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 :

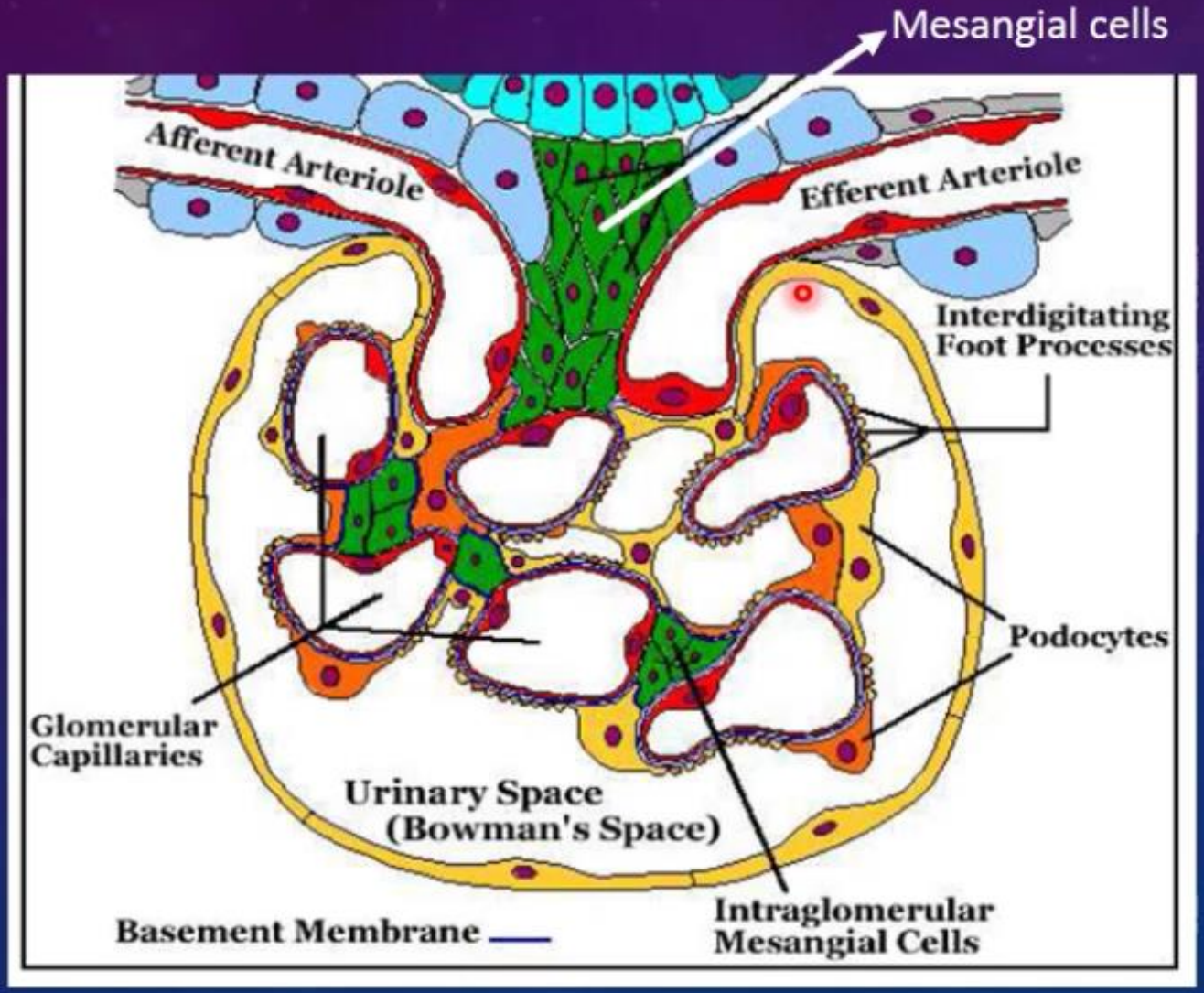
1-A thin layer of fenestrated *endothelial cells*

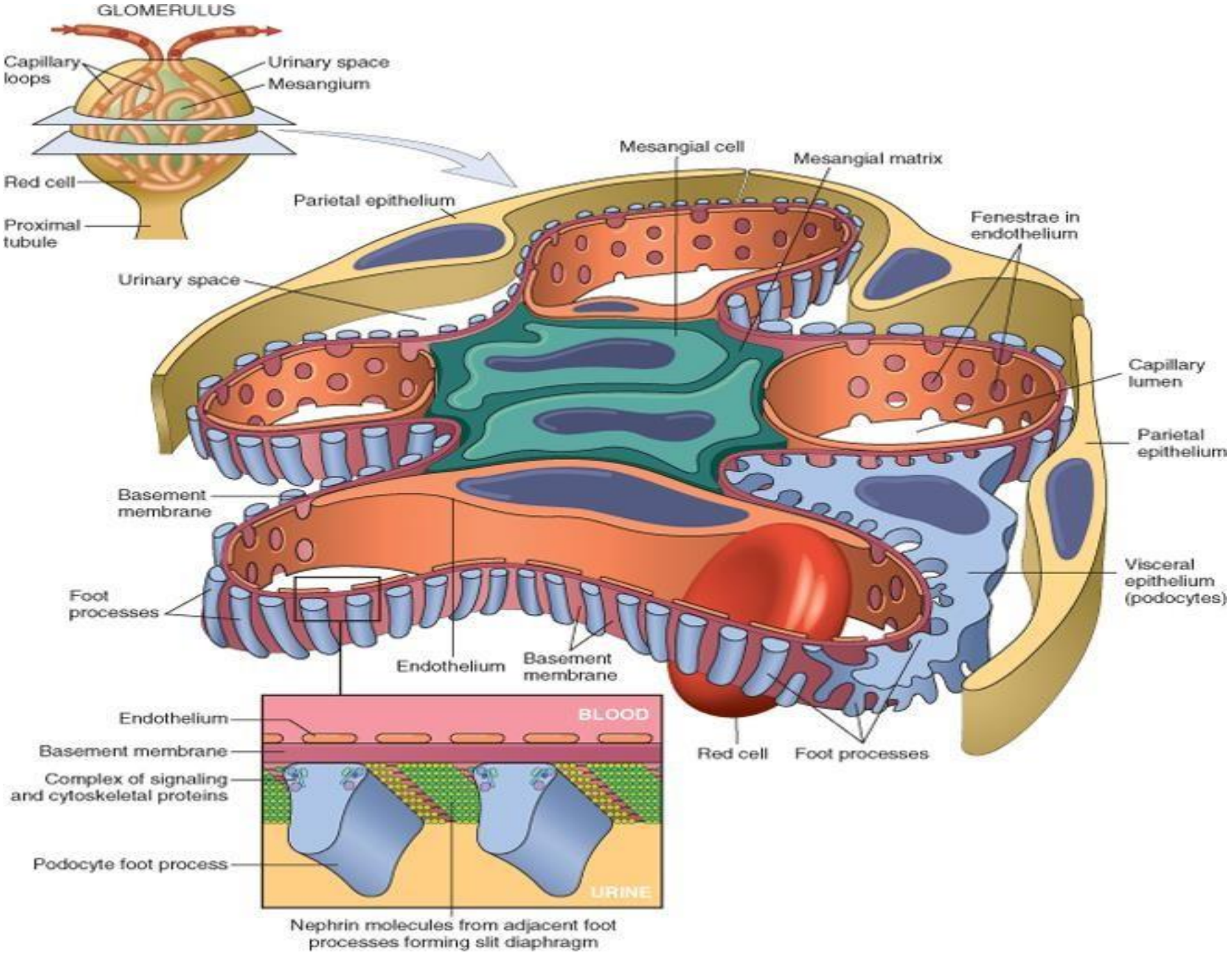
2- *glomerular basement membrane* (GBM)

3- foot processes of podocytes

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

NORMAL GLOMERULUS





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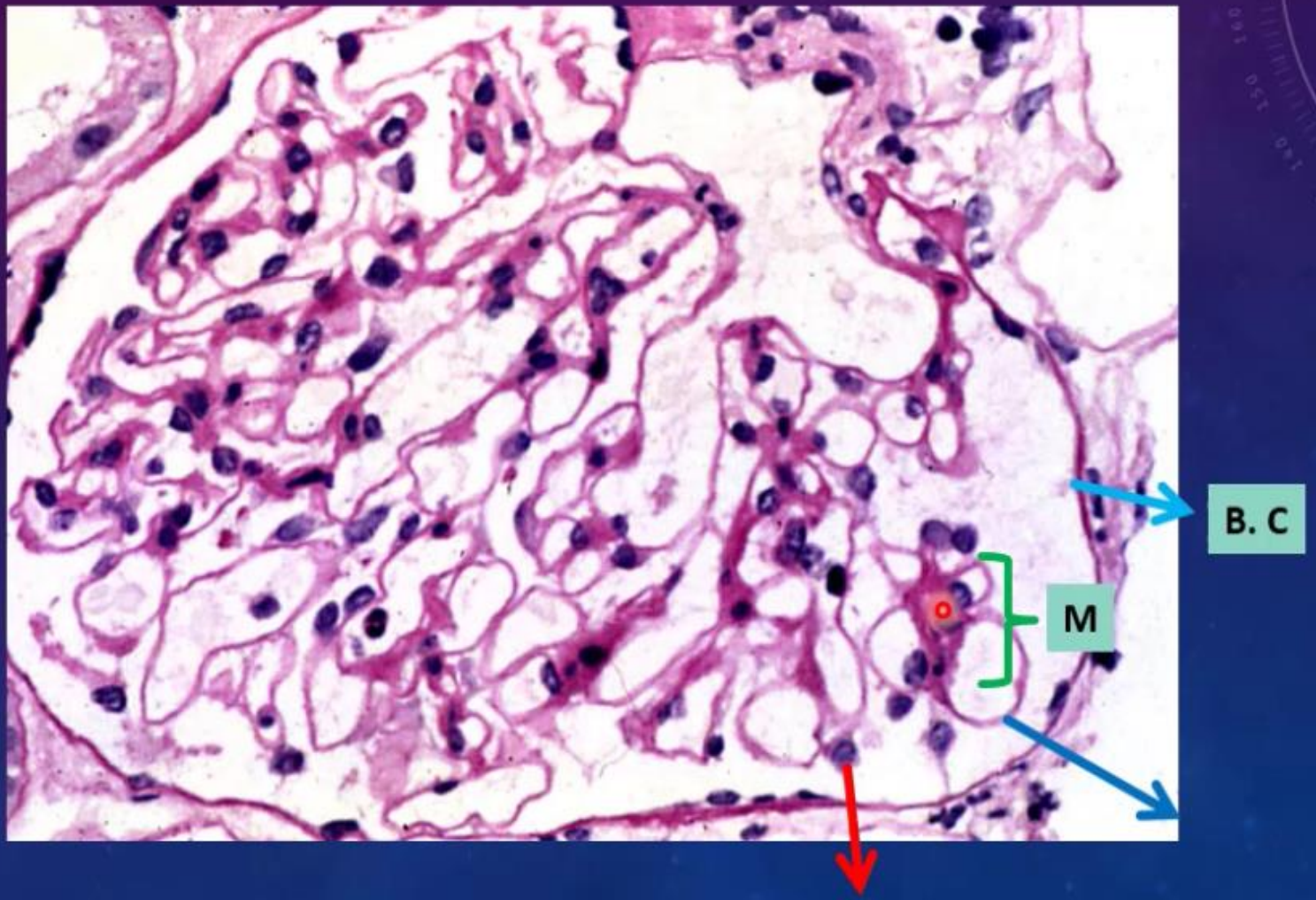
NORMAL GLOMERULUS

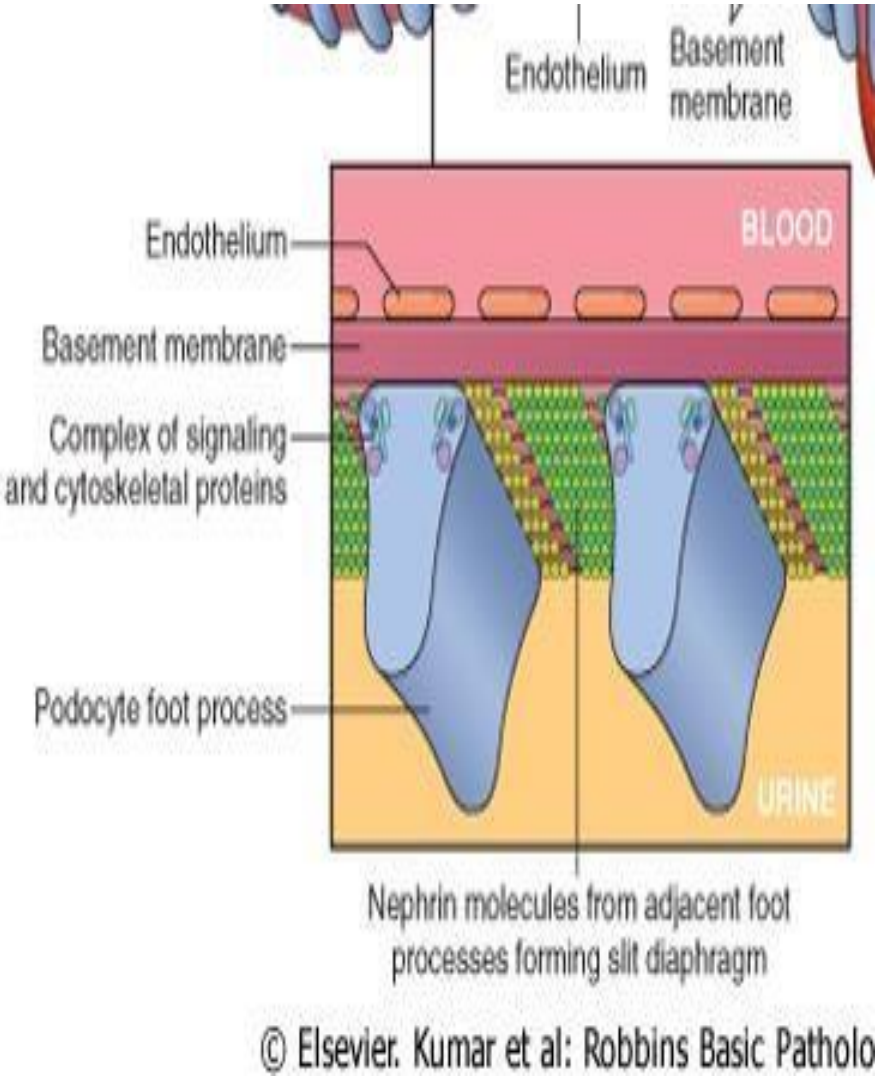


The capillary basement membrane

- **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.**



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:

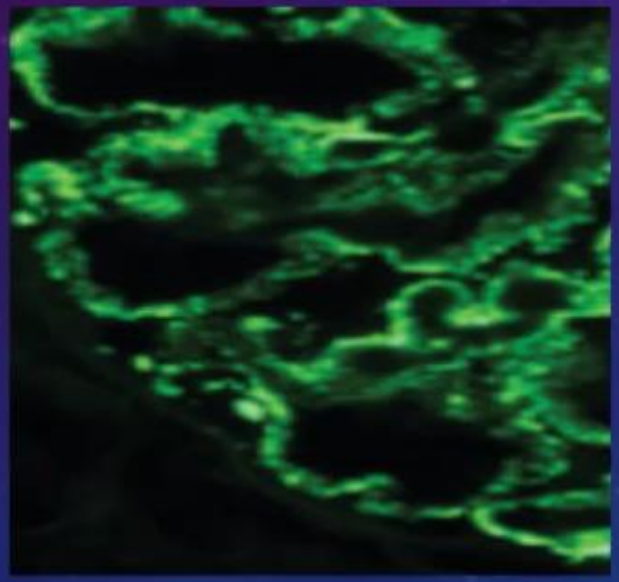
1 the larger the less permeable

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

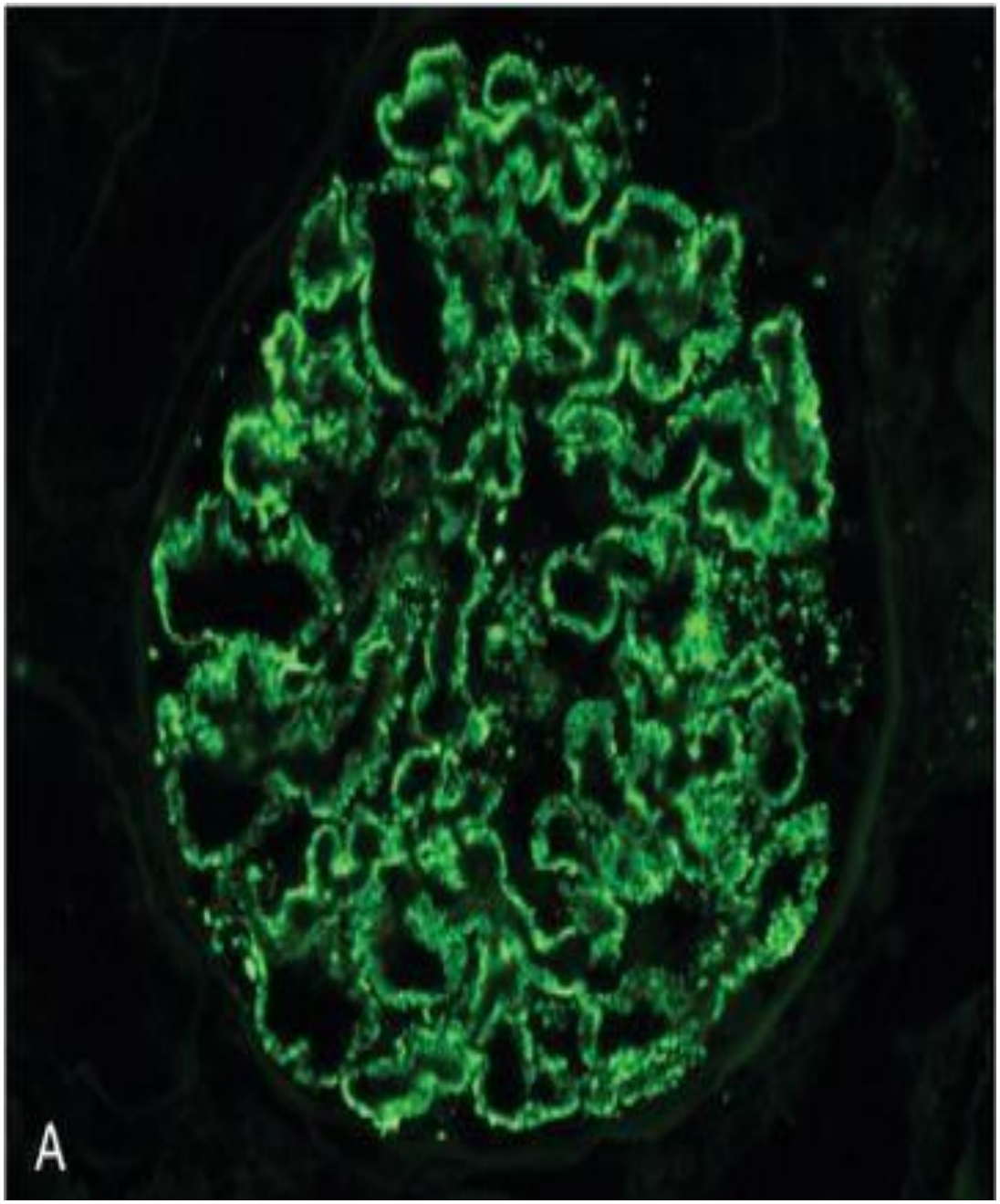
Fluorescein-labeled antibodies used for the antigens that should be routinely examined, including immunoglobulins (primarily IgG, IgM, and IgA), complement components (primarily C3, C1q, and C4), fibrin, and kappa and lambda light chains.



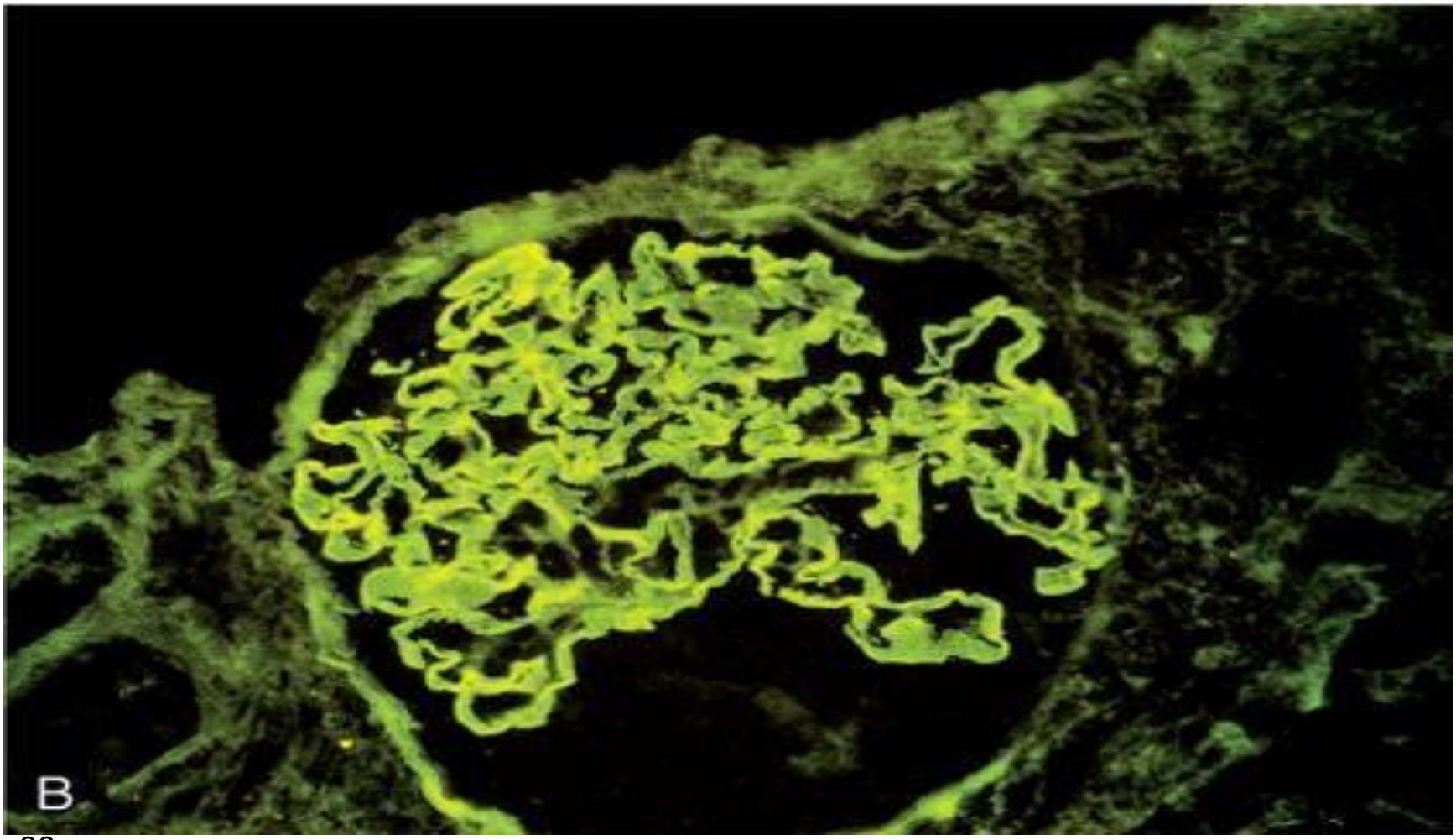
https://en.wikipedia.org/wiki/Immunofluorescence#/media/File:Immunofluorescence.jpg

Immunofluorescence microscopy

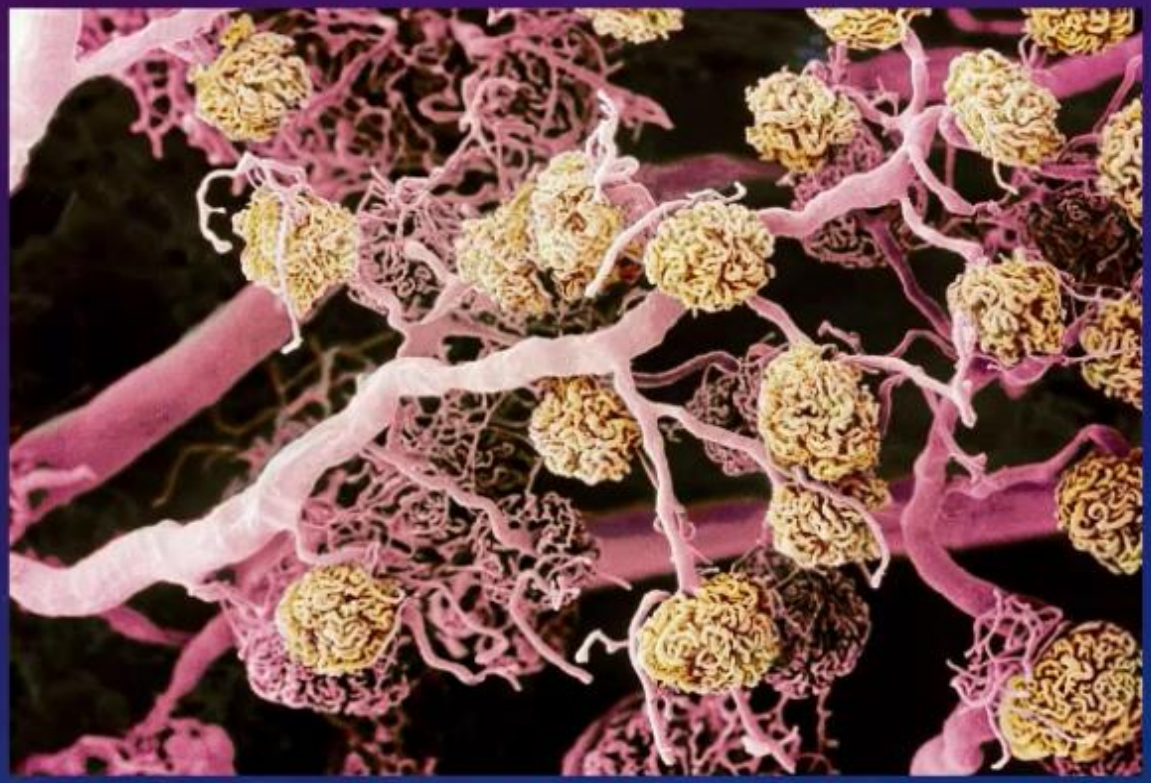
GRANULAR PATTERN OF DEPOSITION



immunofluorescence linear deposition of immune complexes

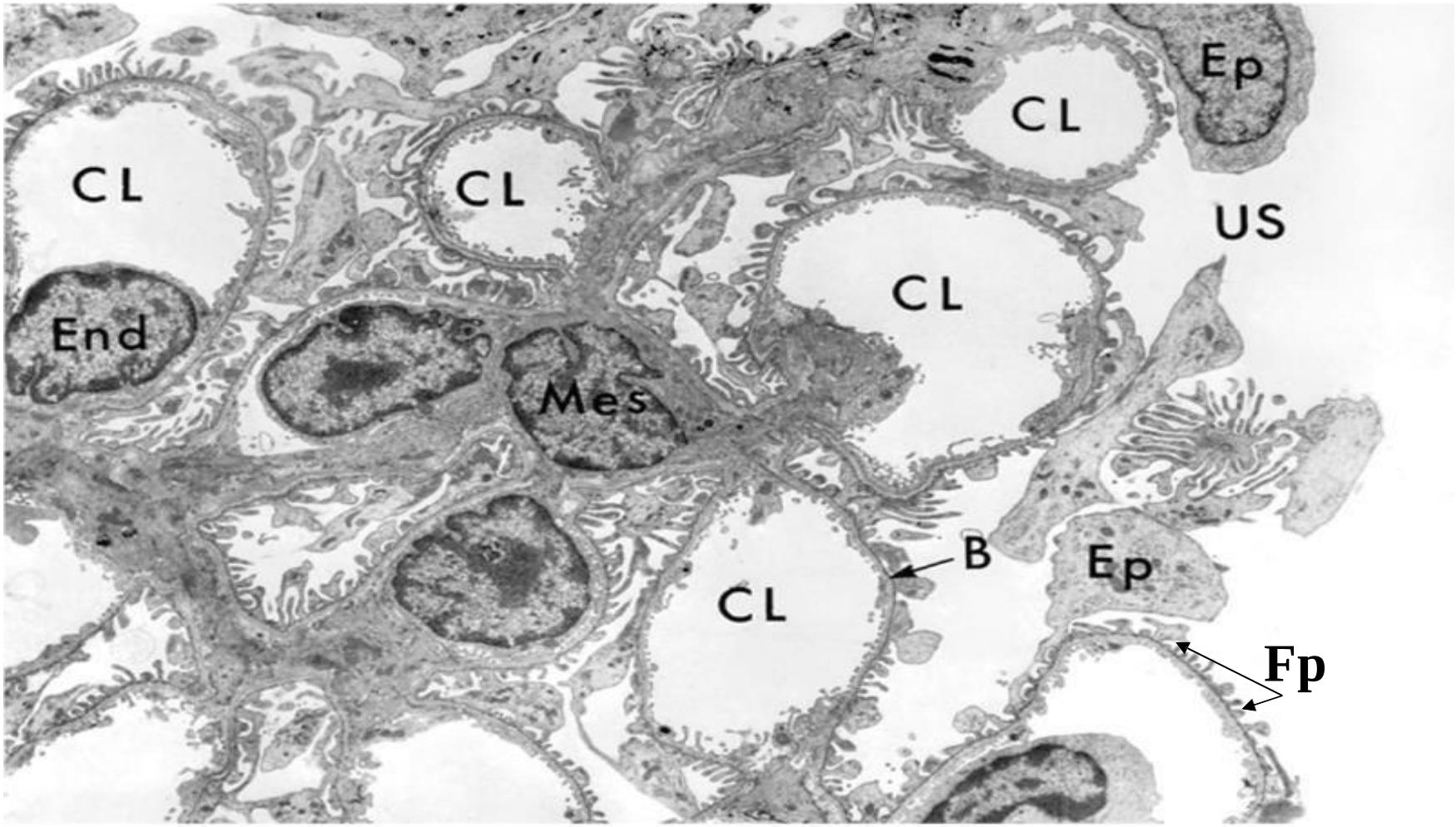


ELECTRON MICROSCOPY



EM-GLOMERULUS

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



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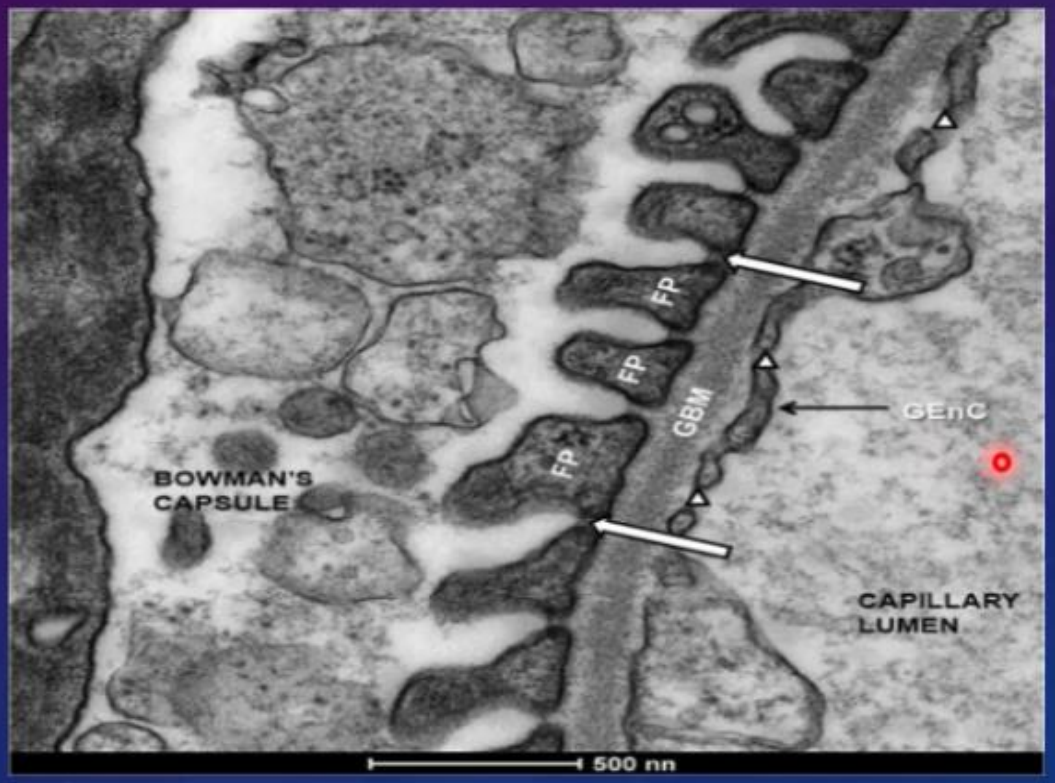
NORMAL GBM BY EM



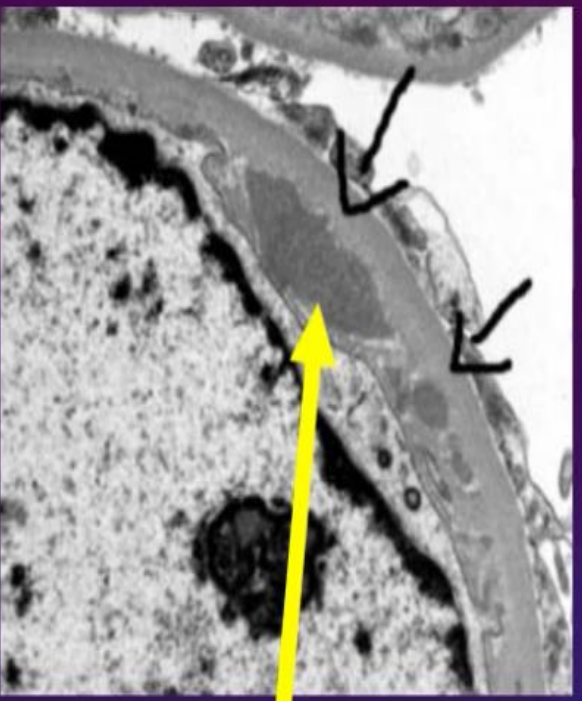
- **Electron Microscopy:**
- **reveals the immune complexes as electron-dense deposits or clumps that lie at one of three sites:**

1 in the mesangium.

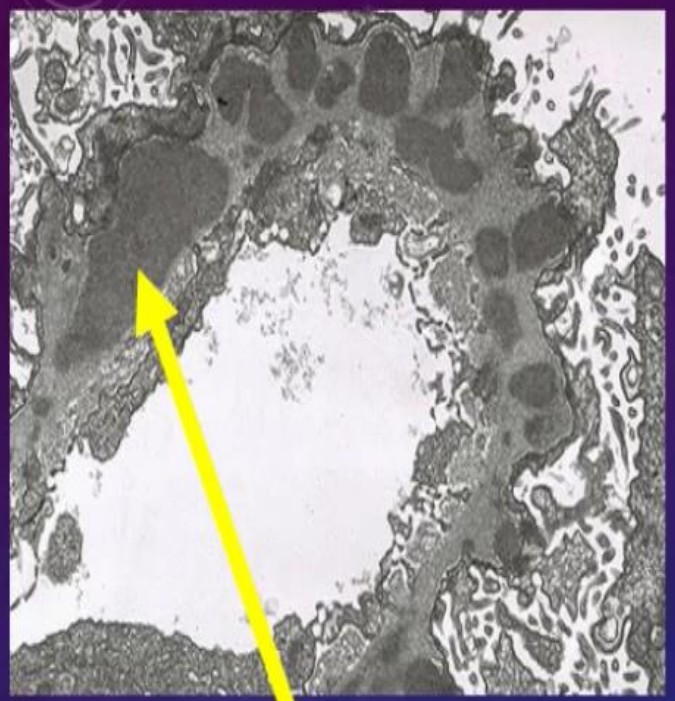
2 between the endothelial cells and the GBM (subendothelial deposits).

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

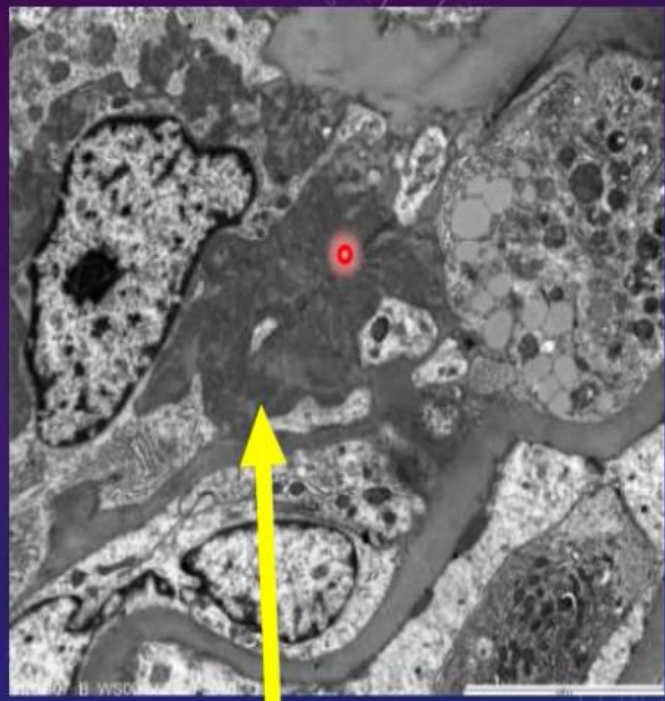
- **The pattern of immune complex deposition is helpful in distinguishing various types of GN**



Subendothelial



Subepithelial



Mesangial

Pathogenesis of Glomerular Diseases

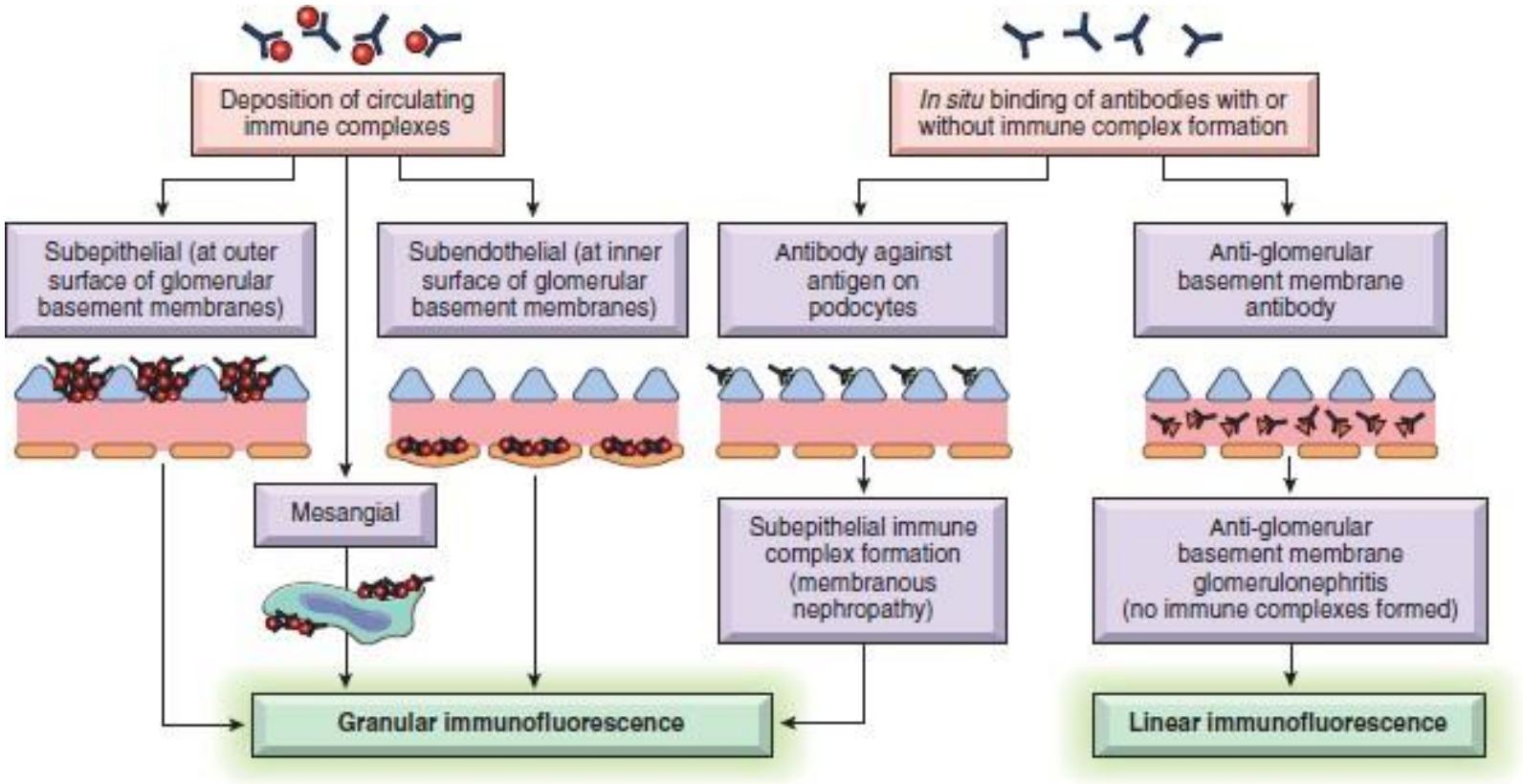
1- Antibody-associated → detected by immunoflourescence microscopy

(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



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.