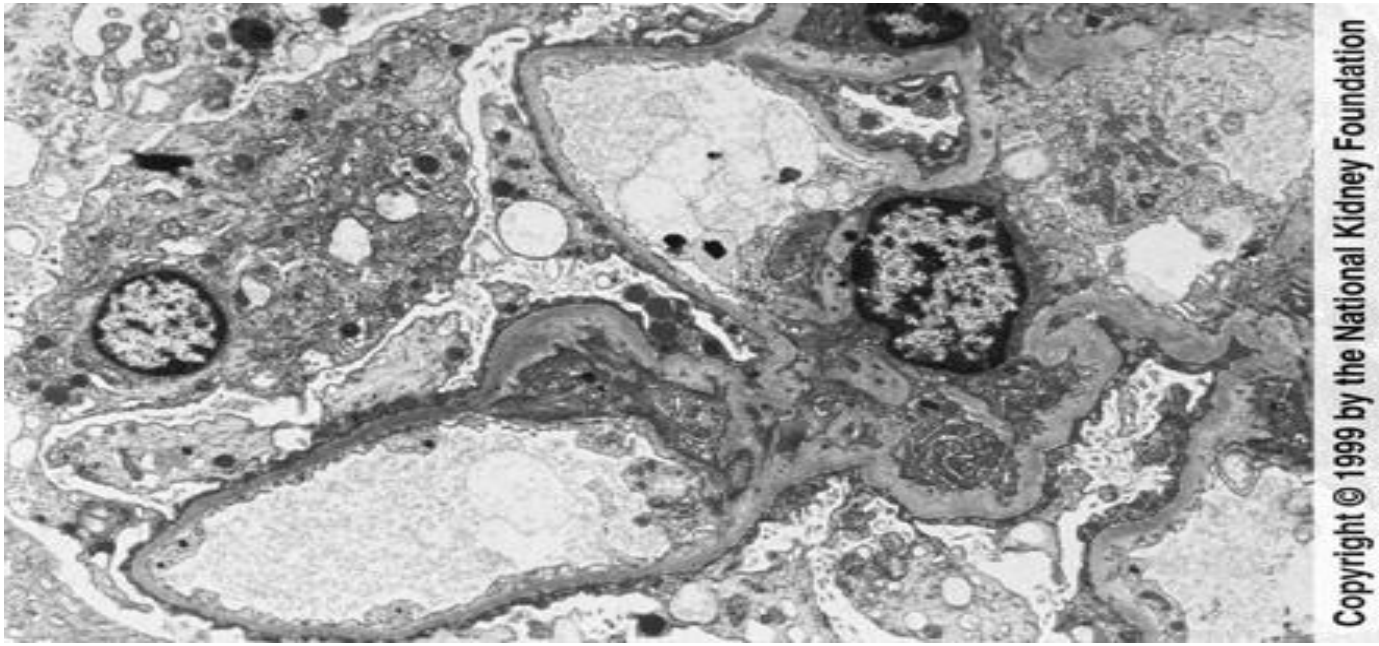

Glomerular schematic 5
Detachment of cell from GBM
Collapsed capillary and scar
Proliferation of subepithelial cells
FOCAL SCLEROSING GLOMERULONEPHRITIS
Afferent arteriole
Efferent arteriole

FSGS

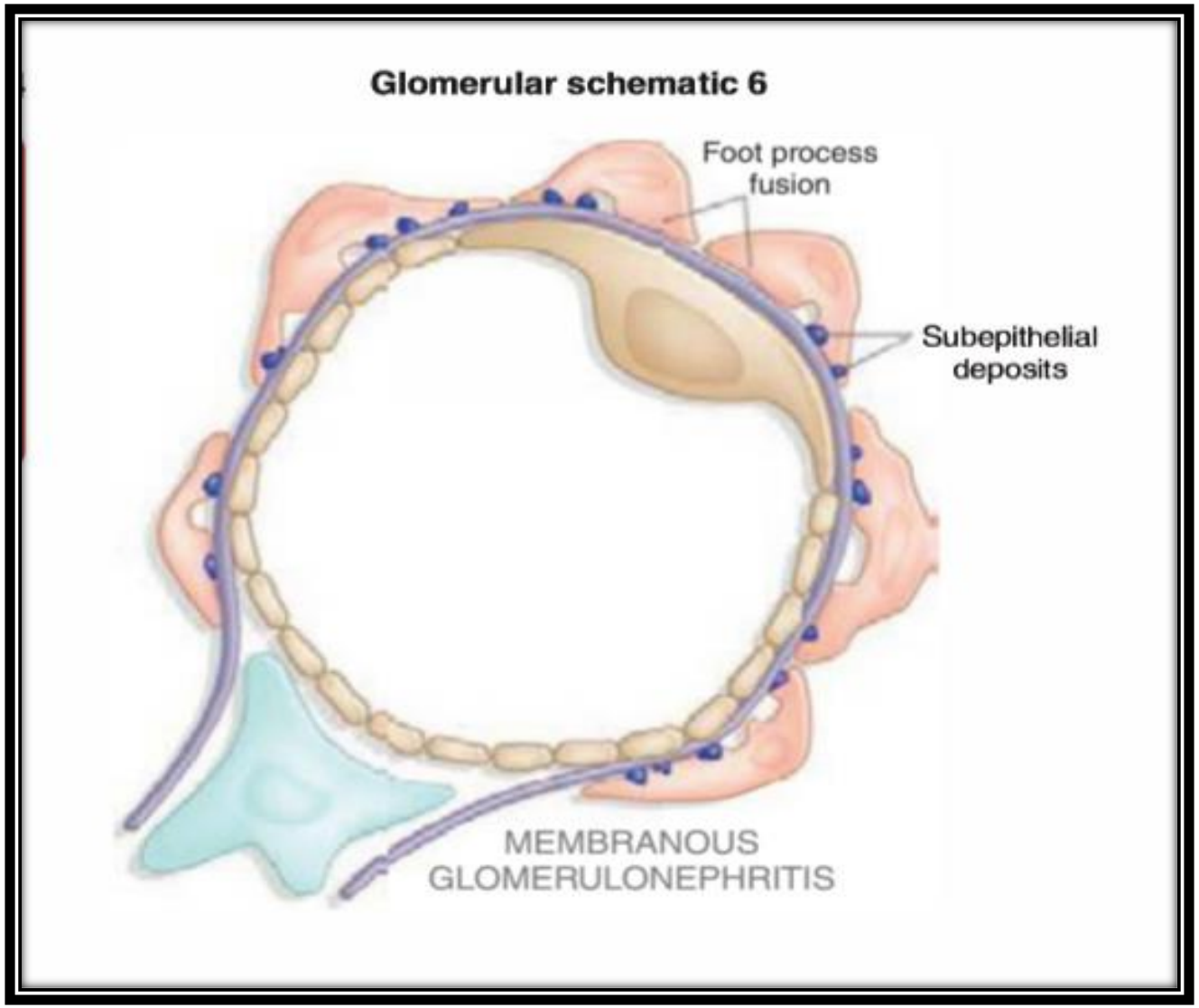


- More advanced lesions of FSGS are present in this biopsy, with a central glomerulus showing global sclerosis, the glomerulus on the left showing well-defined peripheral segmental sclerosis, and the glomerulus on the right showing no lesions in this section. There is moderate interstitial fibrosis and tubular atrophy.

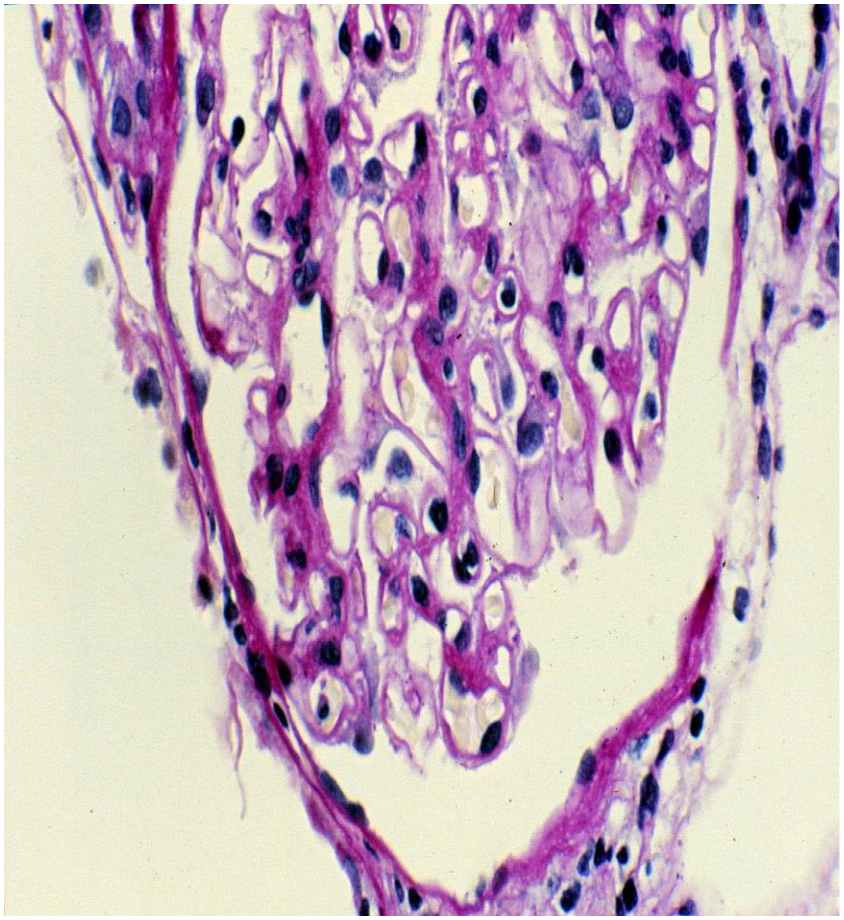
FSGS –EM.



- The mesangial matrix is mildly increased without deposits in this case of FSGS. Endothelial cells are unremarkable, and visceral epithelial cells show extensive blunting and effacement of foot processes with early microvillous transformation.

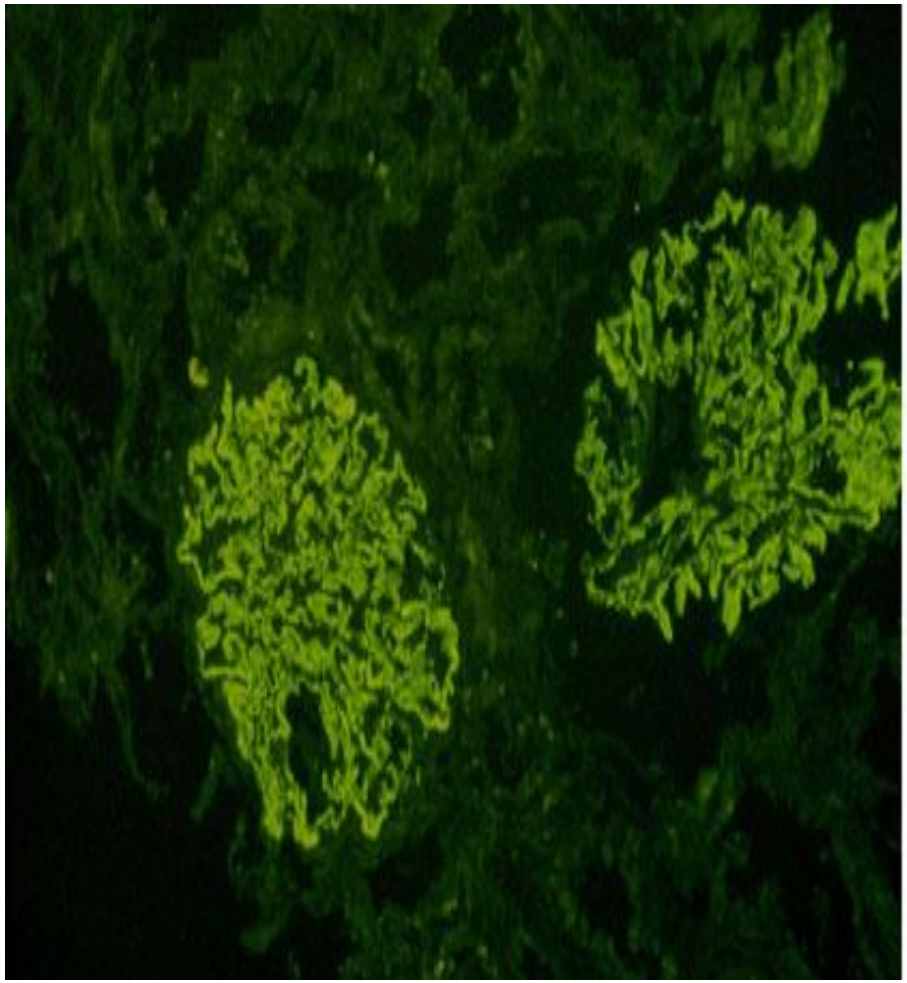

Glomerular schematic 6
Foot process fusion
Subepithelial deposits
MEMBRANOUS GLOMERULONEPHRITIS

Membranous glomerulonephritis



- In this case of stage I membranous glomerulonephritis, the capillary wall is slightly prominent and appears more rigid than normal. However, deposits cannot be directly visualized on this periodic acid-Schiff stain (original magnification x400).

Membranous glomerulonephritis-IF



Diffuse coarsely granular capillary wall IgG deposits in stage II-III membranous glomerulonephritis

- **Minimal-change disease:**

  Normal light microscopy,

  effaced foot processes on EM

- **Membranous nephropathy**

  Subepithelial Deposits on light, IF, EM

- **Membranoproliferative glomerulonephritis :**

  Thickened mesangial matrix,

  splitting (double contour) of the glomerular basement membrane,

  C3 granular staining on IF

- **Focal segmental glomerulosclerosis:**
  Sclerosis in portions of glomeruli,
  C3 in areas of sclerosis on IF

- **IgA nephropathy:**
  IgA in mesangium on IF

- **Fibrillary glomerulonephritis:**
  Fibrillar deposits in mesangium,
  negative congo red staining on IF

TREATMENT:

- **1. secondary cases**
- **2. Treatment of complications**
- **3. Rest:**
- **4. Diet:**
- **5.Diuretics**
- **6. Salt poor albumin:**

- **7.Corticosteroids:**
- no response to previous lines of treatment.
- Minimal change glomerulonephritis gives the best response while mesangiocapillary glomerulonephritis is always steroid resistant.
- secondary glomerulonephritis, 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.
- In primary (idiopathic) minimal change nephritis 40-60 mg daily prednisone are given orally (for children 1-2 mg/kg/d), for 4-6 weeks followed by gradual withdrawal.
- **8. Other immunosuppressive drugs :**
- cyclophosphamide, azathioprine and ciclosporin in selected cases

COMPLICATIONS:

- **1.Subnutritional State:**
- Due to poor dieting, and urinary losses of protein and other substances.
- **2. Infection:**
- Especially upper respiratory, urinary, skin and peritoneal infections.
- Recurrent infection is due to nutritional deficiencies, urinary loss of immunoglobulins and complements.
- **3.Premature atherosclerosis:**
- it is due to hyperlipidaemia.
- This complication occurs mainly in cases with frequent relapses or cases resistant to treatment.

- **4.Clotting episodes:**
- recurrent deep vein thrombosis (DVT), or renal vein thrombosis and pulmonary embolism.
- due to:
- a. Increased concentration of coagulation factors resulting from an increased hepatic synthesis e.g. fibrinogen, factor III, and VIII.
- b. Urinary loss of antithrombin III and protein C which normally act against intravascular clotting.
- c. Abnormal vascular endothelium.
- d. Hypovolemic state.

- **5. Hypovolaemia:**
- Which causes postural hypotension.
- **6. Drug related complications:**
- a. Diuretics : hypovolaemia, hypokalaemia, or hyponatraemia.
- b. Corticosteroids: diabetes mellitus, cataract, D.U., infections, and bone disease.
- c. Other Immunosuppressive drugs: as cyclophosphamide which may cause haemorrhagic cystitis, alopecia, infection and malignancy.

- **7. Acute renal failure:**
- due to:
- severe hypovolaemia
- acute interstitial nephritis
- **8. Bone disease:**
- Due to hypocalcemia. It causes secondary hyperparathyroidism.
- **9. Anemia:**
- Due to nutritional deficiencies and urinary loss of transferrin.

THANK YOU