Renal Pathology- Lecture 1

Contents:

1- Concepts of renal pathology

2- Introduction to glomerulus pathology

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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 (macroscopic) hematuria
- mild to moderate proteinuria (< 3.5 gm of protein/day in adults)
- azotemia
- edema
- hypertension

Nephritic Syndrome: Presentation

- **PHAROH**
- ***P**roteinuria*
  - *<3.5g/1.73m2/day*
- ***H**ematuria*
  - *Abrupt onset*
- ***A**zotemia*
  - *Increased creatinine and urea*
- ***R**BC Casts*
- ***O**liguria*
- ***H**TN*

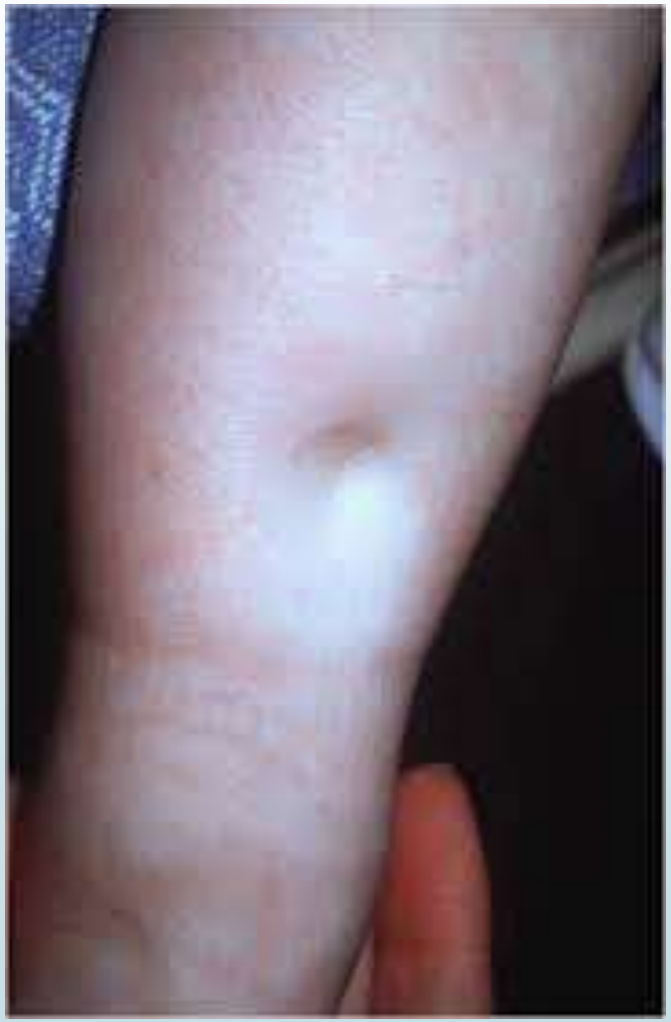
Peripheral Edema/Puffy Eyes

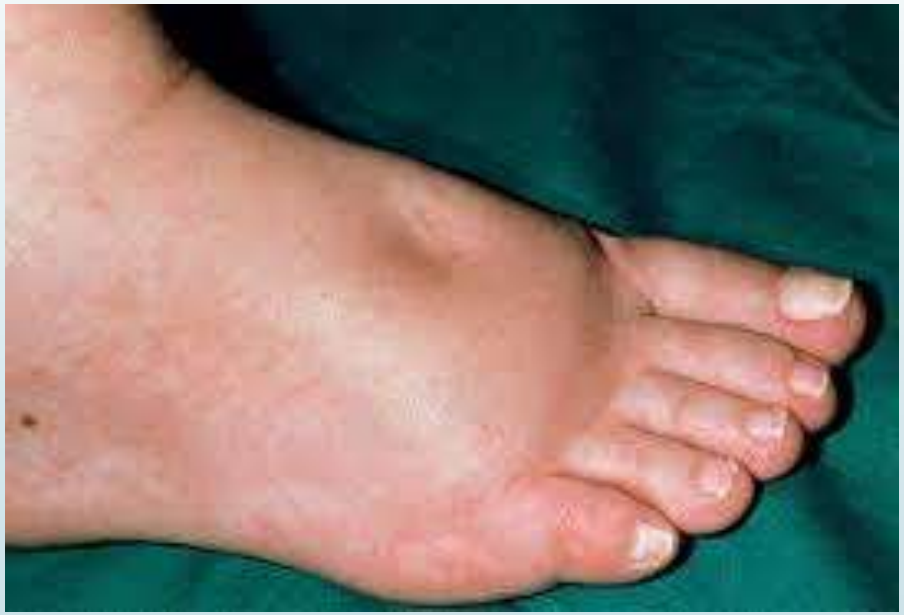
"Smoky Urine"

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).

Nephrotic syndrome





- ***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

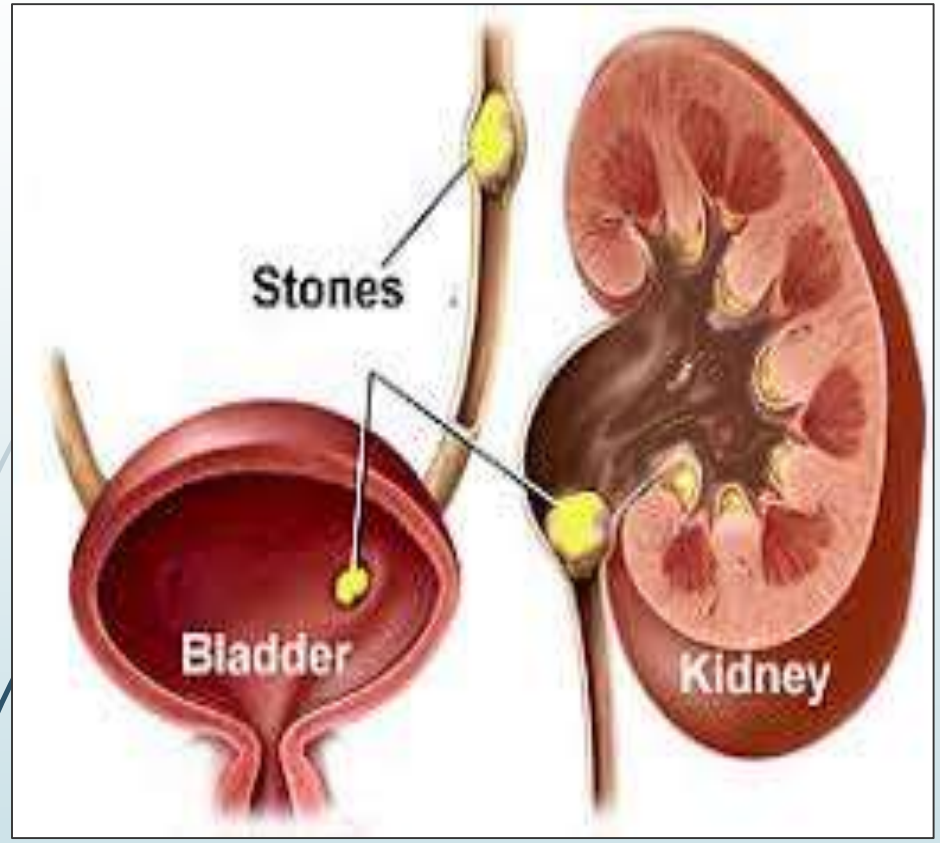
6- Chronic renal failure

- 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 (pain)

2-hematuria

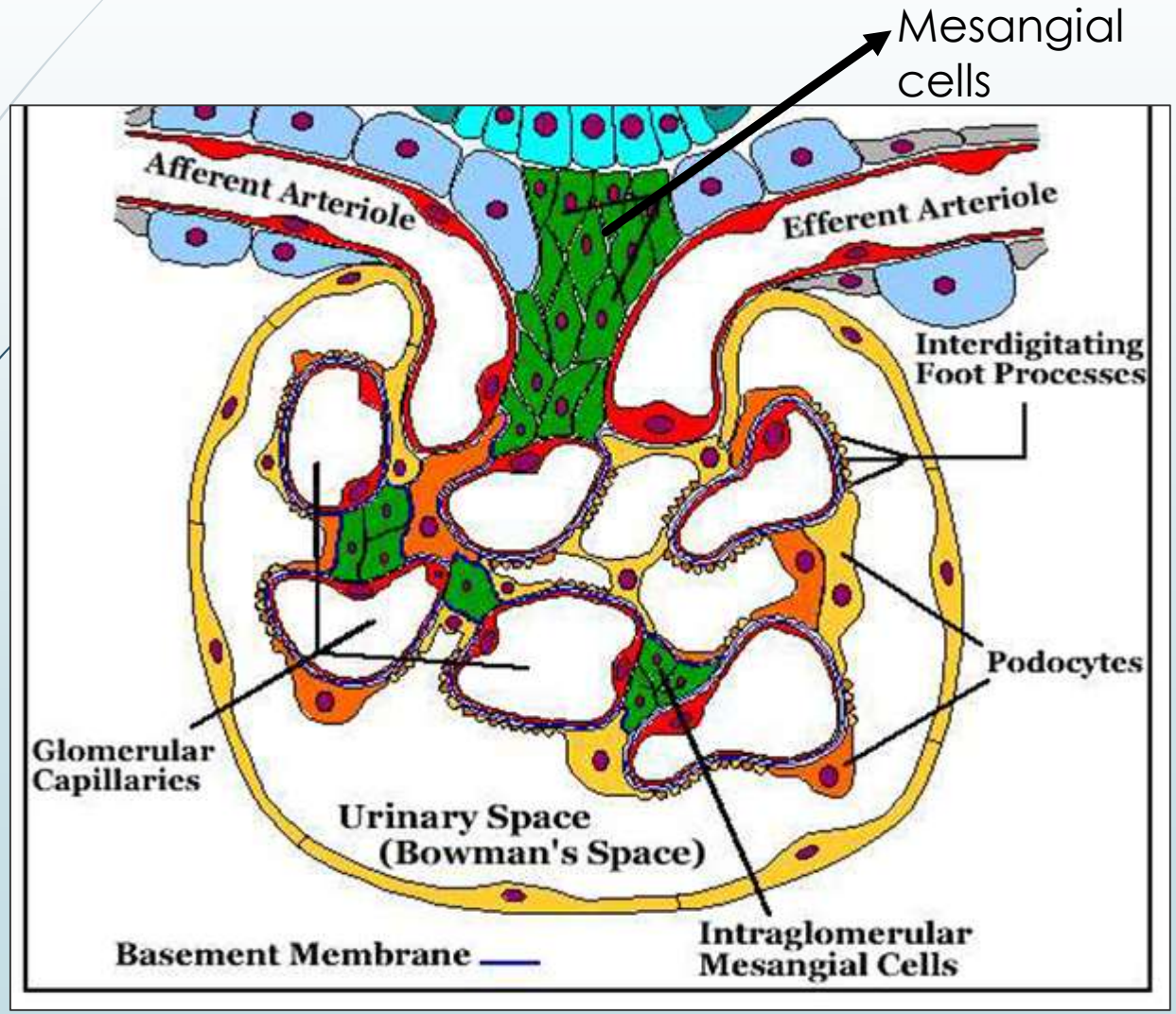
3-possible recurrent stone formation

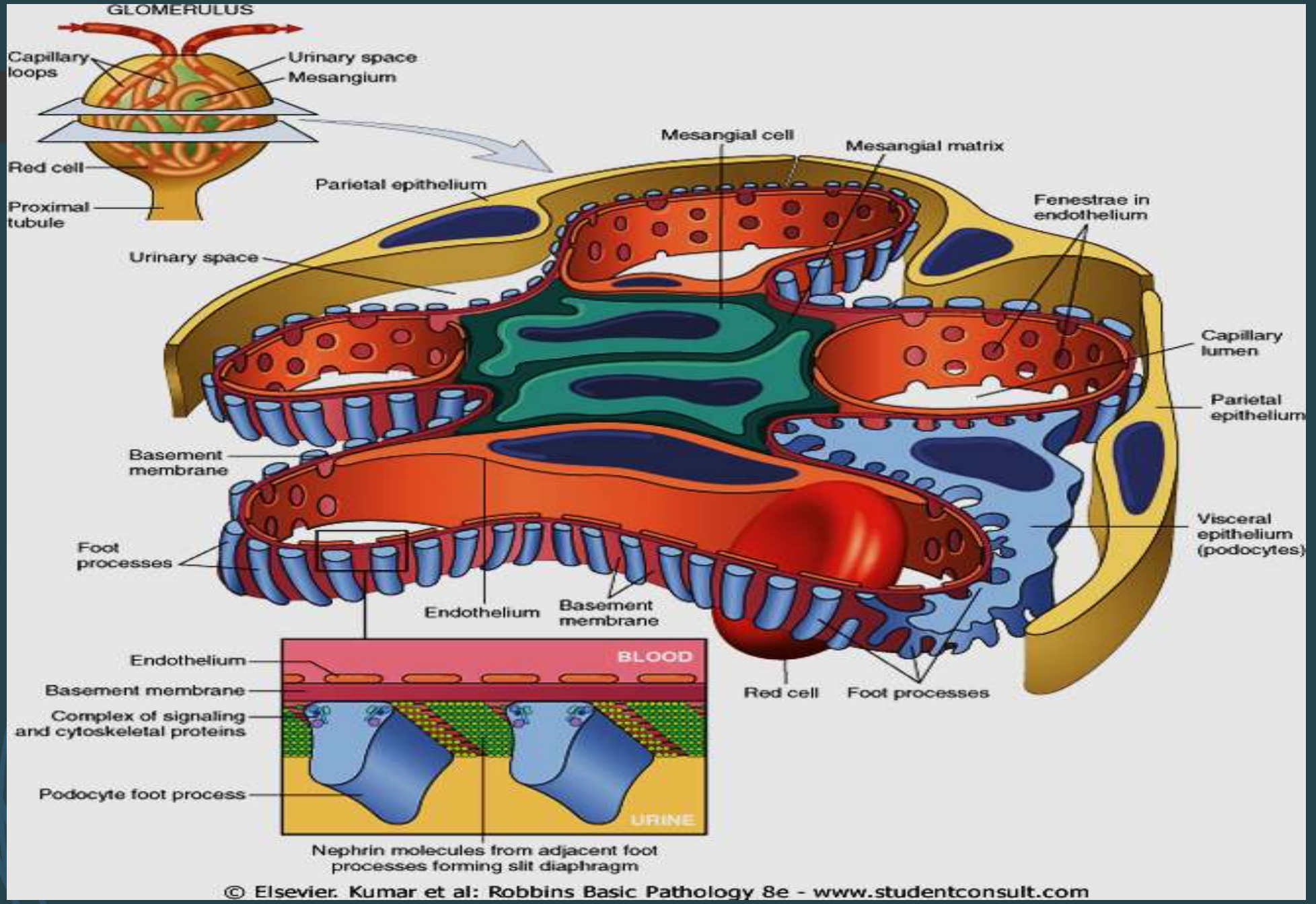
Glomerular diseases

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 ultra-filtrate first collects.

Normal glomerulus




GLOMERULUS
Capillary loops
Urinary space
Mesangium
Red cell
Proximal tubule
Mesangial cell
Mesangial matrix
Parietal epithelium
Fenestrae in endothelium
Urinary space
Capillary lumen
Parietal epithelium
Basement membrane
Visceral epithelium (podocytes)
Foot processes
Endothelium
Basement membrane
Red cell
Foot processes
Endothelium
BLOOD
Basement membrane
Complex of signaling and cytoskeletal proteins
Podocyte foot process
URINE
Nephrin molecules from adjacent foot processes forming slit diaphragm
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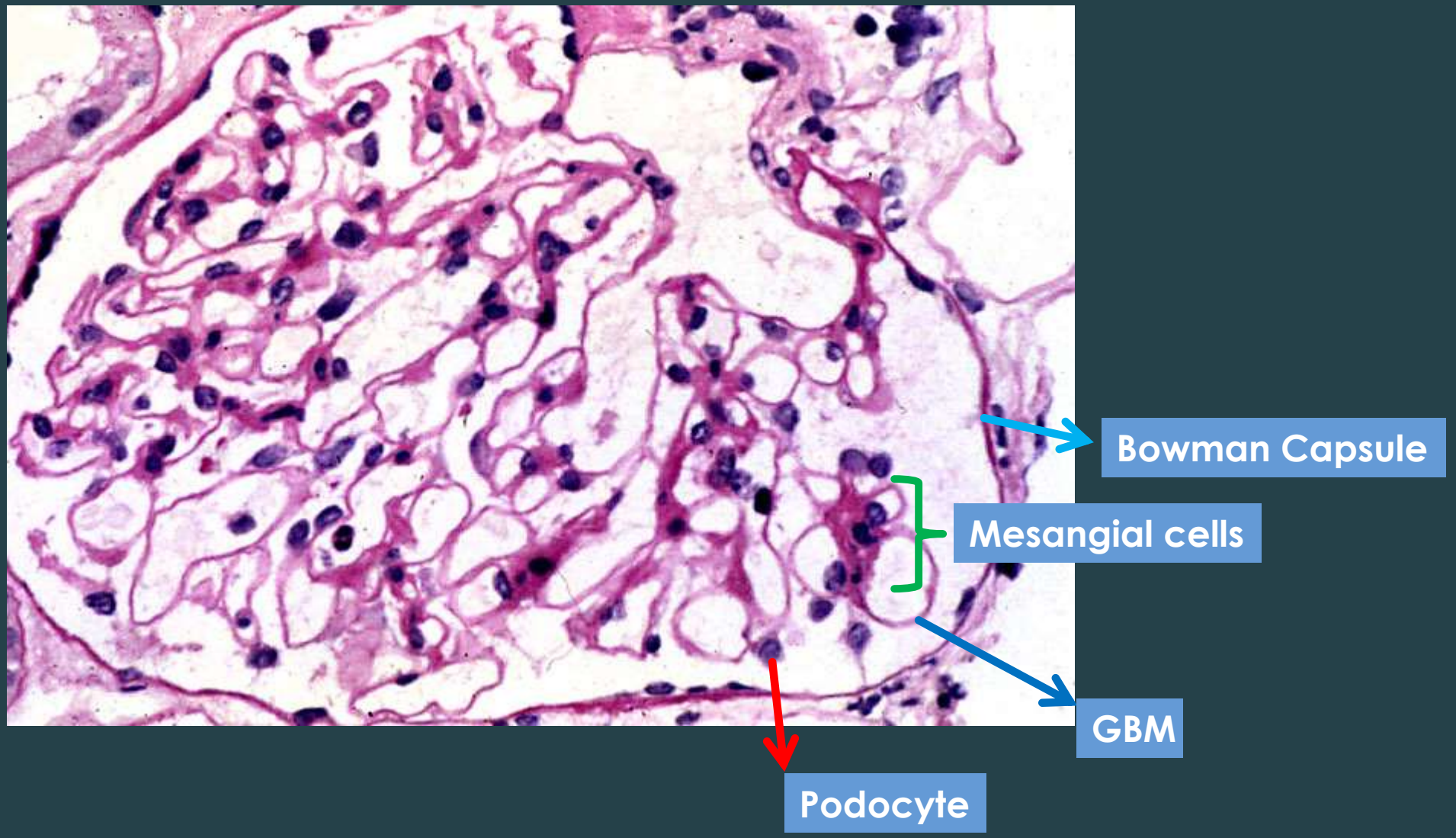
Pathological tests used in the evaluation for renal medical diseases:

1- Light microscopy (LM)

2- Immunofluorescence microscopy (IF)

3- Electron microscopy (EM) (usually Transmission electron microscope)

Normal glomerulus- light microscopy



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

1-A thin layer of fenestrated *endothelial cells*

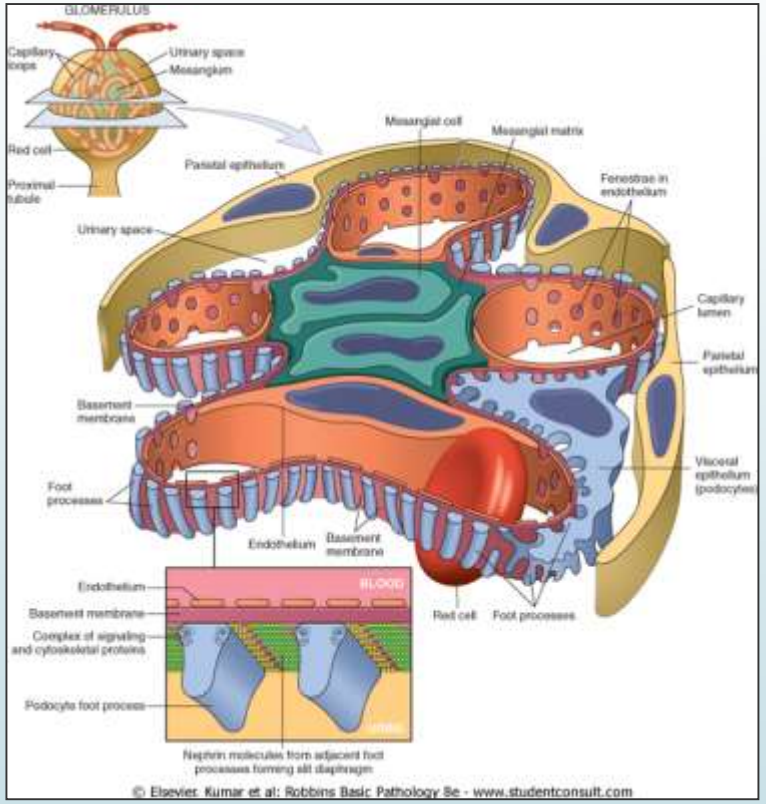
2- *glomerular basement membrane* (GBM)

3- foot processes of podocytes

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

Glomerular filtration membrane/ unit

- 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 mainly of Nephrin.



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

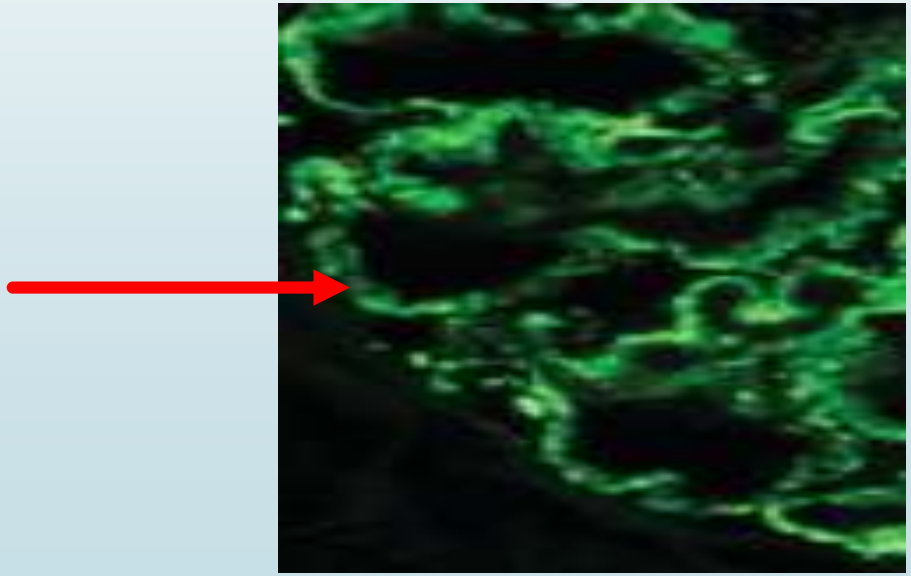
2- the more cationic the more permeable.

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

Immunofluorescence microscopy

- Fluorescein-labeled antibodies used for the antigens that should be routinely examined include immunoglobulins (primarily IgG, IgM, and IgA), complement components (primarily C3, C1q, and C4), fibrin, and kappa and lambda light chains.

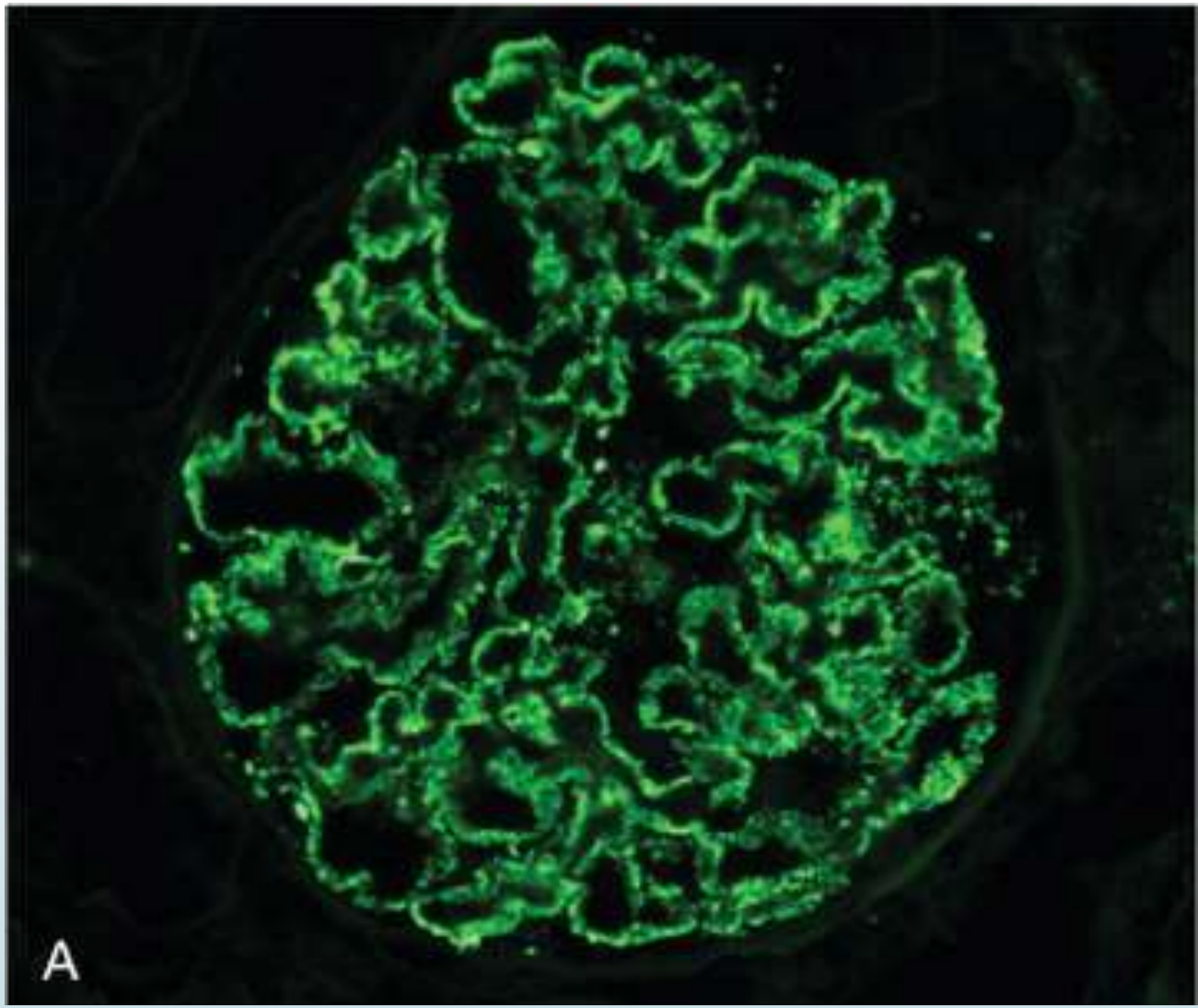
- Important in detecting immune complex-mediated glomerular disorders
- The pattern and location of immune complex deposition is helpful in distinguishing various types of GN



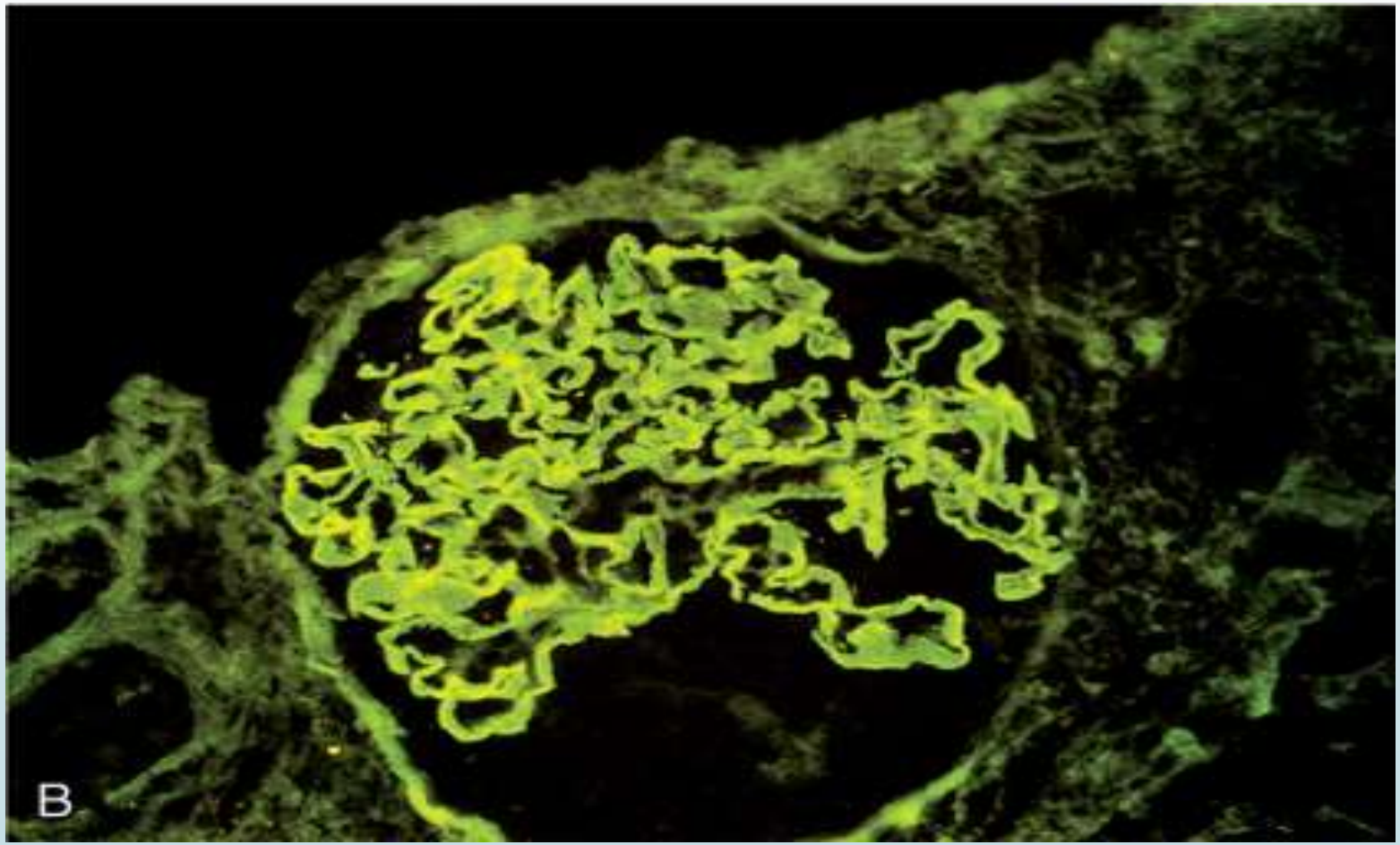
https://en.wikipedia.org/wiki/Immunofluorescence#/media/File:Immunofluorescence.jpg

Immunofluorescence microscopy

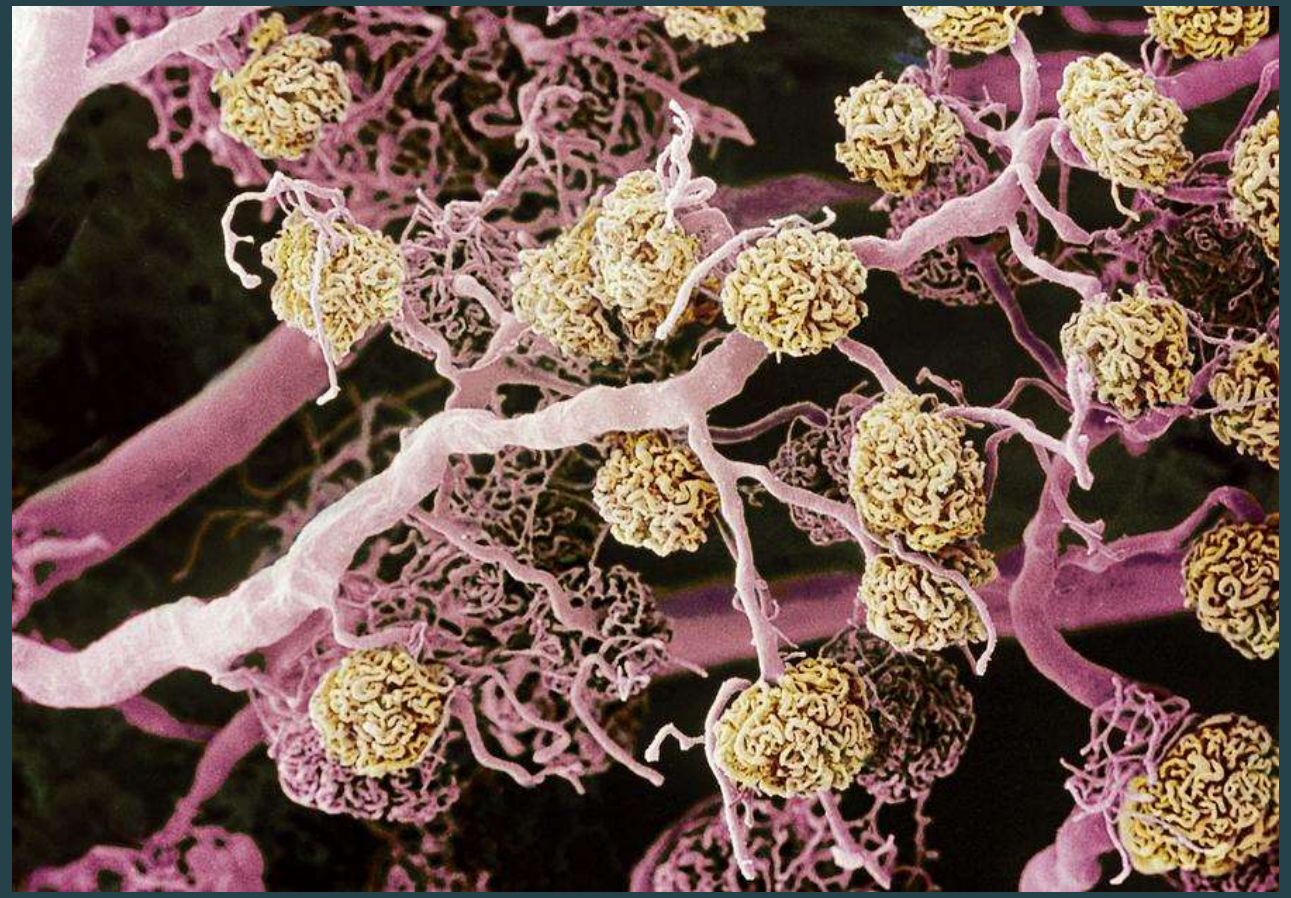
granular pattern of deposition



immunofluorescence linear deposition of immune complexes

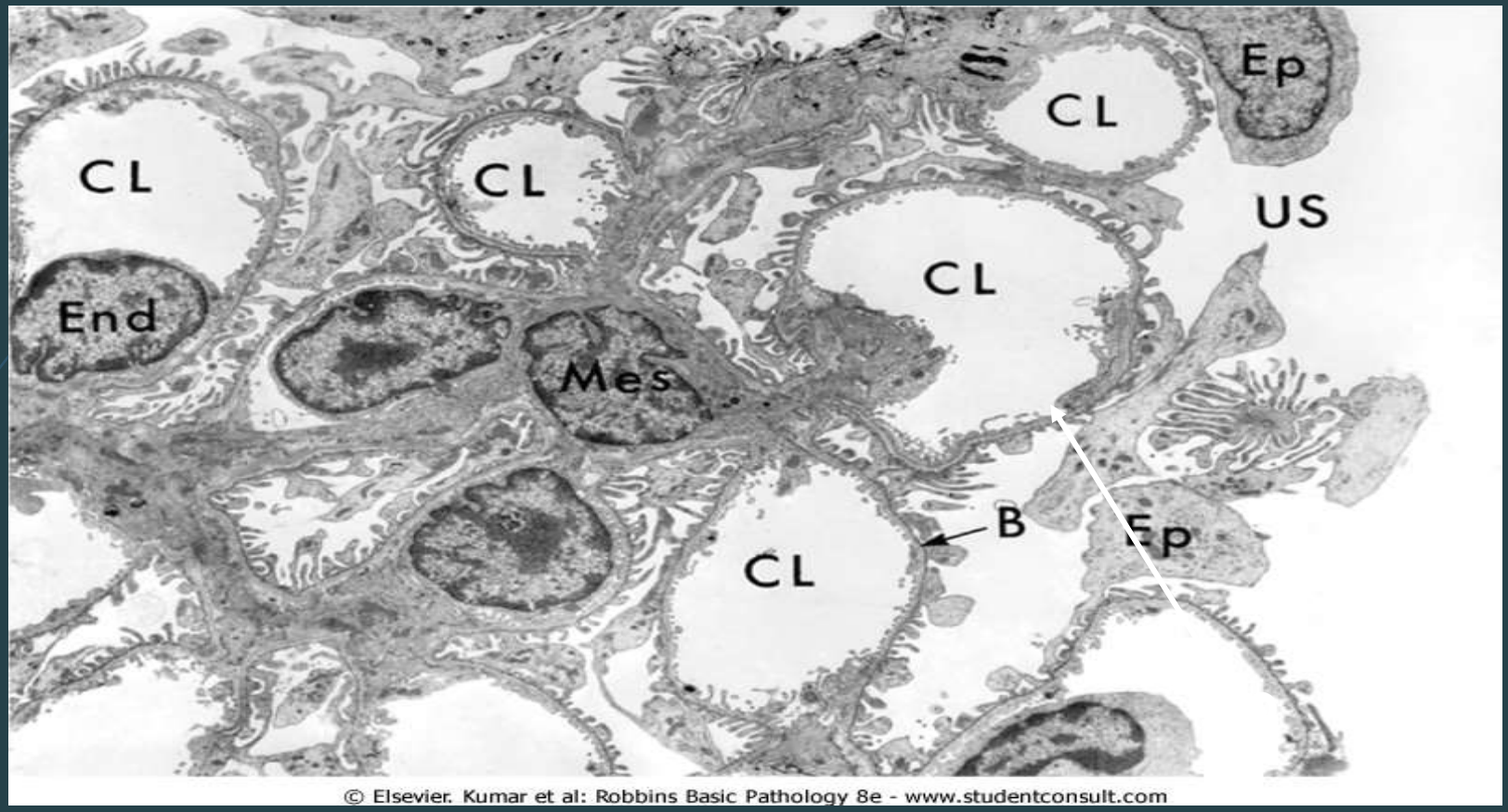


Electron Microscopy



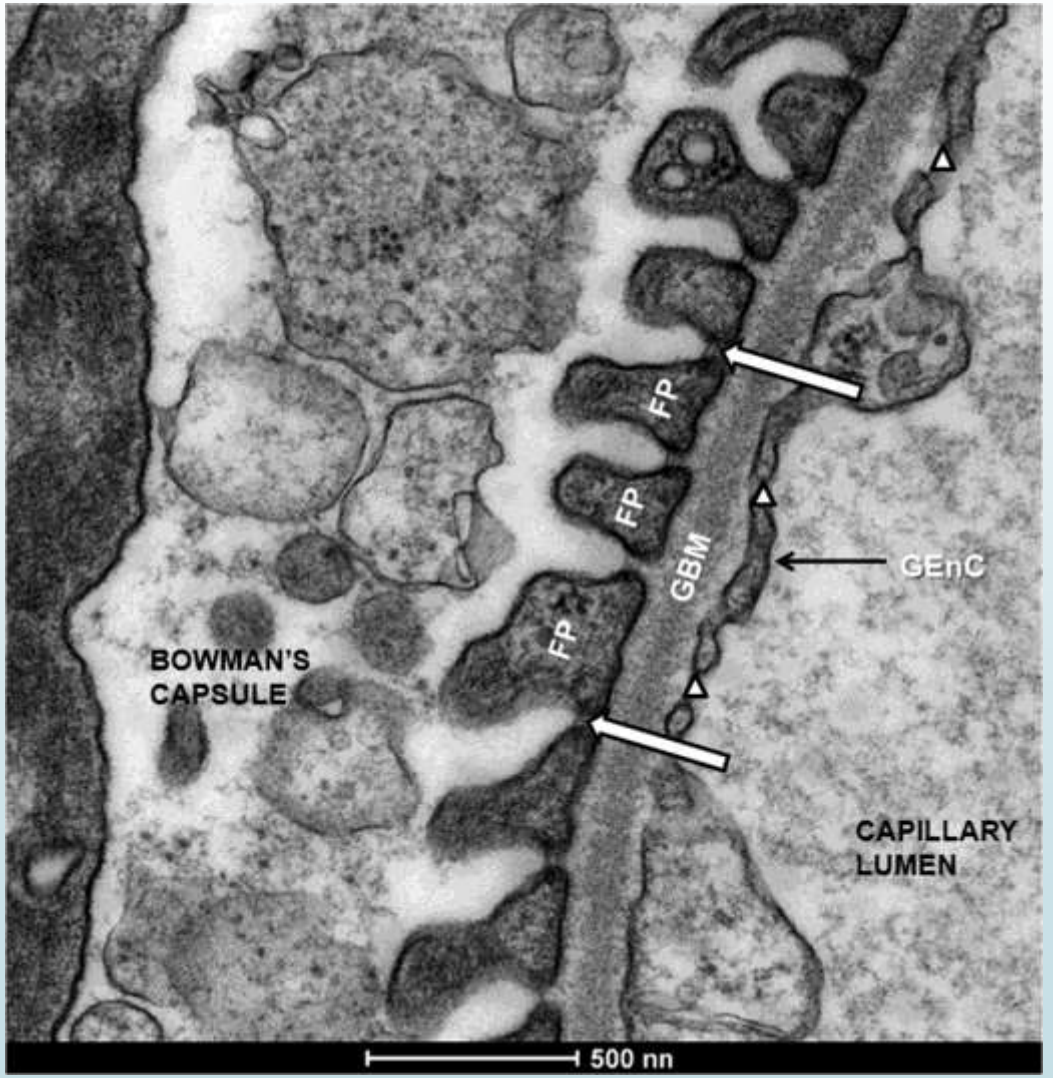
EM- normal GLOMERULUS

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



https://en.wikipedia.org/wiki/Transmission_electron_microscopy

Normal GBM by EM



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

1-in the **mesangium.**

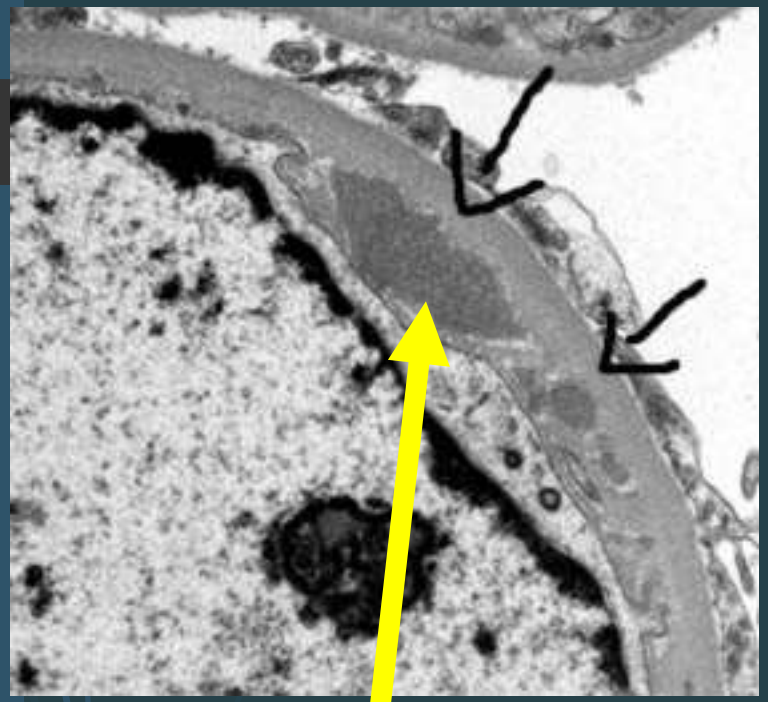
2-between the endothelial cells and the GBM

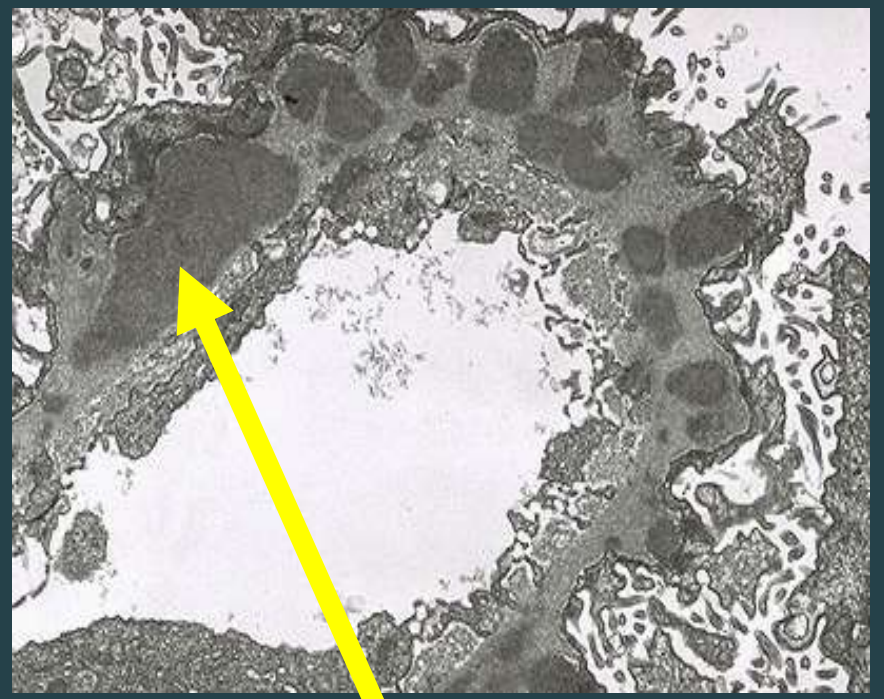
(**subendothelial deposits**).

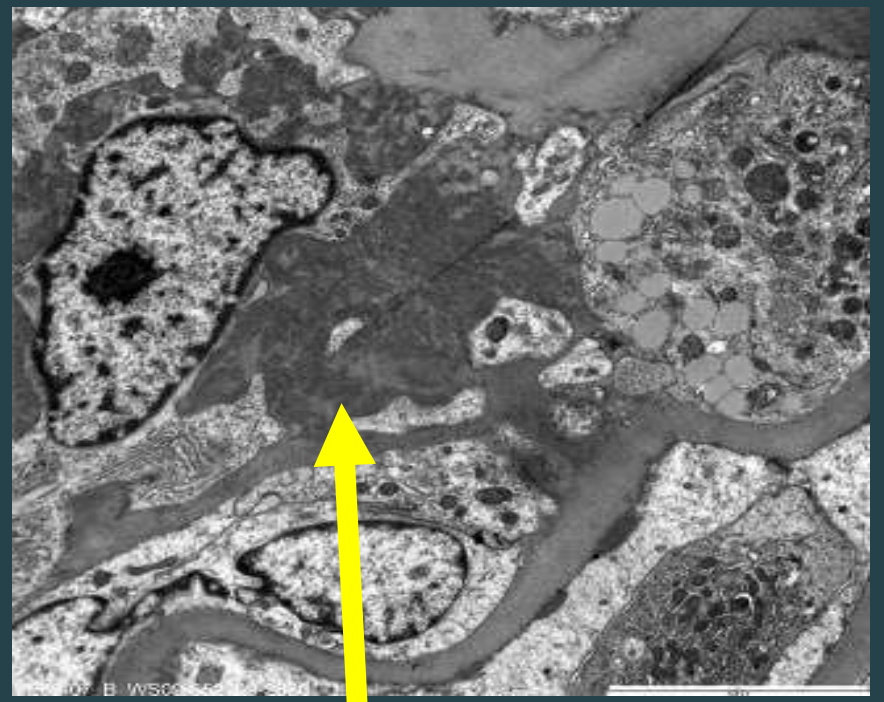
3-between the outer surface of the GBM and

the podocytes (**subepithelial deposits**).

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







Subendothelial

Subepithelial

Mesangial

Pathogenesis of Glomerular Diseases

1- Antibody-associated → detected by immunoflourescence microscopy

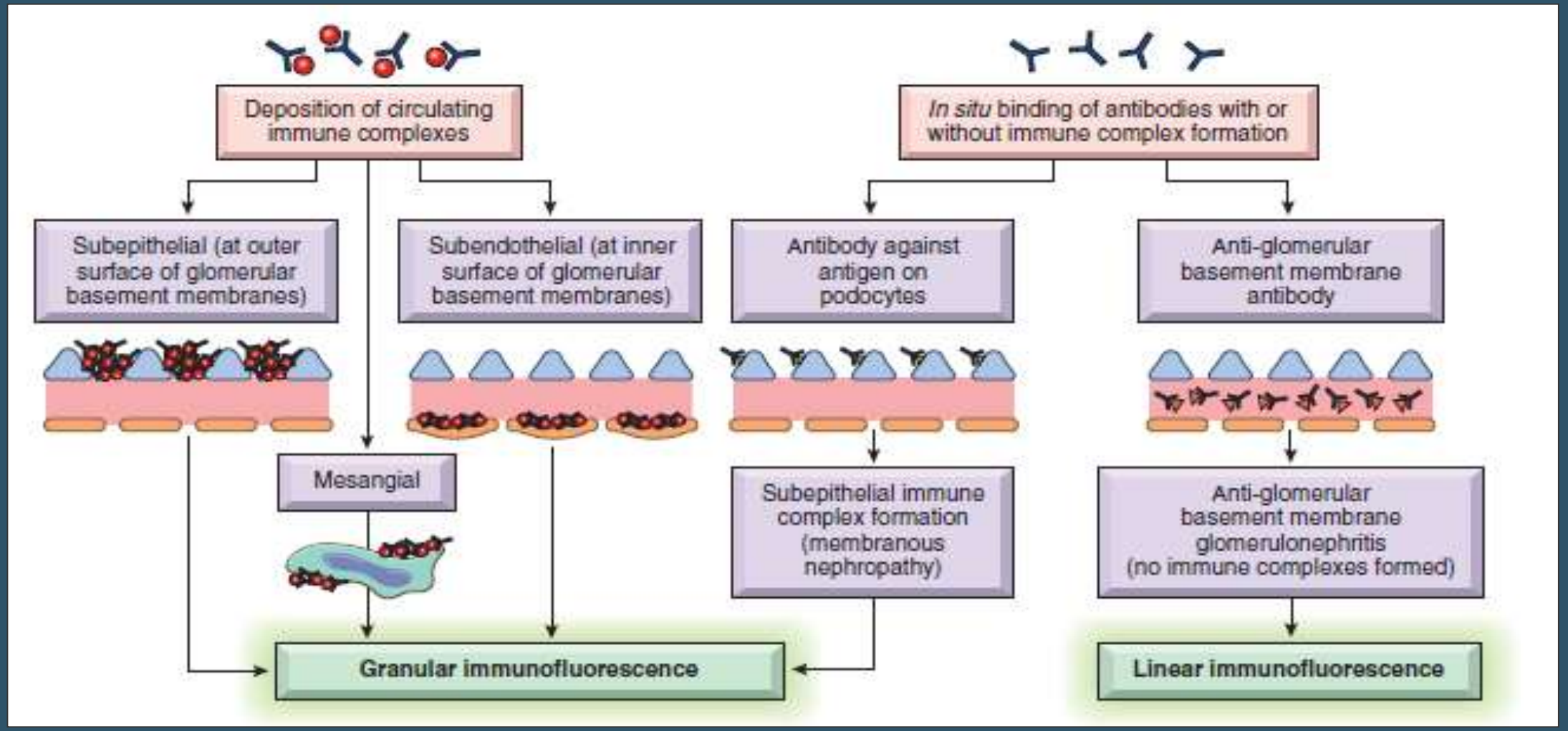
Sources of those Abs:

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

(2) Abs reacting in situ within the glomerulus.

(3) Abs directed against glomerular cell components.

Antibody- mediated glomerular injury



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)

Pathogenesis of Glomerular Diseases

2- Non-immune Mechanisms of Glomerular Injury

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.