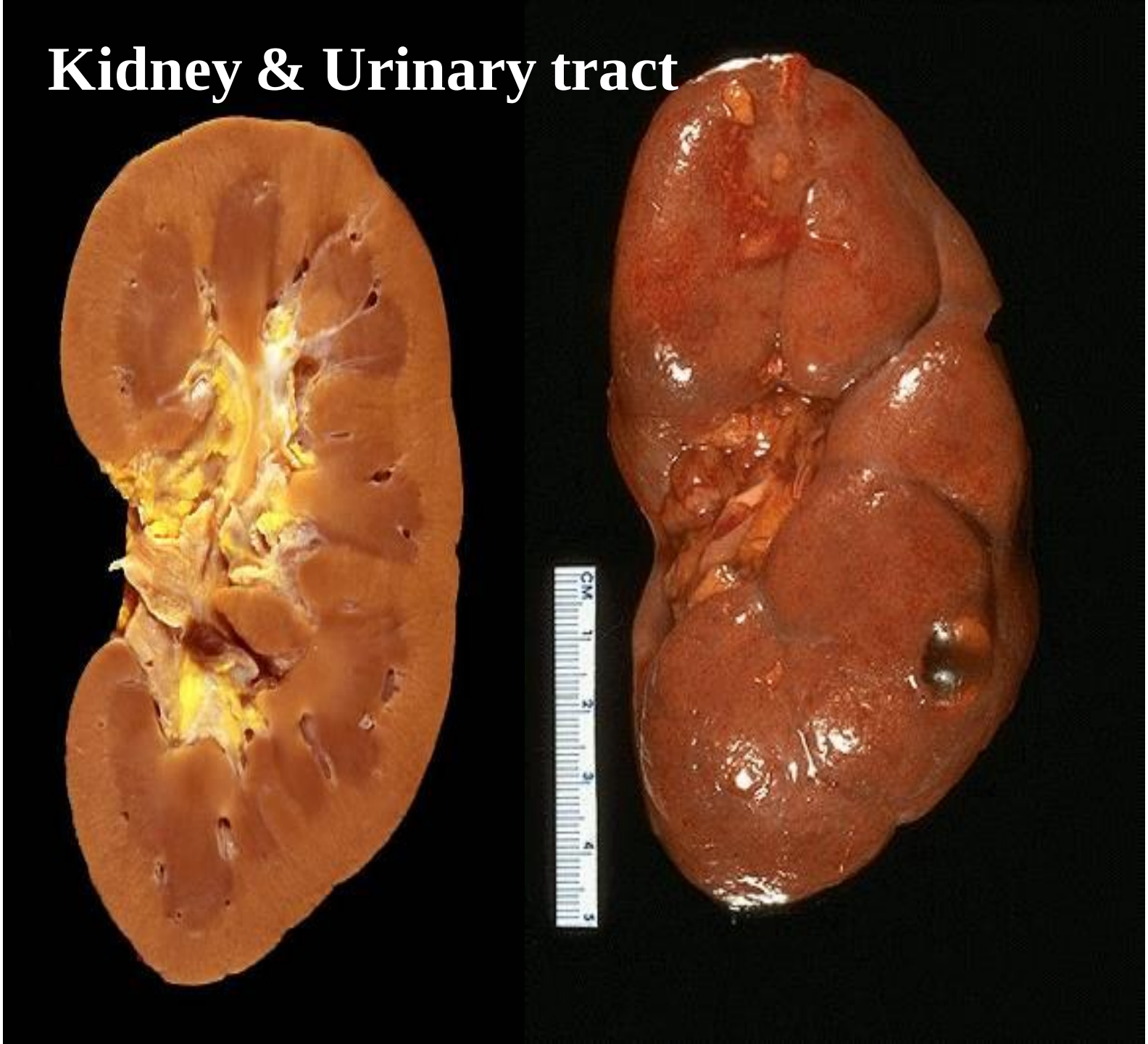
# Kidney & Urinary tract



# CLINICAL MANIFESTATIONS OF RENAL DISEASES

- ***1-Azotemia***
- **refers to an elevation of blood urea nitrogen(BUN) and creatinine levels**
- **It is largely related to a decreased glomerular filtration rate (GFR).**
- ***2-uremia***
- **when azotemia progresses to clinical manifestations and systemic biochemical abnormalities.**

- **Uremia is characterized by:**

**1- failure of renal excretory function**

**2- metabolic and endocrine alterations**

**3- 2ry gastrointestinal manifestations (e.g., uremic gastroenteritis)**

**4- 2ry neuromuscular manifestations (e.g., peripheral neuropathy)**

**5- 2ry cardiovascular manifestations (e.g., uremic fibrinous pericarditis)**

# The major renal syndromes

- ***1-Nephritic syndrome:***
- **a glomerular syndrome characterized by:**
- **acute onset .**
- **gross hematuria.**
- **mild to moderate proteinuria (< 3.5 gm of protein/day in adults)**
- **azotemia.**
- **edema.**
- **hypertension.**

# *2-Nephrotic syndrome*

- **a glomerular syndrome characterized by:**
- **heavy proteinuria (excretion of >3.5 gm of protein/day in adults)**
- **hypoalbuminemia**
- **severe edema**
- **hyperlipidemia**
- **lipiduria (lipid in the urine).**

- ***3-Asymptomatic hematuria* or *proteinuria:***
- **A manifestation of mild glomerular abnormalities.**
- ***4-Rapidly progressive glomerulonephritis (crescentic GN)***
- **loss of renal function in a few days or weeks**
- **It is manifested by :**
- **microscopic hematuria.**
- **dysmorphic RBC and RBC casts in urine sediment.**
- **mild-moderate proteinuria**

# *5-Acute renal failure*

- **oliguria (<400 ml/day) or anuria (no urine flow).**
- **recent onset of azotemia.**

- **It can result from :**
- **1-glomerular injury**
- **2-interstitial injury**
- **3-vascular injury (thrombotic microangiopathy)**
- **4-acute tubular necrosis**

- ***6- Chronic renal failure***

- **prolonged symptoms and signs of uremia.**
- **the end result of all chronic renal diseases .**

- ***7- Urinary tract infection***
- **bacteriuria and pyuria (bacteria and WBCs in urine).**
- **symptomatic or asymptomatic.**
- **Types :**
- **1- *pyelonephritis (*kidney ).**
- **2- *cystitis* (bladder).**

# *8-Nephrolithiasis*

- **= Renal stones.**
- **manifested by:**
- **1-renal colic.**
- **2-hematuria.**
- **3-recurrent stone formation.**

# *Glomerular diseases*

# CONCEPTS

# GLOMERULAR DISEASES

- one of the most common causes of chronic kidney disease.
- **The glomerulus** =anastomosing network of capillaries invested by two layers of epithelium: podocytes and parietal epithelium
- Bowman space (urinary space)= the cavity in which plasma ultrafiltrate first collects.

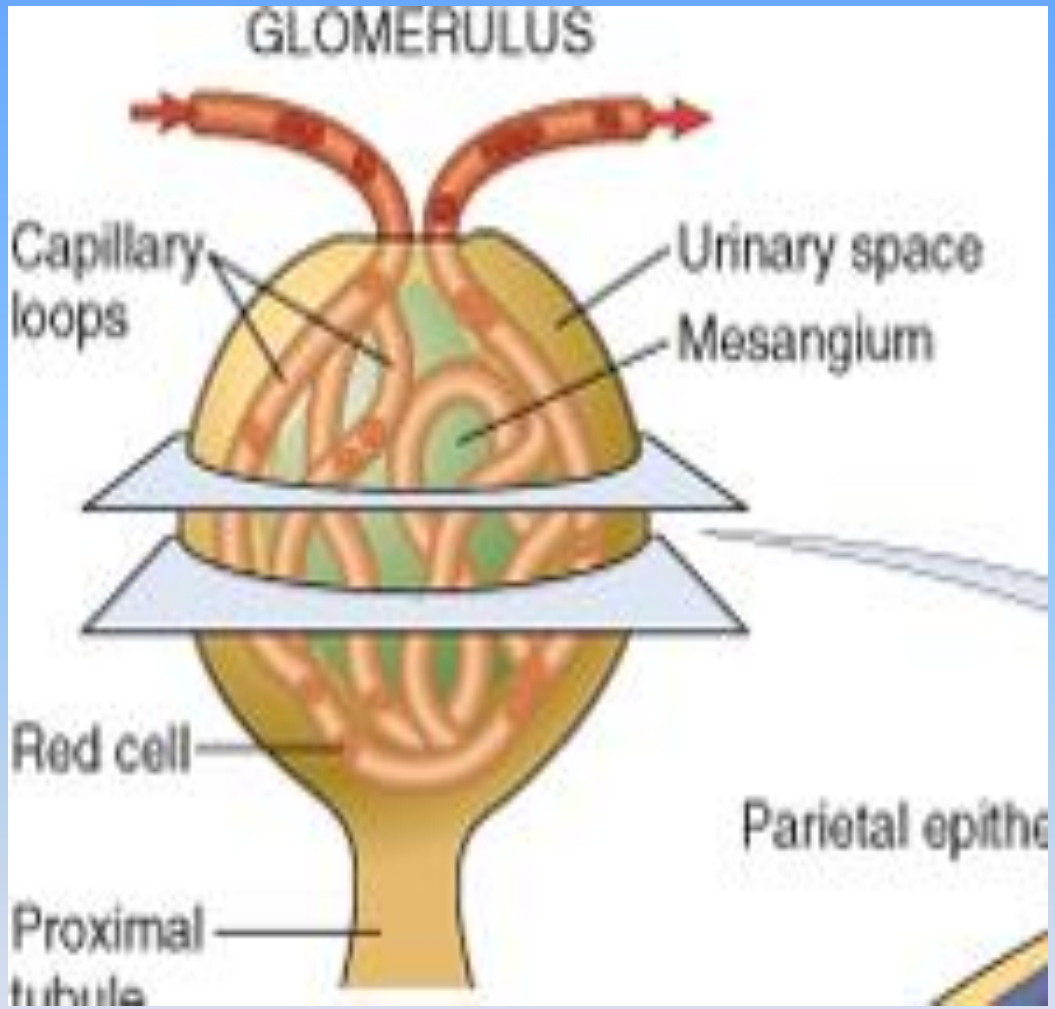
- The glomerular capillary wall is the filtration unit and consists of :

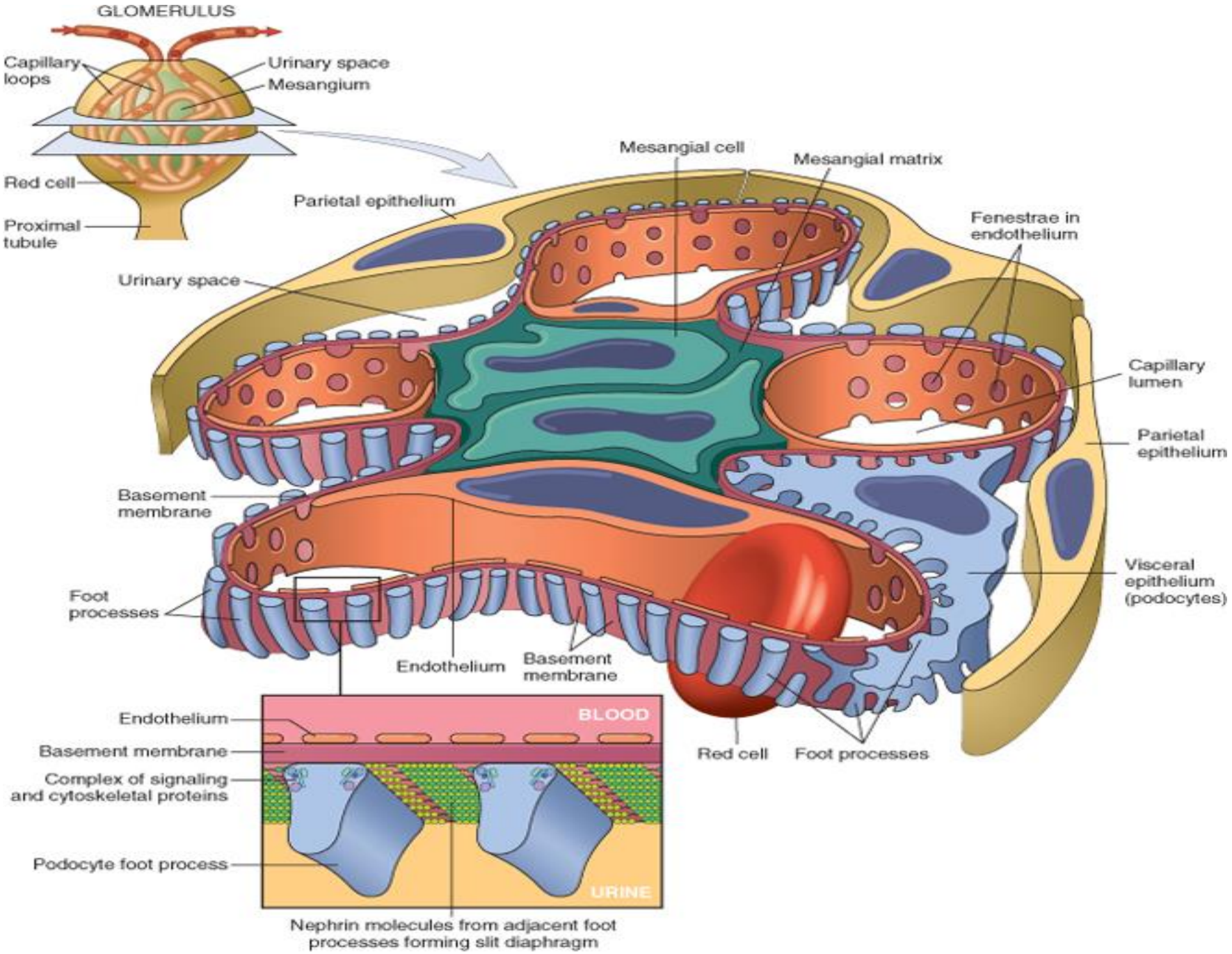
**1-A thin layer of fenestrated *endothelial cells***

**2- *glomerular basement membrane* (GBM)**

**3- foot processes of podocytes**

**4-Supportive cells (*mesangial cells*) lying between the capillaries**


GLOMERULUS
Capillary loops
Urinary space
Mesangium
Red cell
Parietal epithe
Proximal

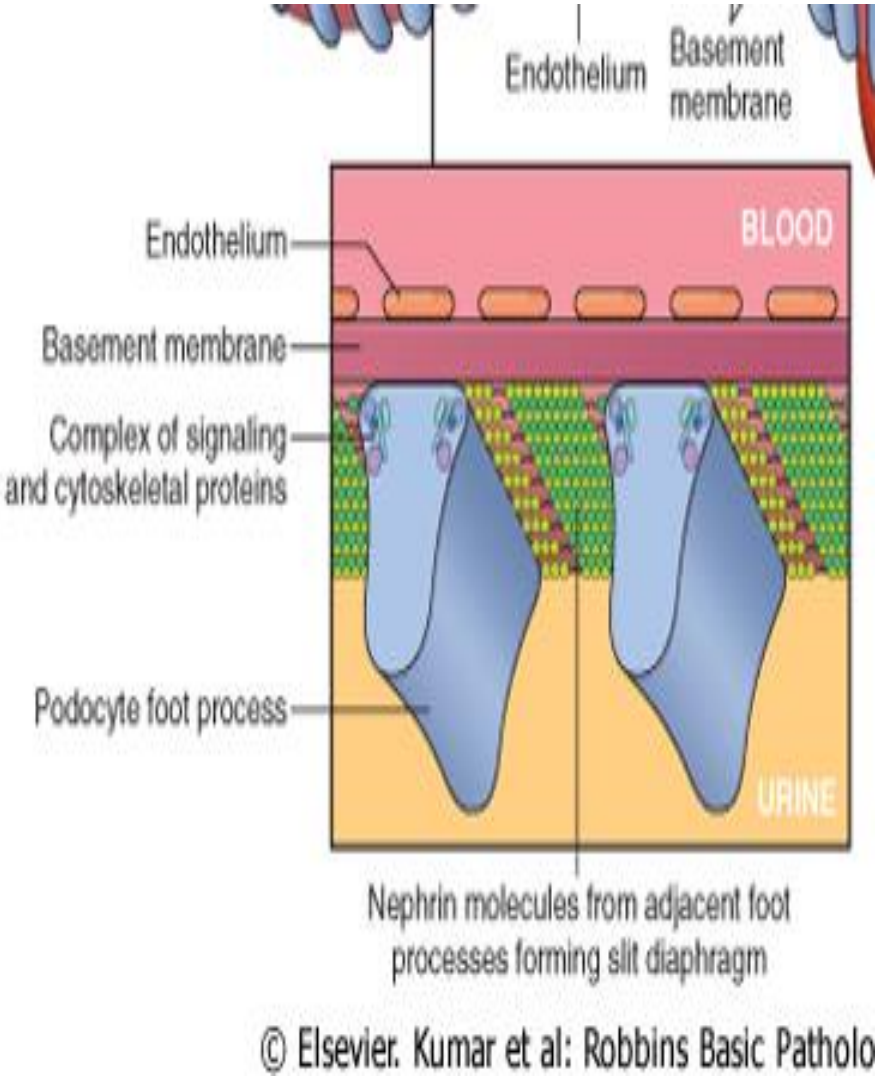


# The capillary basement membrane

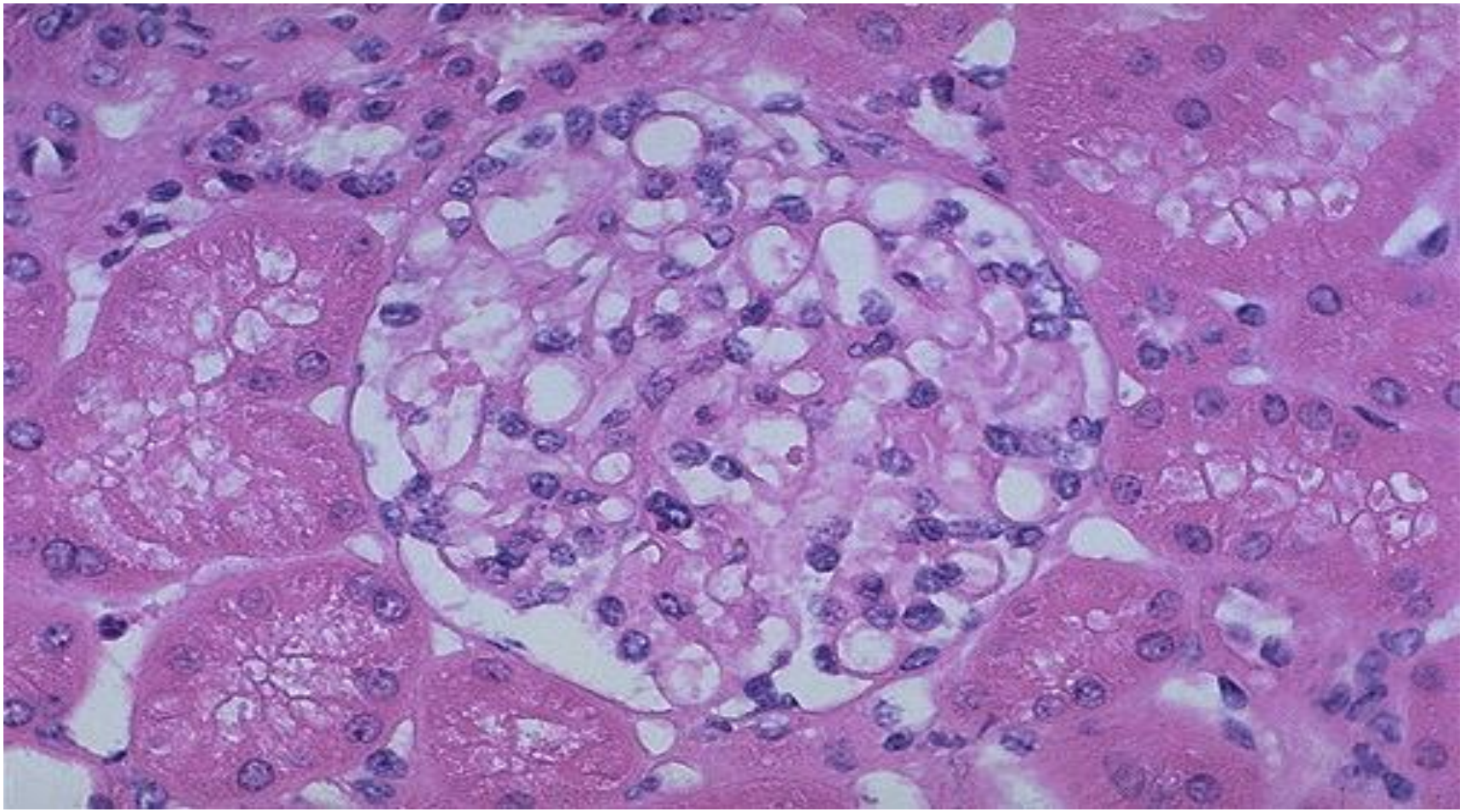
- **consists of collagen (type IV), laminin, polyanionic proteoglycans, fibronectin, and glycoproteins.**

- **interdigitating foot processes of The *visceral epithelial cells* (podocytes), embedded in and adherent to GBM**

- ***foot processes* are separated by *filtration slits* which are bridged by a thin slit diaphragm composed in large part of nephrin.**

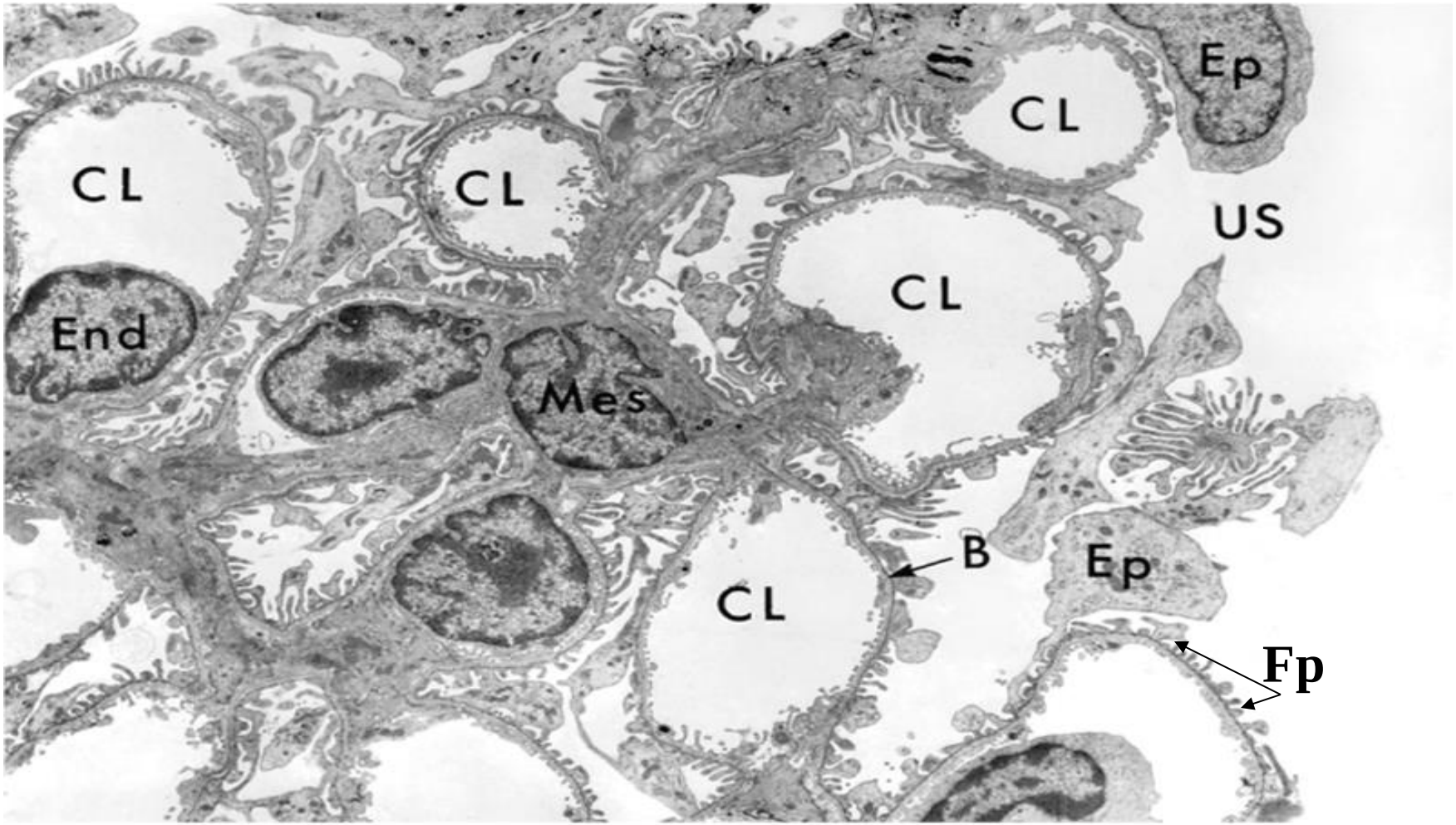


**Normal glomerulus by LM.**
**The glomerular capillary loops are thin and delicate.**
**Endothelial and mesangial cells are normal in number. The surrounding tubules are normal.**



**EM-GLOMERULUS**

**CL-capillary lumen, End-endothelium, US-urinary space, B-basement membrane, Ep-epithelial cell, Mes-mesangial cell, Fp-foot process.**



# The major characteristics of glomerular filtration

**1- high permeability to water and small solutes**

**2- complete impermeability to molecules of large size and molecular charge (e.g. albumin)**

- **So:**

**1- the larger the less permeable**

**2- the more cationic the more permeable.**

- **Nephrin and its associated proteins, including podocin, have a crucial role in maintaining the selective permeability of the glomerular filtration barrier.**

# Pathogenesis of Glomerular Diseases

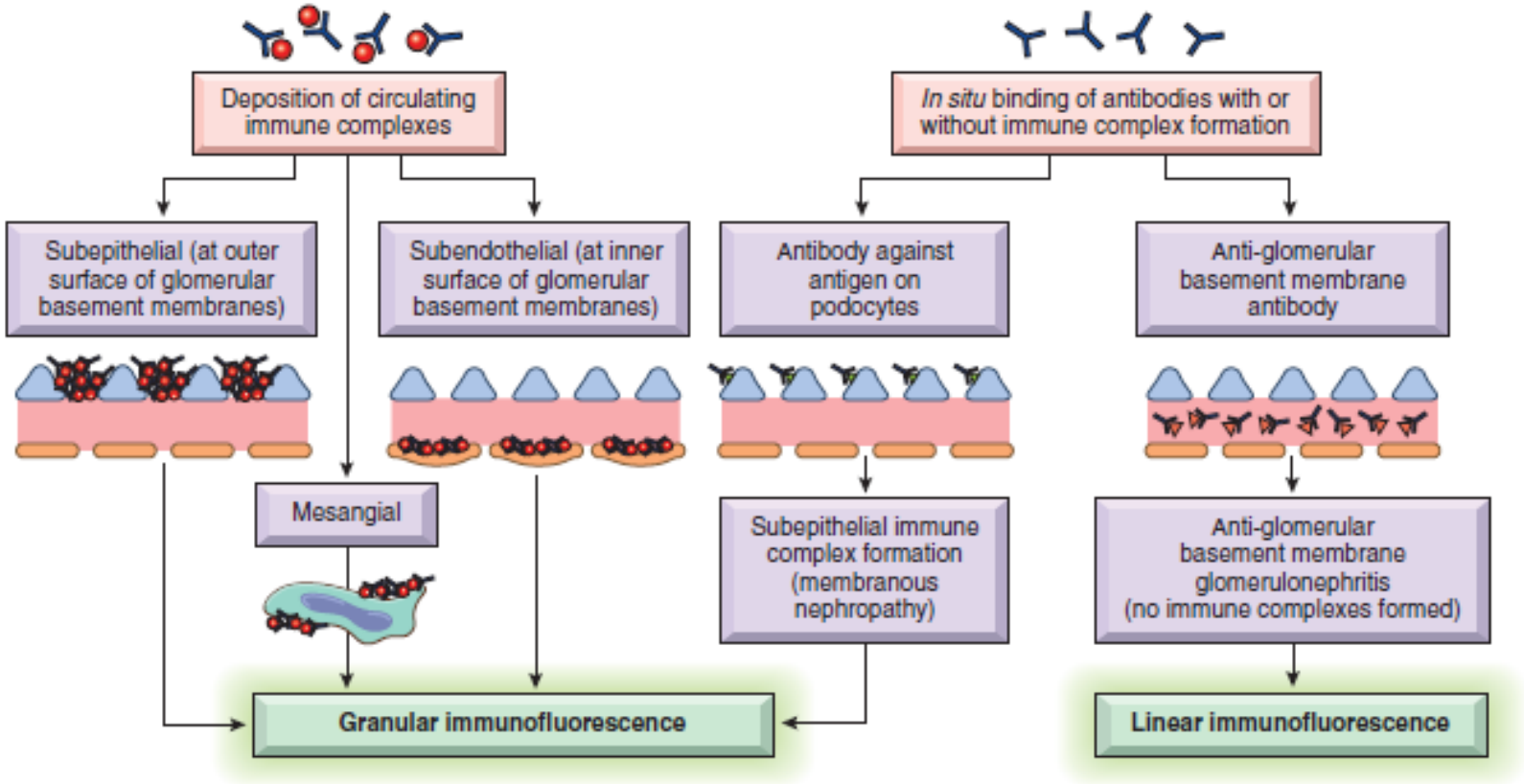
**1- Antibody-associated → detected by immunoflourescence microscopy**

**(1) deposition of soluble circulating Ag-Ab complexes in the glomerulus.**

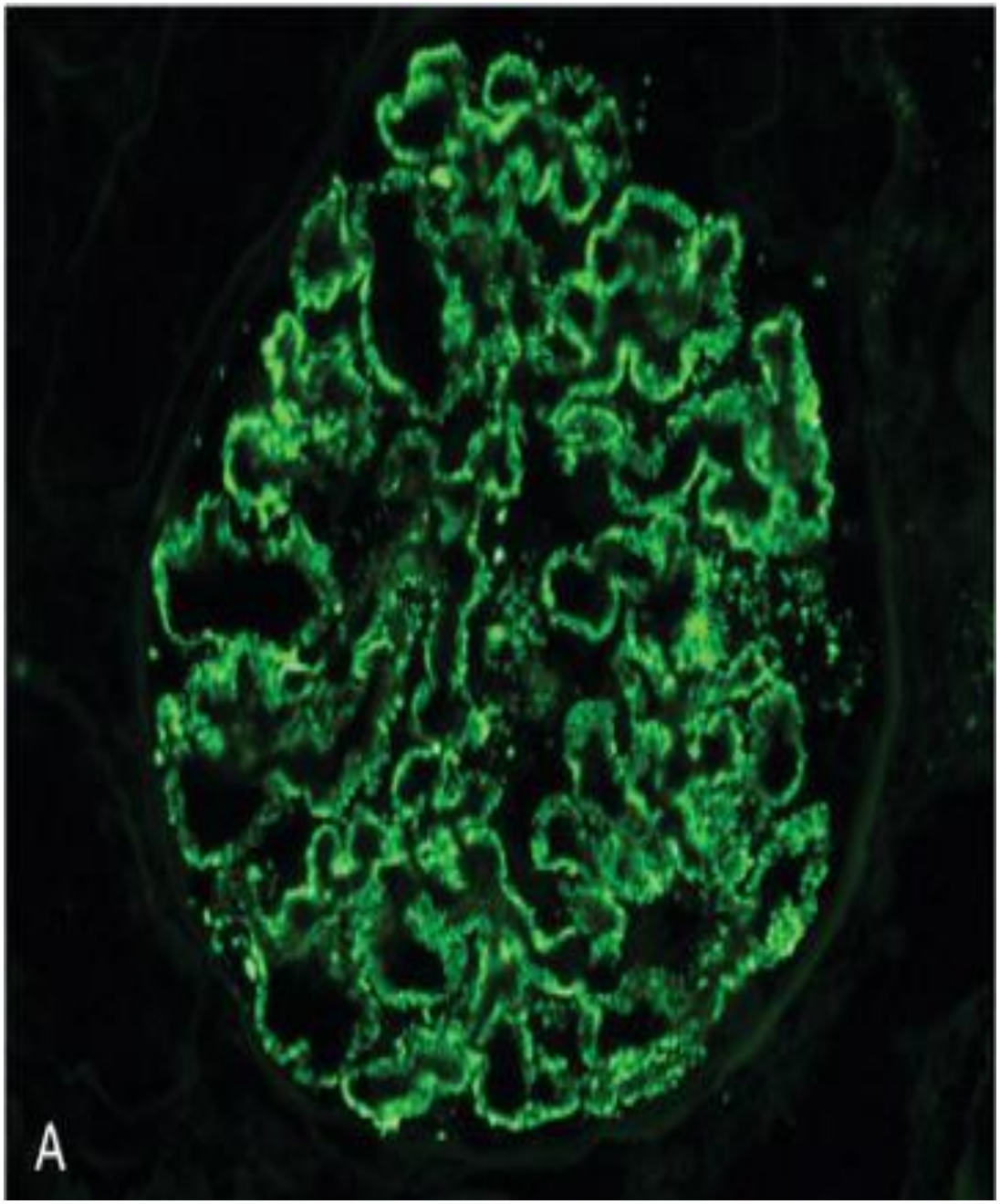
**(2) Abs reacting in situ within the glomerulus.**

**(3) Abs directed against glomerular cell components.**

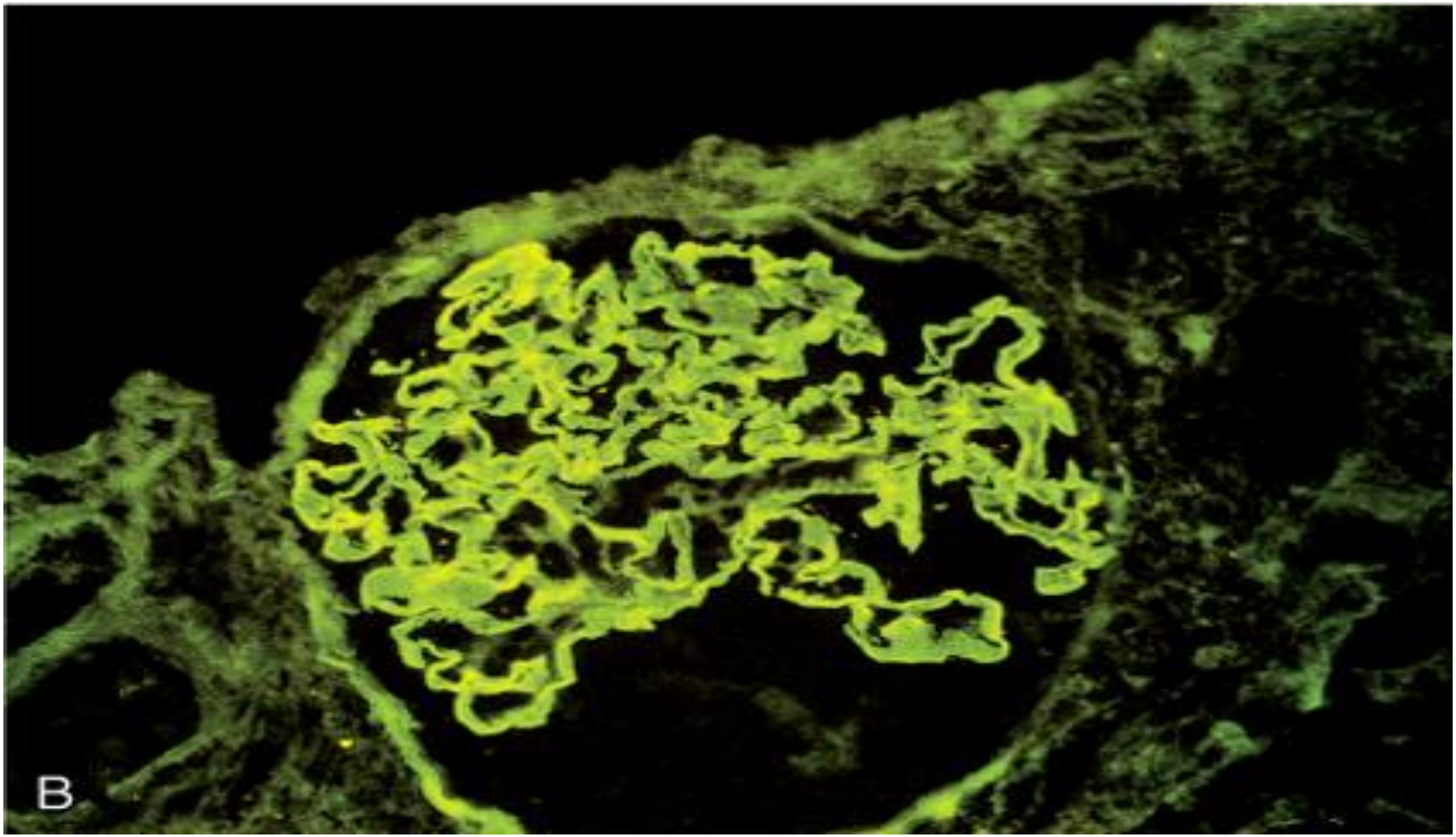
# Antibody- mediated glomerular injury



# Immunofluorescence microscopy



**immunofluorescence linear deposition of immune complexes**



- **Electron Microscopy:**
- **reveals the immune complexes as electron-dense deposits or clumps that lie at one of three sites:**

**1-in the mesangium.**

**2-between the endothelial cells and the GBM (subendothelial deposits).**

**3-between the outer surface of the GBM and the podocytes (subepithelial deposits).**

- **The pattern of immune complex deposition is helpful in distinguishing various types of GN**

# Pathogenesis of Glomerular Diseases

## 2- Non-immune Mechanisms of Glomerular Injury

### 1) Podocyte Injury:

- Causes: toxins; cytokines; or poorly characterized circulating factors; mutations
- effacement of foot processes, results in the development of proteinuria (loss of normal slit diaphragms)

## 2) Nephron Loss:

Eventually leads to segmental or global (complete) sclerosis of glomeruli→ further reduction of nephron mass, initiating a vicious cycle of progressive glomerulosclerosis.

# Nephrotic Syndrome

# The Nephrotic Syndrome

- a clinical complex that includes the following:
- (1) **massive proteinuria** with daily protein loss in the urine of 3.5 gm or more in adults.
- (2) **hypoalbuminemia** with plasma albumin levels less than 3 gm/dL.
- (3) **generalized edema**
- (4) **hyperlipidemia and lipiduria**.
- (5) little or no azotemia, hematuria, or hypertension.

# Causes of Nephrotic Syndrome

- **1- Primary Glomerular Diseases**
- **2- Systemic Diseases with Renal Manifestations**

# Primary Diseases That Present Mostly With Nephrotic Syndrome

1- Minimal-change disease

2- Focal segmental glomerulosclerosis (FSGS).

3- Membranous nephropathy

4- membranoproliferative GN type 1 (?) (usually a combination of nephrotic/ nephritic syndrome)

# Causes of Nephrotic Syndrome

## 1-primary glomerular diseases

| Cause | Prevalence (%) Children | Prevalence (%) Adults |
|---|---|---|
| Primary Glomerular Disease | | |
| Membranous GN | 5 | 30 |
| Minimal-change disease | 65 | 10 |
| Focal segmental glomerulosclerosis | 10 | 35 |
| Membranoproliferative GN | 10 | 10 |
| IgA nephropathy | 10 | 15 |

# Causes of Nephrotic Syndrome

## B-Systemic Diseases with Renal Manifestations:

- **Diabetes mellitus:**
- **Amyloidosis**
- **Systemic lupus erythematosus**
- **drugs (gold, penicillamine, "street heroin")**
- **Infections (malaria, syphilis, hepatitis B, HIV)**
- **Malignancy (carcinoma, melanoma)**
- **Miscellaneous (e.g. bee-sting allergy)**

# Minimal-Change Disease (Lipoid Nephrosis)

- **benign disorder.**

- **The most frequent cause of the nephrotic syndrome in children (ages 1-7 years).**

- ***Pathogenesis:*** **still not clear.**

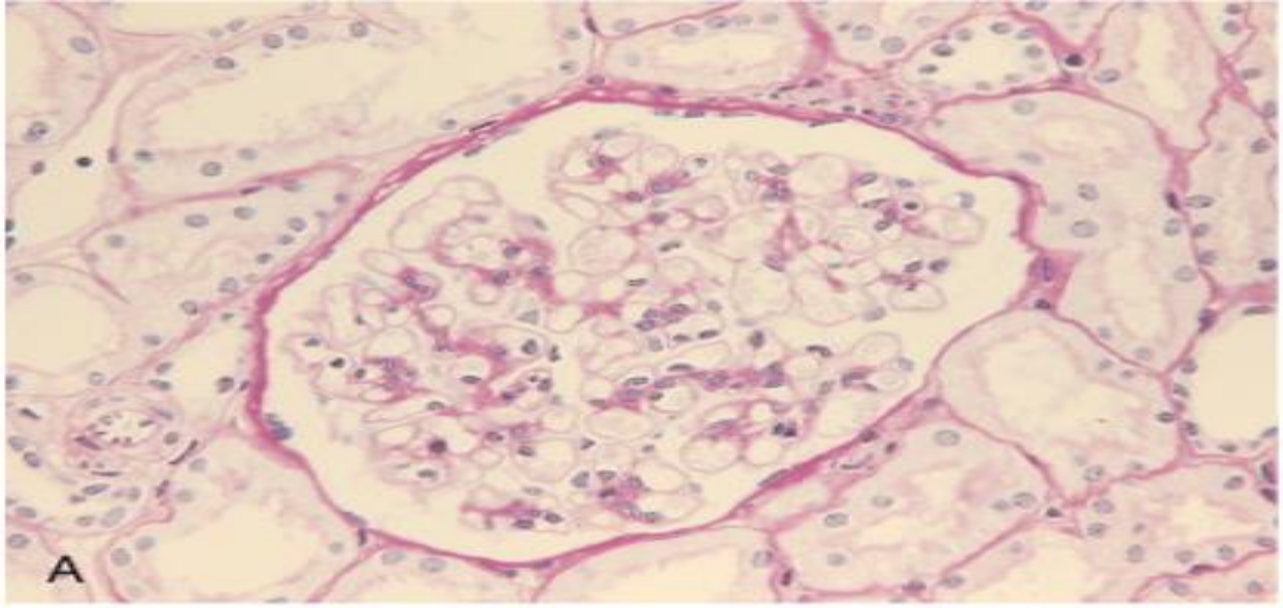
**? T-cell derived factor that causes podocyte damage and effacement of foot processes.**

# Morphology

- **LM**
- the glomeruli appear normal.

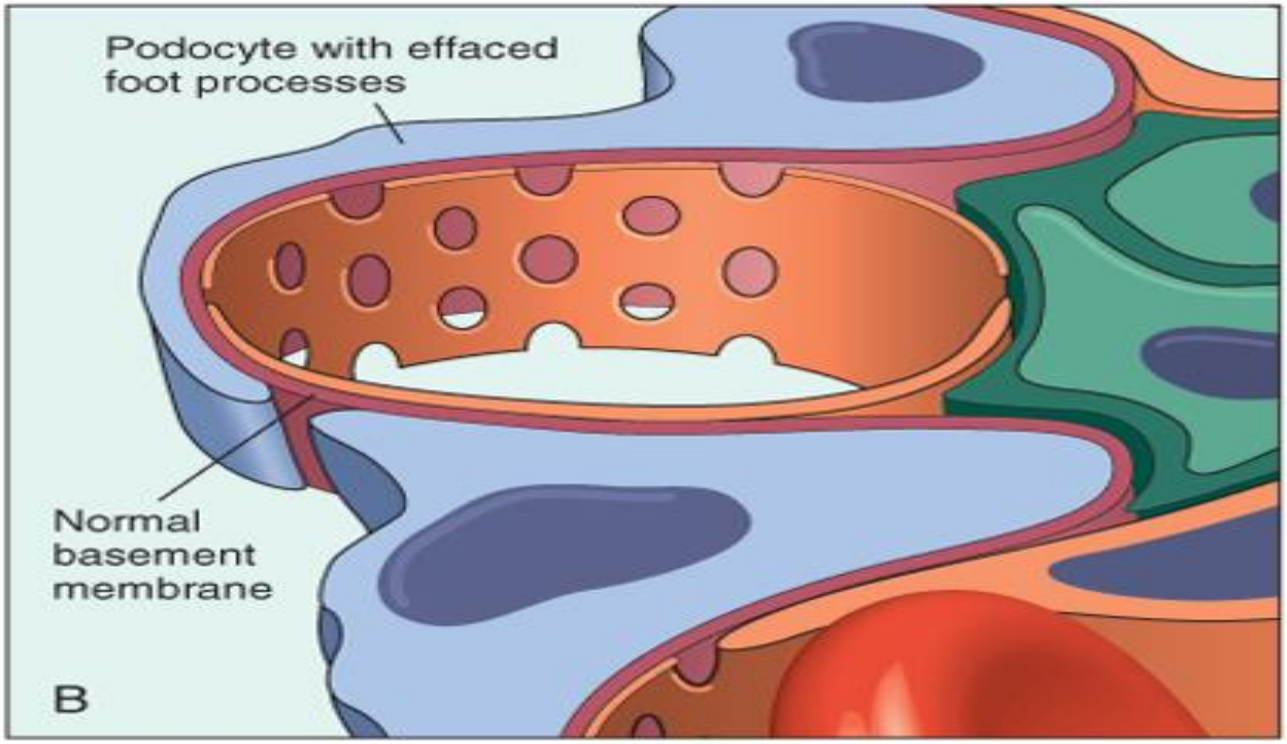
- **IF**
- negative
- **EM**
- **uniform and diffuse effacement of the foot processes of the podocytes** .
- No immune deposits

# Minimal change disease.




**A**

glomerulus appears normal, with a delicate basement membrane



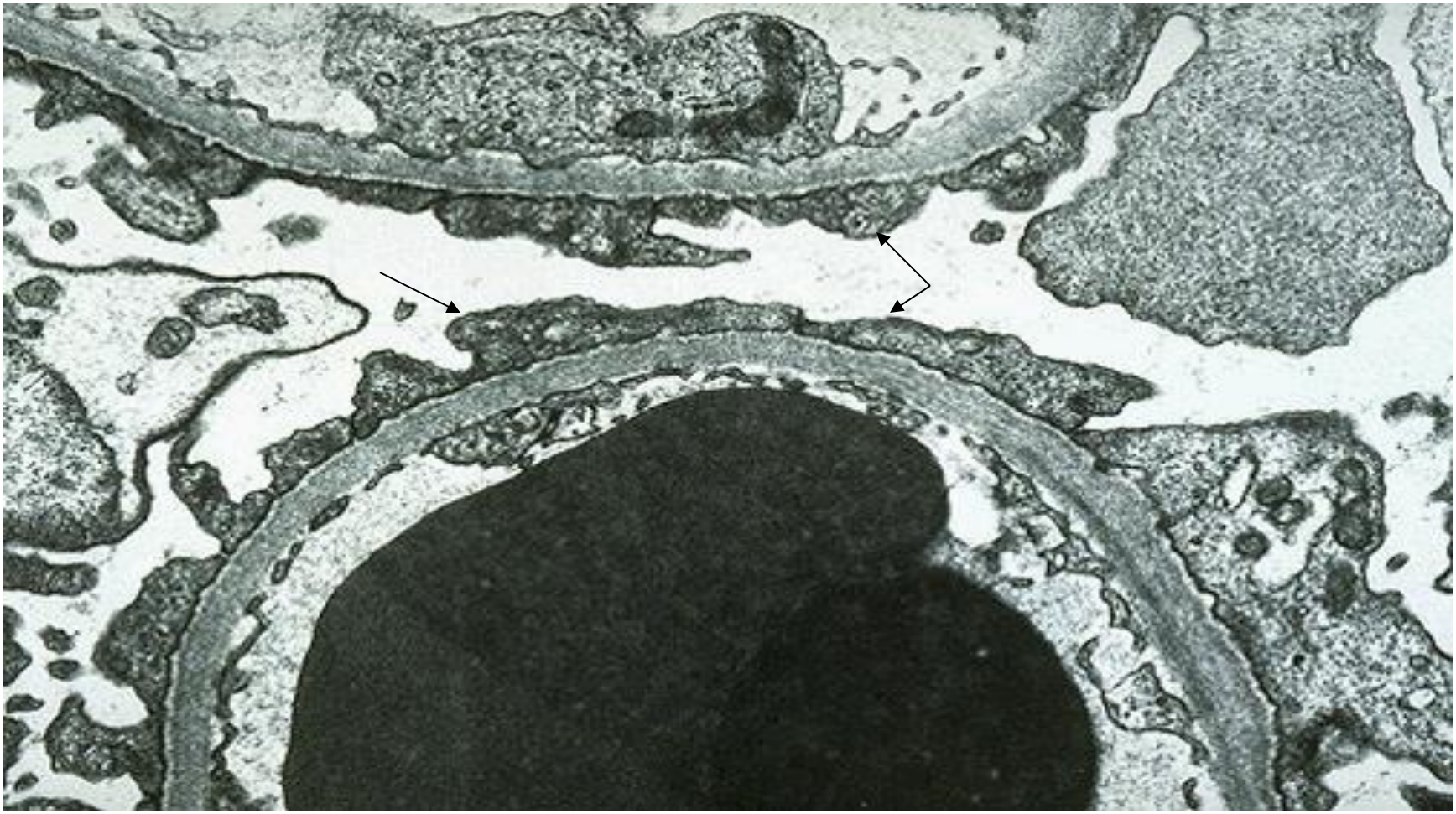

**B**

diffuse effacement of foot processes of podocytes with no immune deposits.

**MCD-EM**

**the capillary loop in the lower half contains two electron dense RBC's. Fenestrated endothelium is present and the BM is normal.**

**The overlying epithelial cell foot processes are fused (arrows).**



# MCD- Clinical Course

- **nephrotic syndrome in an otherwise healthy child.**
- **no hypertension.**
- **renal function preserved**
- **selective proteinuria (confined to albumin)**
- **prognosis is good.**
- **Treatment: corticosteroids (90% of cases respond)**
- **< 5% develop chronic renal failure after 25 years**
- **In Adults with minimal change disease the response is slower and relapses are more common.**

# Focal and Segmental Glomerulosclerosis (FSGS)

- **sclerosis affecting some but not all glomeruli (focal involvement) and involving only segments of glomerulus.**
- **Usually nephrotic syndrome.**
- **It can occur :**
- **as a primary disease( 20% to 30% of NS)**
- **Or: in association with AIDS; heroin abuse; nephron loss; inherited or congenital forms resulting from mutations affecting nephrin; etc**

# MCD vs FSGS

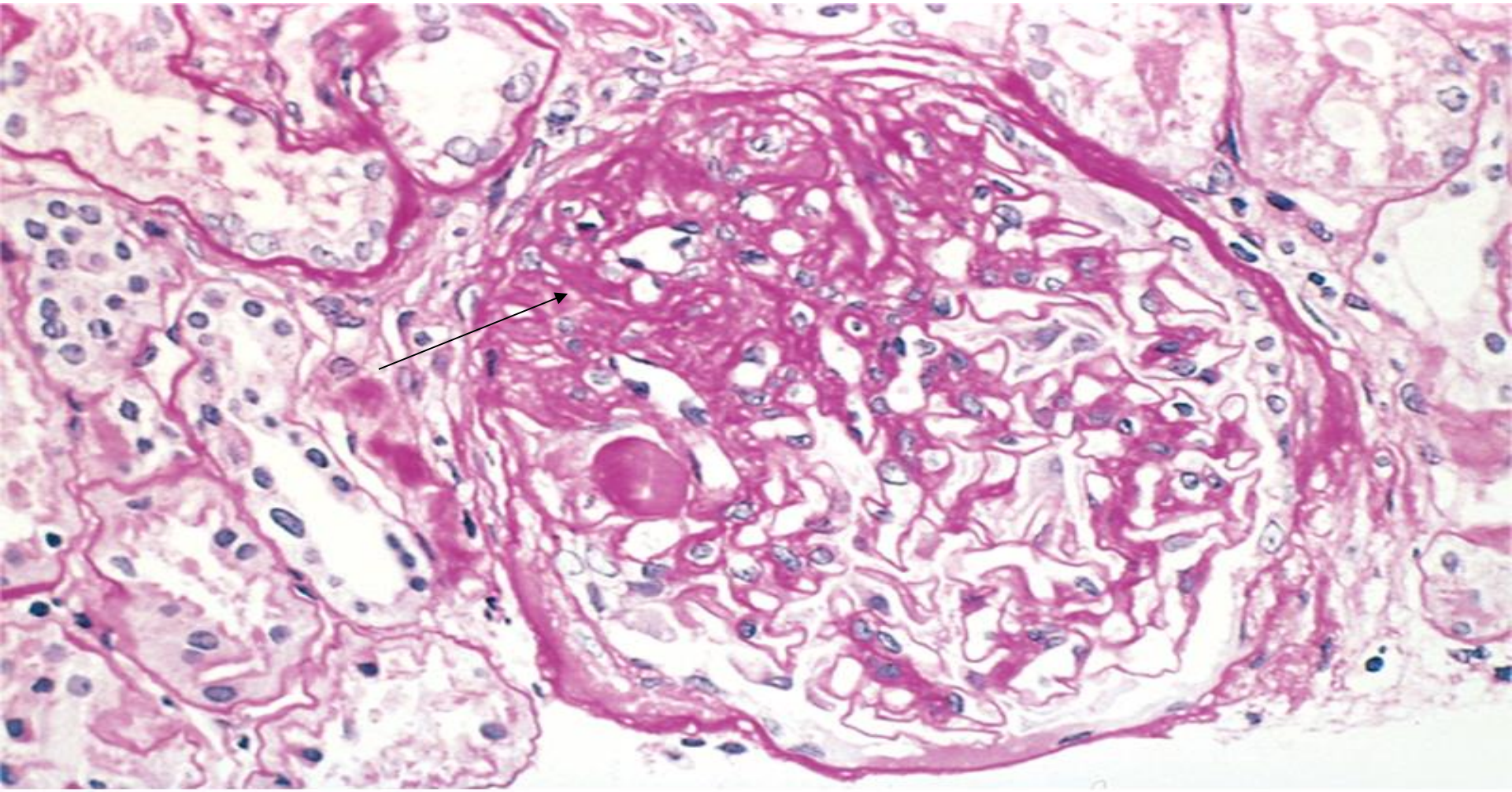
| | *MCD* | **FSGS** |
|---|---|---|
| **hematuria** | - | + |
| **hypertension** | - | + |
| **proteinuria** | selective | nonselective |
| **response to corticosteroid therapy** | good | poor |

- ***Pathogenesis***
- **unknown .**
- ***injury to the podocytes* ?**
- **entrapment of plasma proteins and lipids in foci of injury where sclerosis develops.**

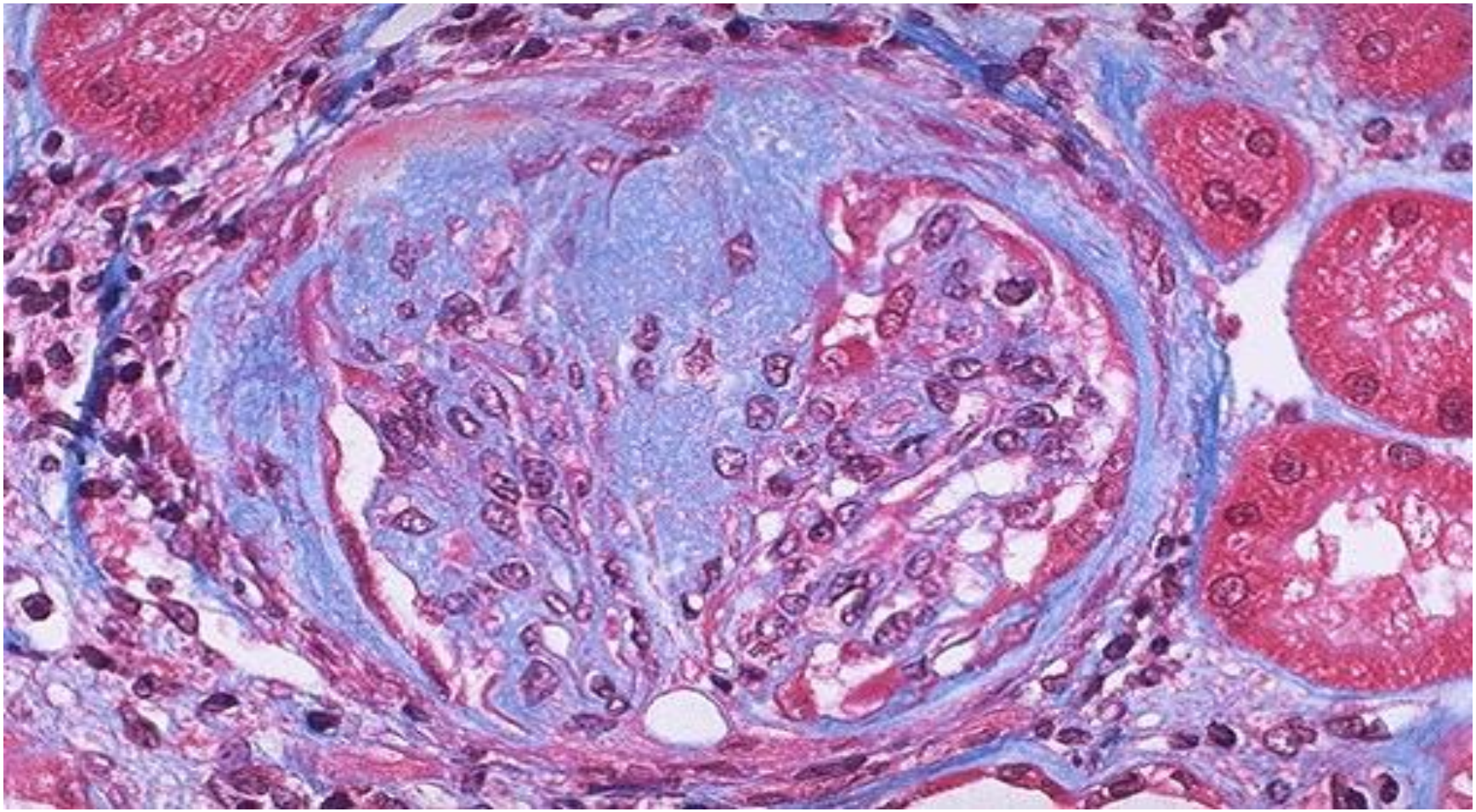
- **Clinical Course**
- **about 50% of individuals suffer renal failure after 10 years**
- **Poor responses to corticosteroid therapy.**
- **Adults do worse than children**

- **Morphology**
- **LM:**
- Sclerosis in some tufts within a glomerulus and sparing of the others ( "**segmental**").
- **increased mesangial matrix**
- **IF microscopy**
- Negative
- **EM**
- **effacement of foot processes**

focal and segmental glomerulosclerosis (PAS stain).
a mass of scarred, obliterated capillary lumens with accumulations of matrix material



**FSGS**
**blue collagen deposition (MT stain).**



# Collapsing glomerulopathy

- a morphologic type of FSGS.
- poor prognosis.
- collapse of glomerular tuft and podocyte hyperplasia.
- It may be :
- 1-idiopathic .
- 2-associated with **HIV infection**.
- 3-drug-induced toxicities.

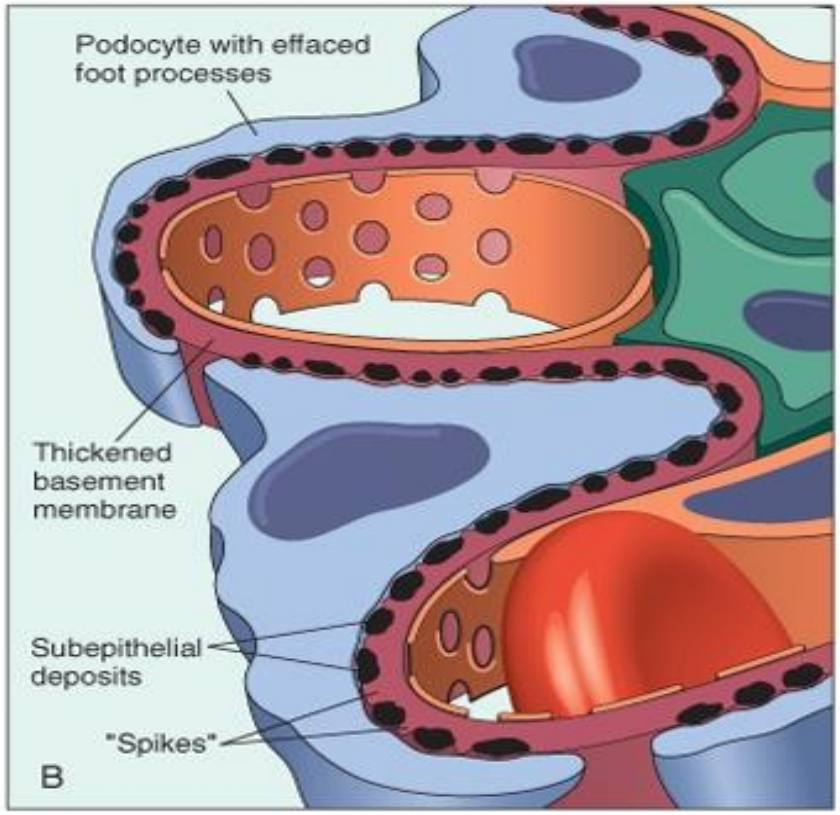
# ***Membranous nephropathy:***

- **Imune complex disease**
- **Types of Membranous glomerulonephritis :**
- **1-Idiopathic (85% of cases): against** podocyte antigen phospholipase A2 receptor (PLA2R) antigen in most cases
- **2-Secondary**

# Secondary Membranous glomerulonephritis :

- **(1) infections (HBV, syphilis, schistosomiasis, malaria).**
- **(2) malignant tumors (lung, colon and melanoma).**
- **(3) autoimmune diseases as SLE .**
- **(4) inorganic salts exposure (gold, mercury).**
- **(5) drugs (penicillamine, captopril,NSAID).**

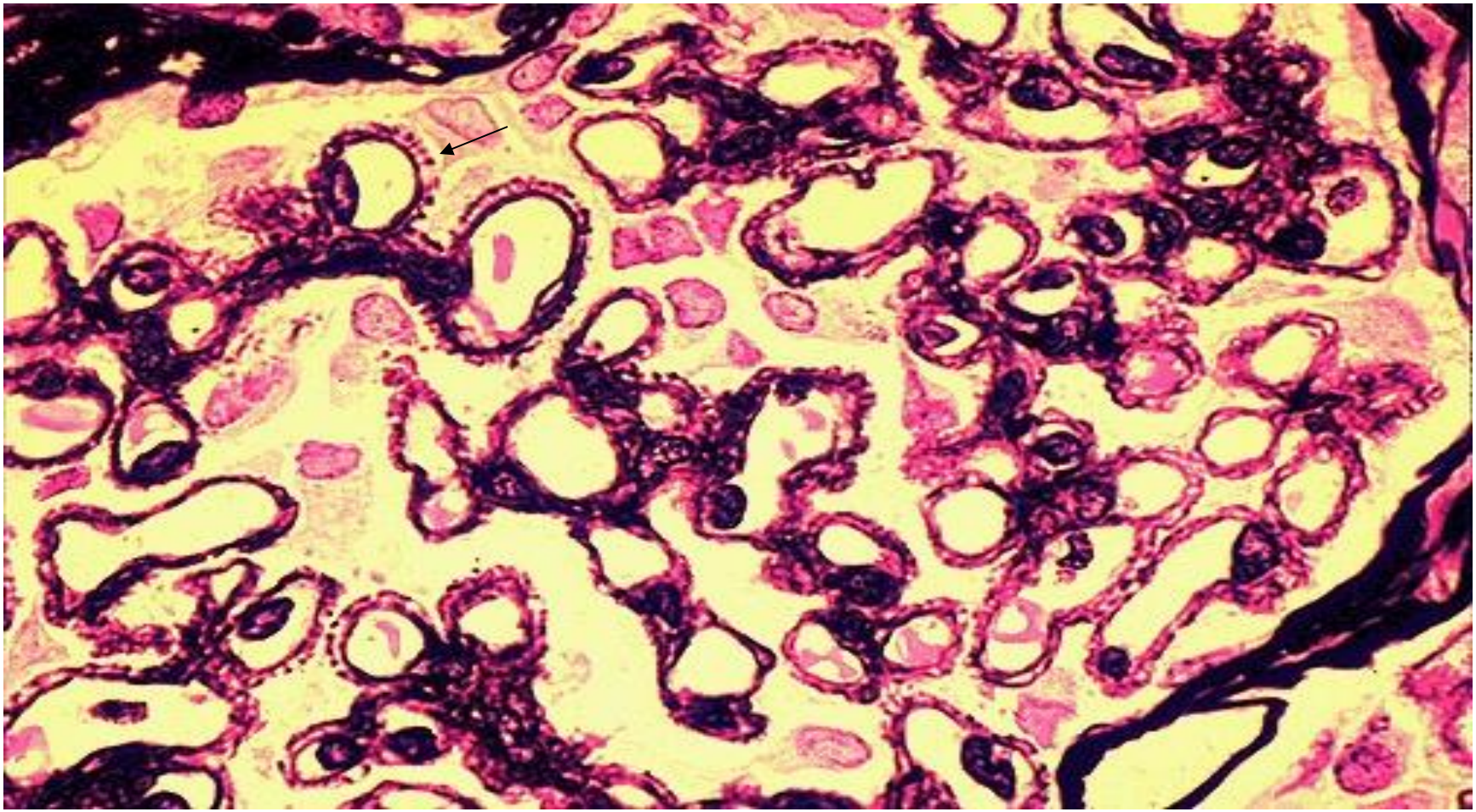
- **Morphology**
- **LM**
- **diffuse thickening of the GBM .**
- **IF**
- **deposits** of immunoglobulins and complement along the GBM (IgG)
- **EM**
- **subepithelial deposits "spike and dome" pattern**.



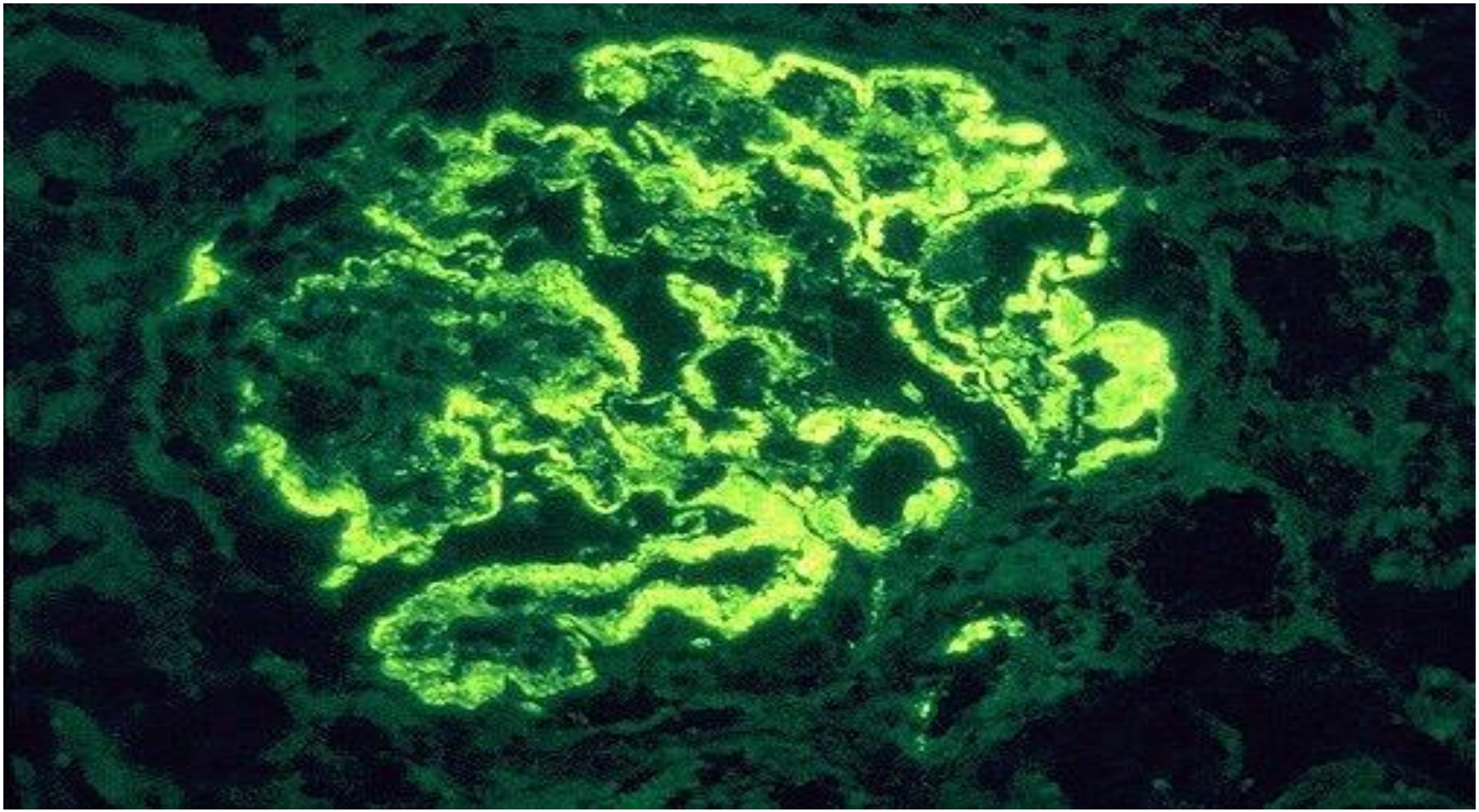



**Membranous nephropathy.**
**subepithelial deposits and the presence of "spikes" of basement membrane material between the immune deposits .**

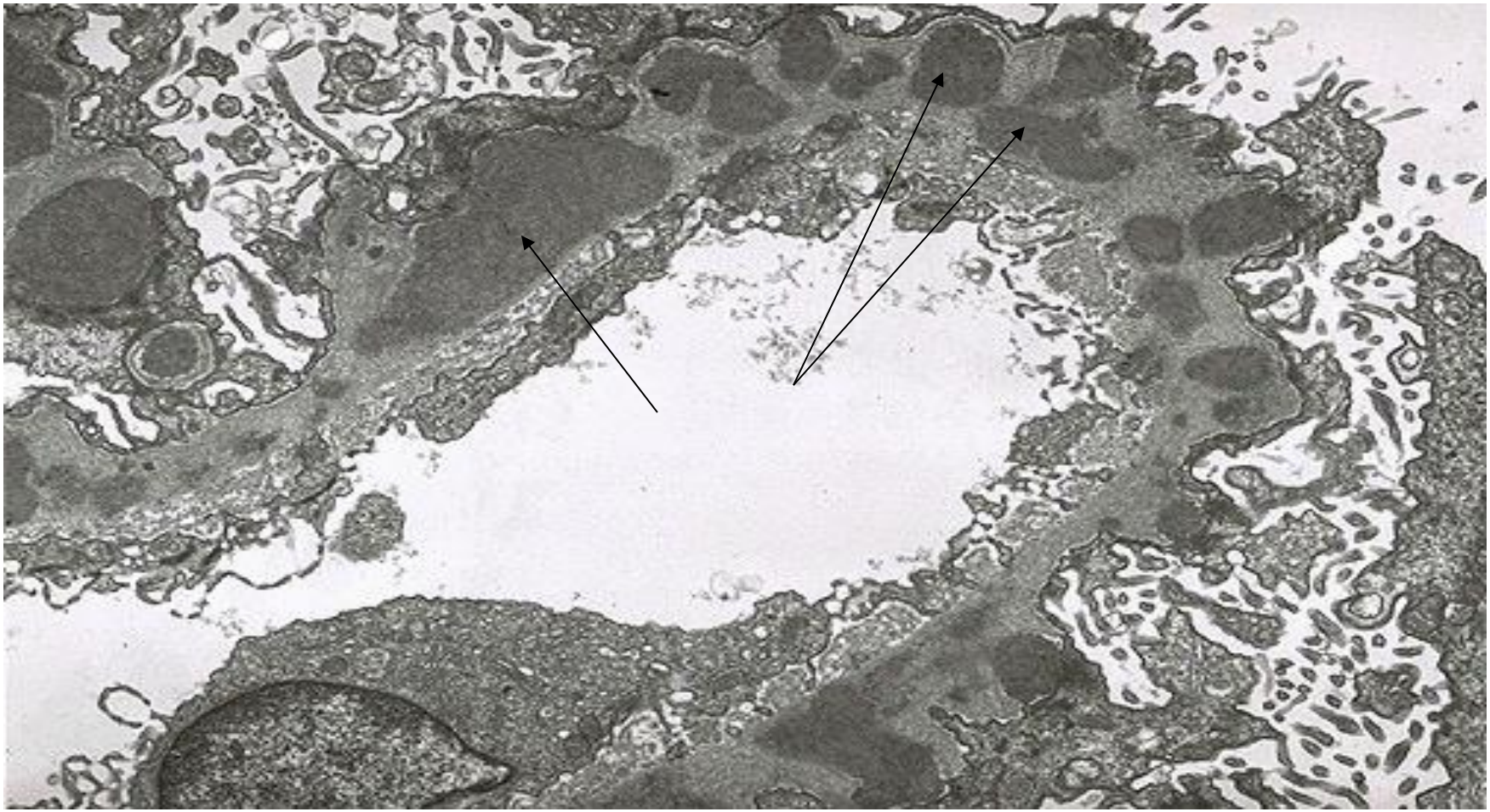
**A silver stain (black). Characteristic "spikes" seen with membranous glomerulonephritis as projections around the capillary loops.**



**Membranous GN**
**IF: deposits of mainly IgG and complements**



**EM-the darker electron dense immune deposits are seen scattered within the thickened basement membrane .**



- **Clinical Course**
- **nephrotic syndrome**
- **proteinuria nonselective.**
- **no response to corticosteroid therapy.**
- **60% of cases→ proteinuria persists**
- **~ 40%→ progressive disease and renal failure 2 to 20 yr.**
- **30% →partial / complete remission of proteinuria.**