Glomerular diseases

CONCEPTS

The doctor basically read the slide

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*

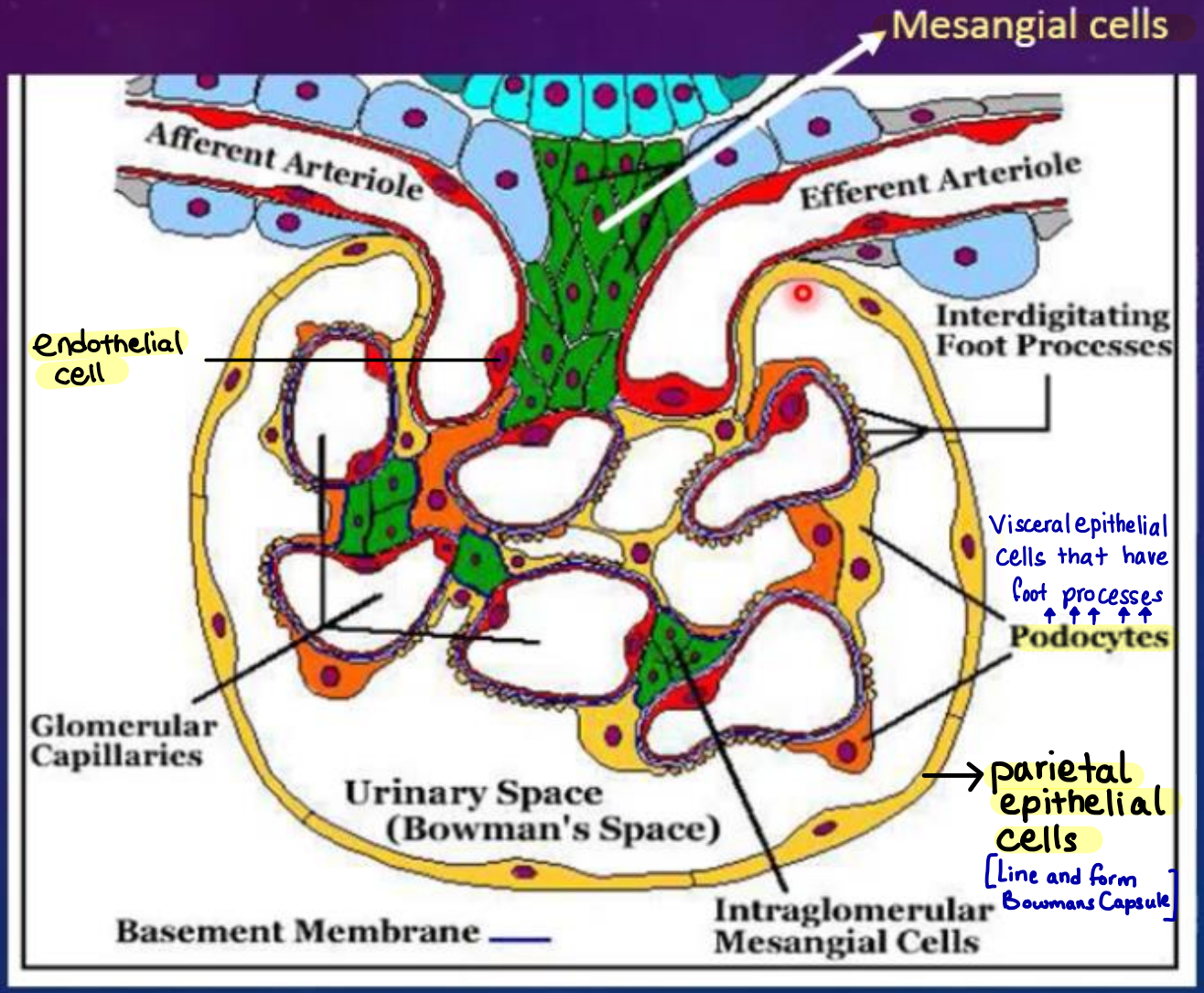
2- *glomerular basement membrane* (GBM)

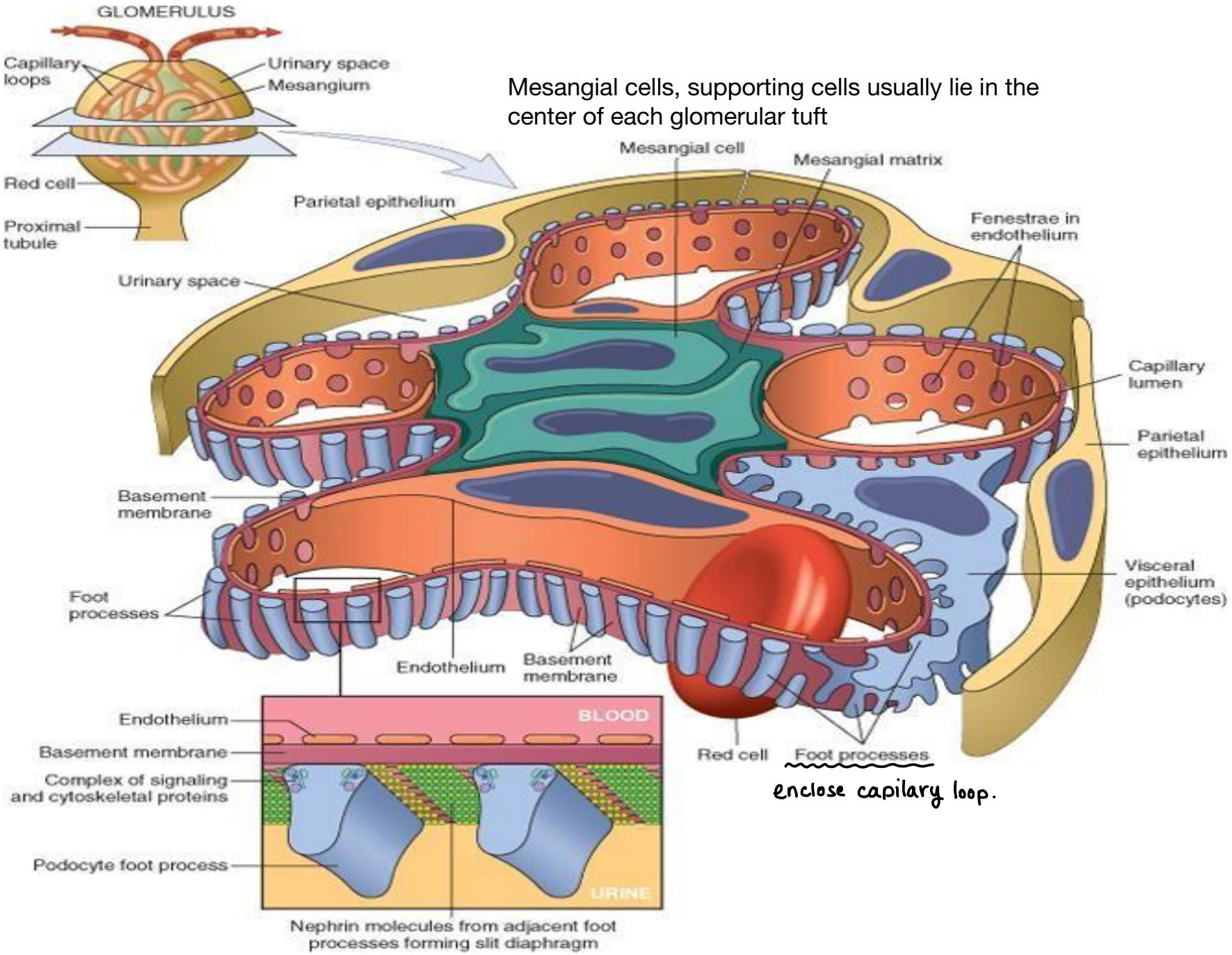
3- foot processes of podocytes

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

Is an Anastomosing network of capillaries that begin with afferent arteriole and end with efferent arteriole
Main function: filtration of blood

NORMAL GLOMERULUS





Mesangial cells, supporting cells usually lie in the center of each glomerular tuft

enclose capilary loop.

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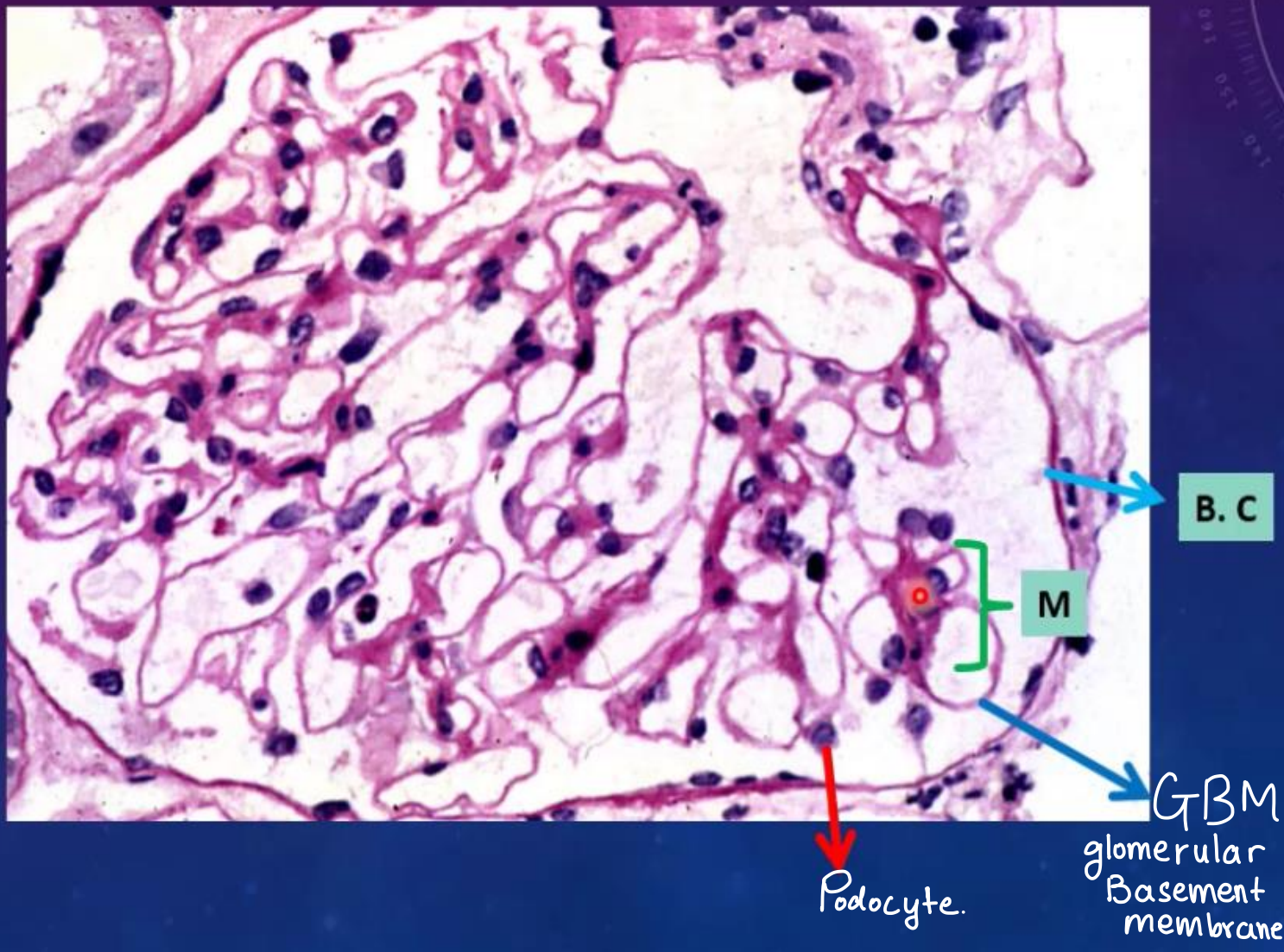
NORMAL GLOMERULUS

seen under Light microscope.



The glomerular filtration membrane/unit

Consists of the following

1- endothelial cells with its fenestrations

2-Basement membrane

3-complex of signaling and cytoskeletal proteins many of which are coming from podocyte foot processes, the most significant protein is nephrin.

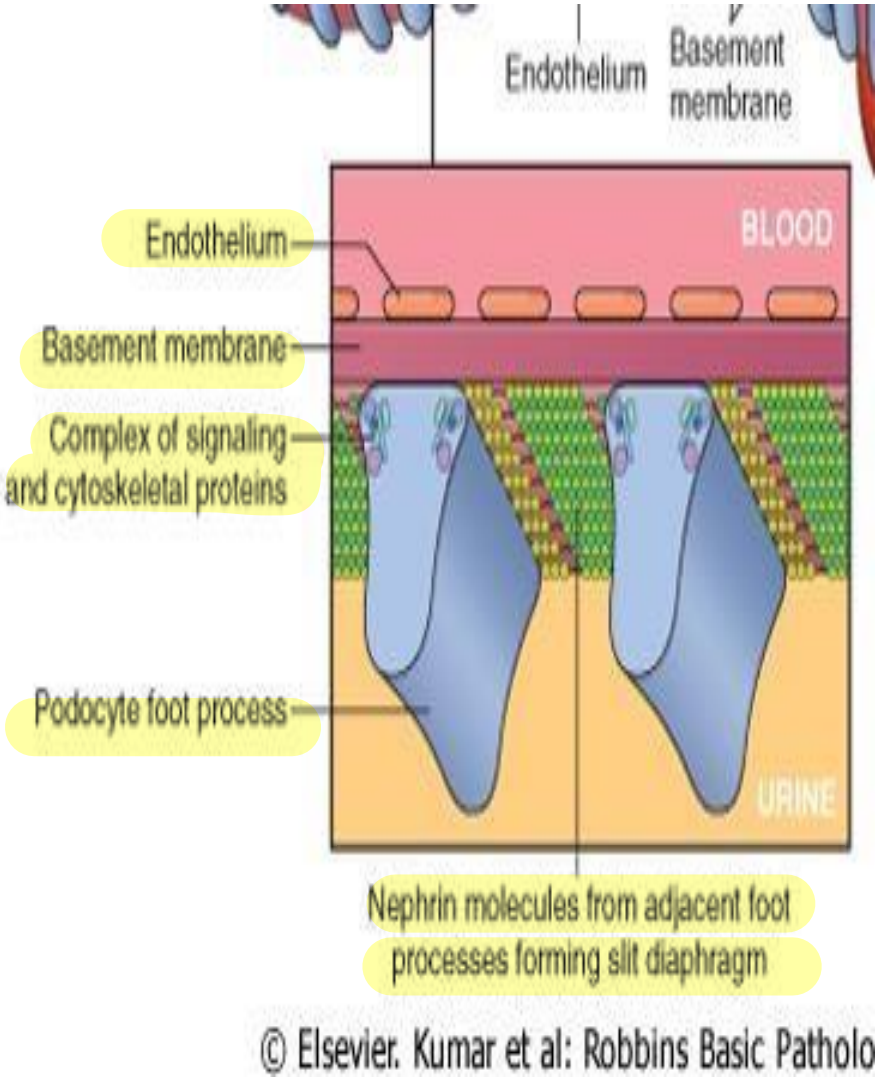
nephrin molecules from adjacent foot processes form the very imp structure called slit diaphragm, which is very important for the permeability of the basement membrane

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) Albumin is (−ve)ly charged thus completely impermeable.

- So:

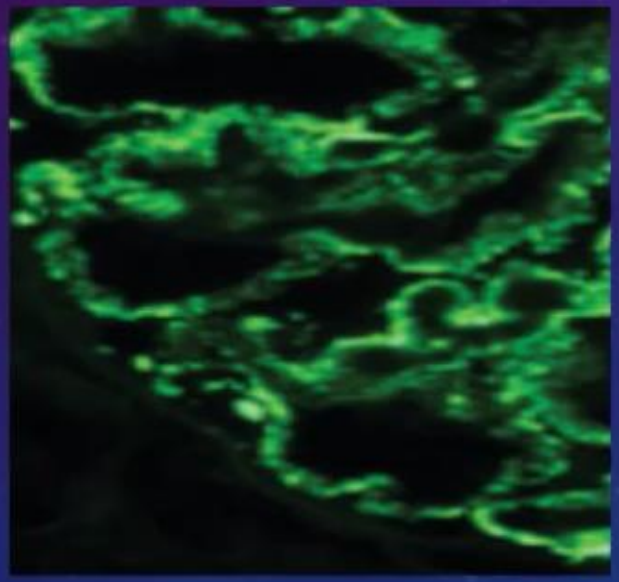
1 the larger the less permeable

2 the more cationic the more permeable. (+ve)

- 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.



Positive immunoflurescence of kidney biopsy(this is an example of one of the patterns seen with IF)

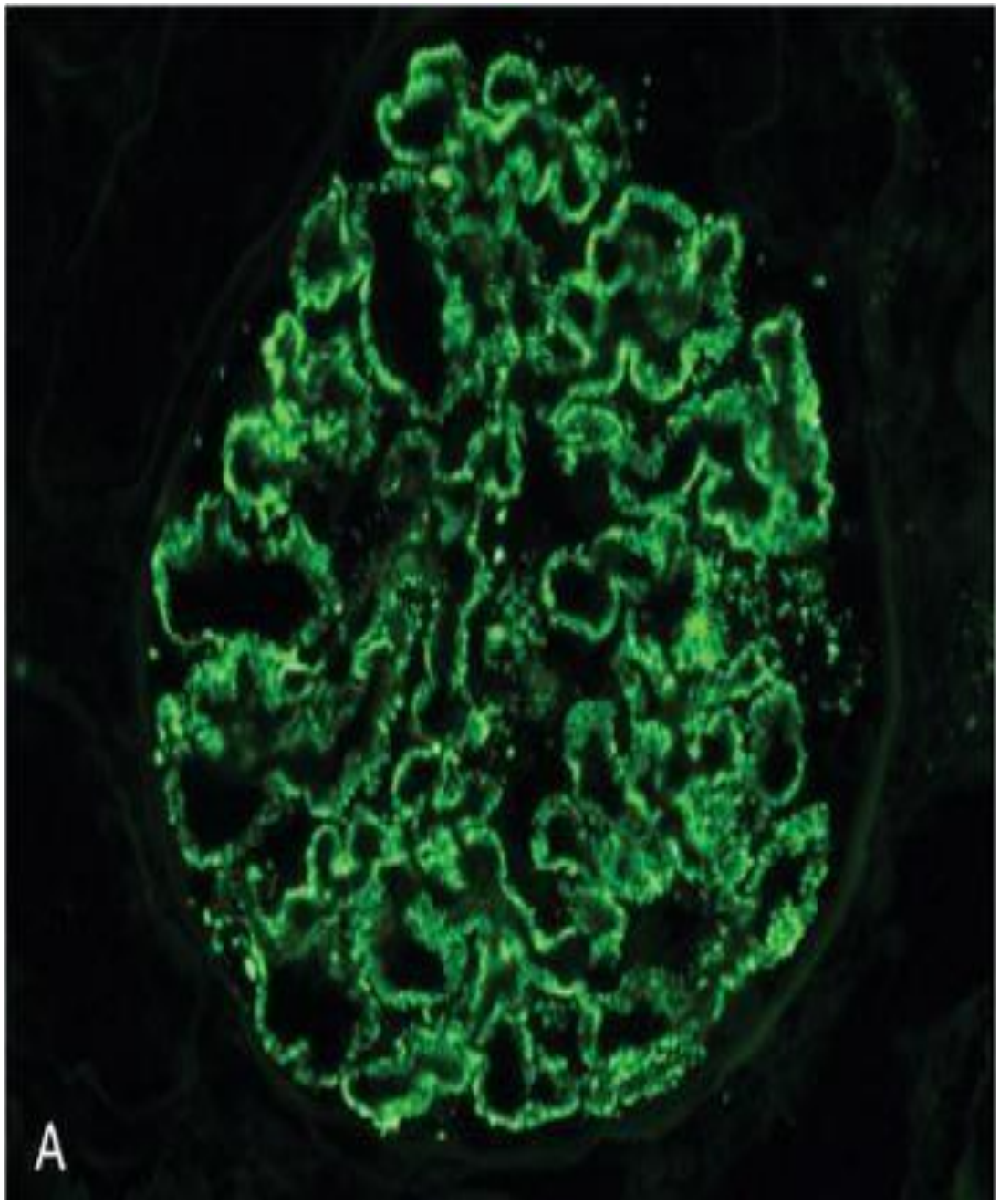
https://en.wikipedia.org/wiki/Immunofluorescence#/media/File:Immunofluorescence.jpg

Immunofluorescence microscopy

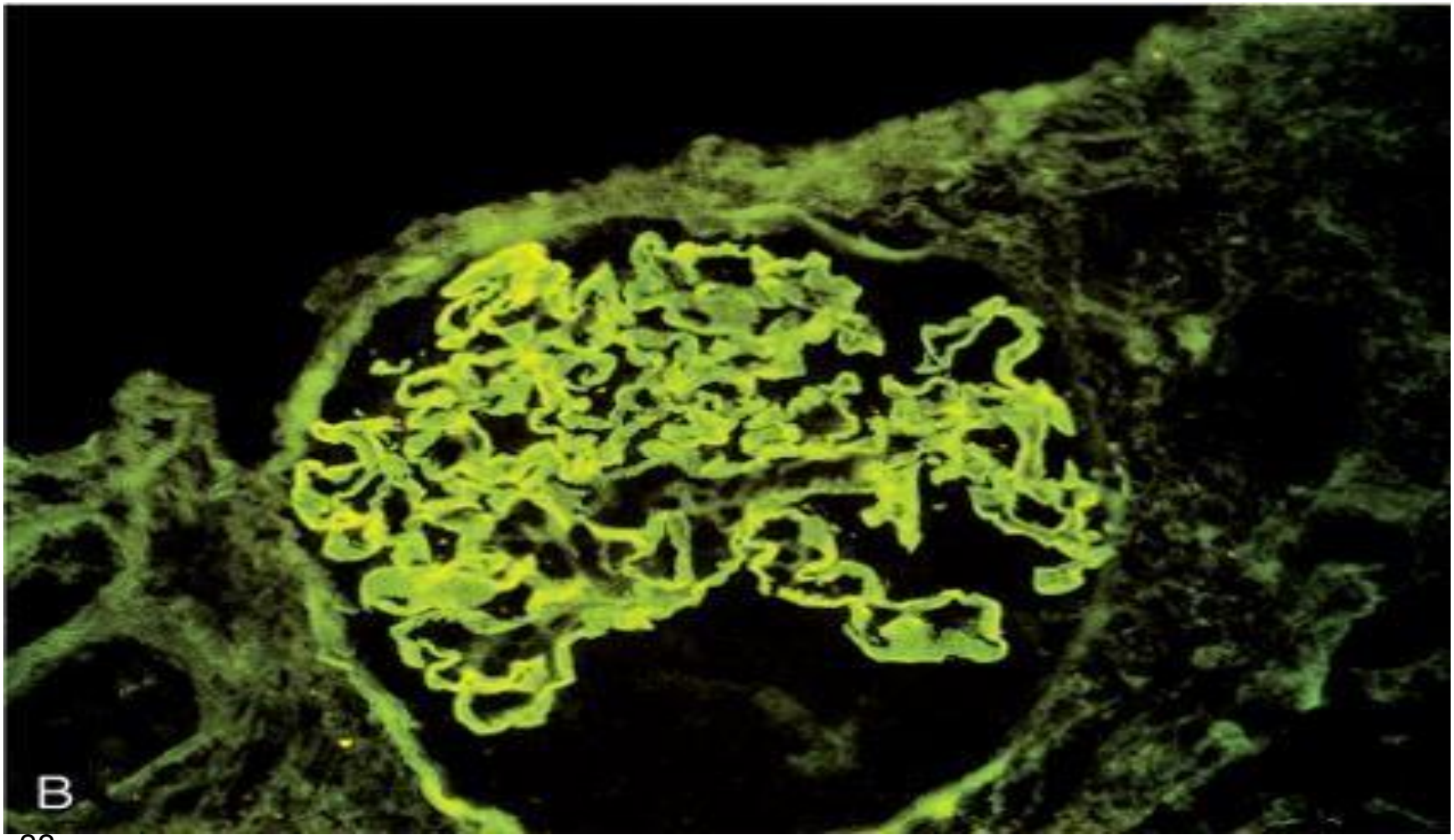
Patterns according to Morphological differences

1- GRANULAR PATTERN OF DEPOSITION

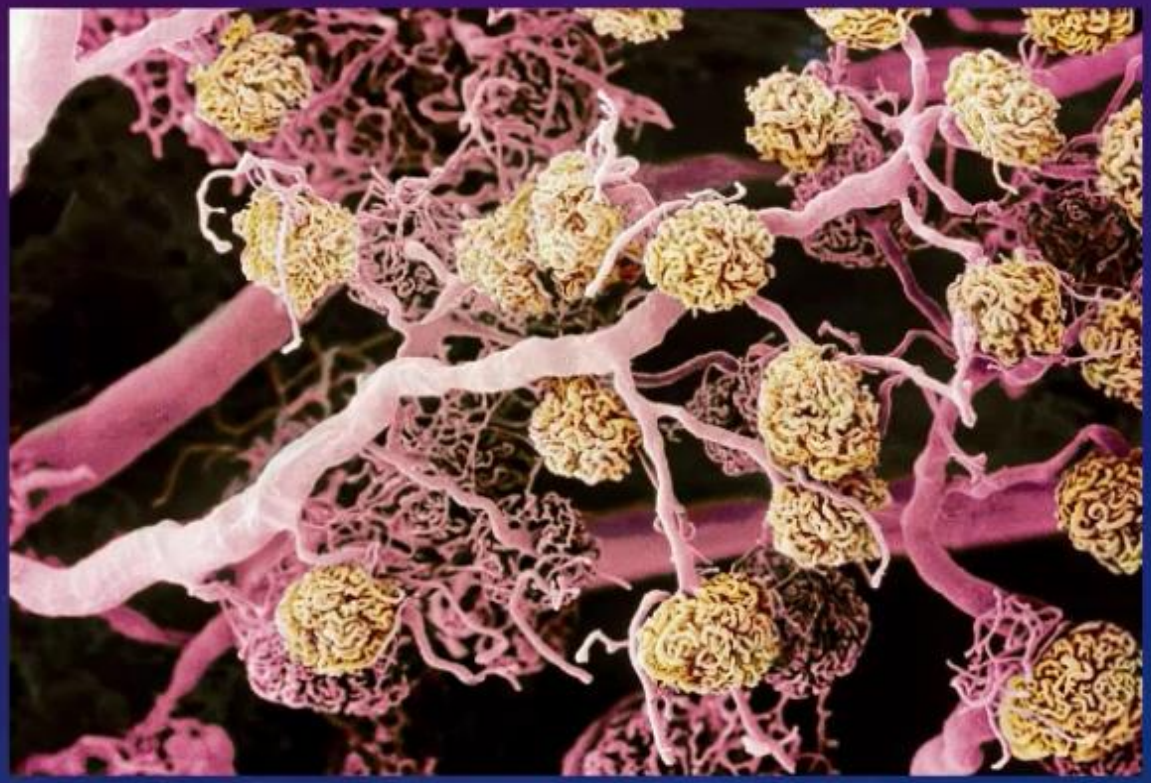
In the form of small or larger dots



2- **immunofluorescence linear deposition of immune complexes**



ELECTRON MICROSCOPY

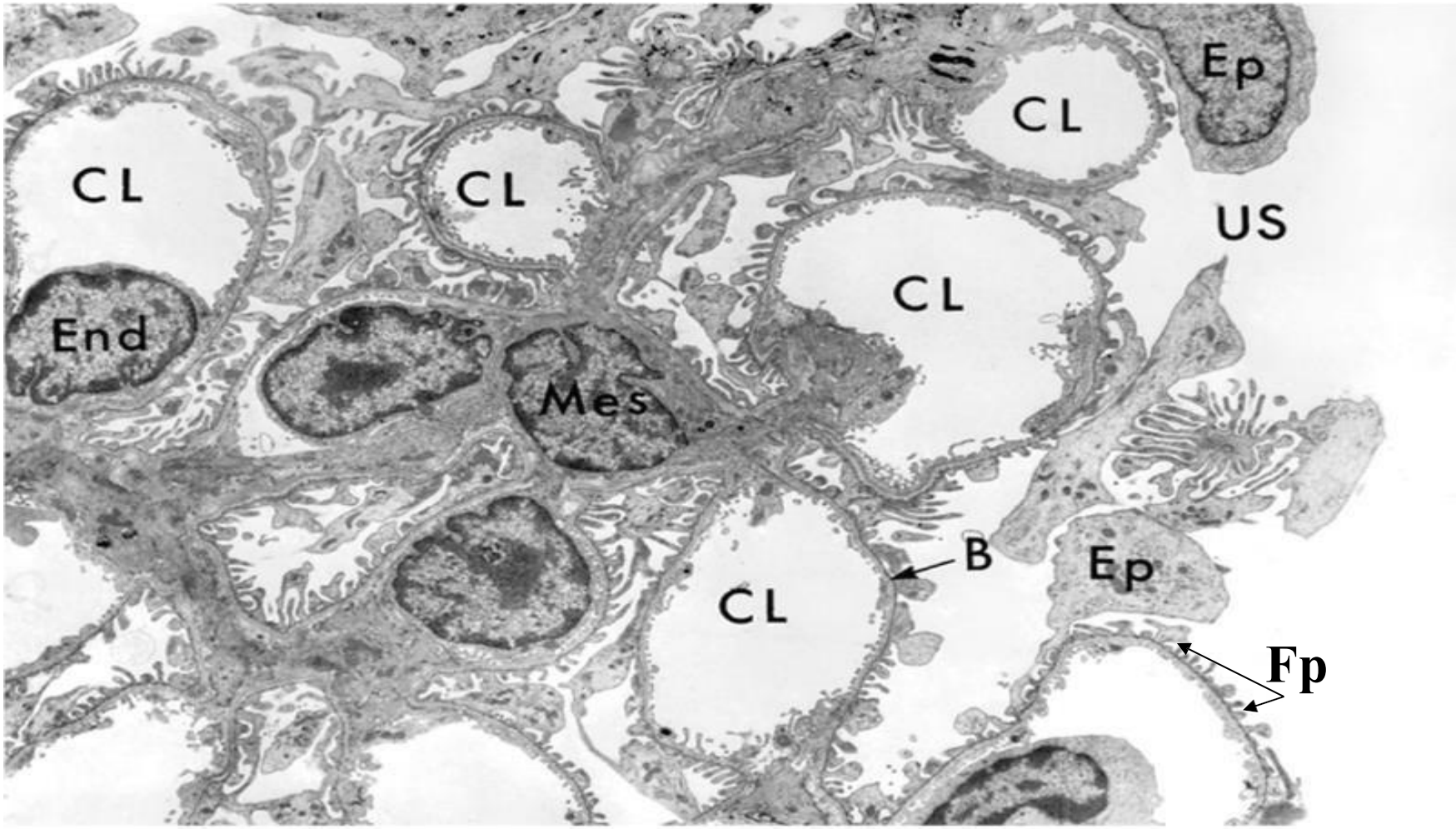


EM-GLOMERULUS

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

(podocytes)

Mesangial cells surrounded by capillary loops



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NORMAL GBM BY EM

foot processes of podocytes

endothelial cell fenestrations

glomerular Basement Membrane.

Bowmans capsule.

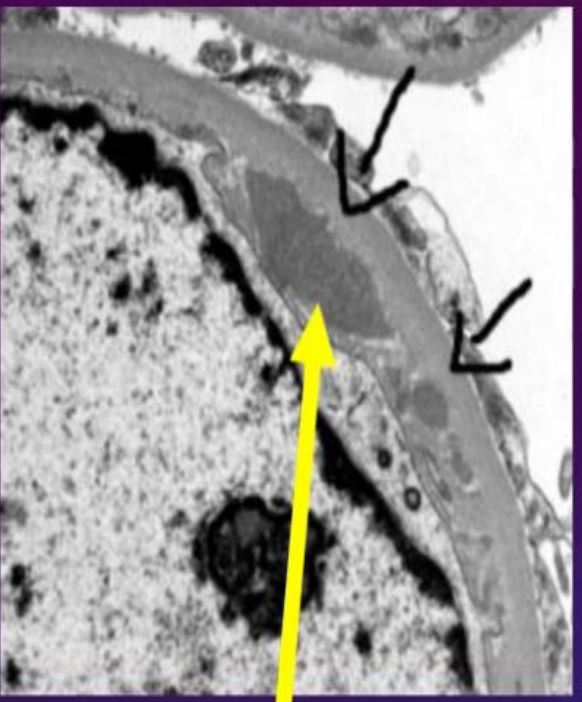
- **Electron Microscopy:**
- **reveals the immune complexes as electron-dense deposits or clumps that lie at one of three sites:**

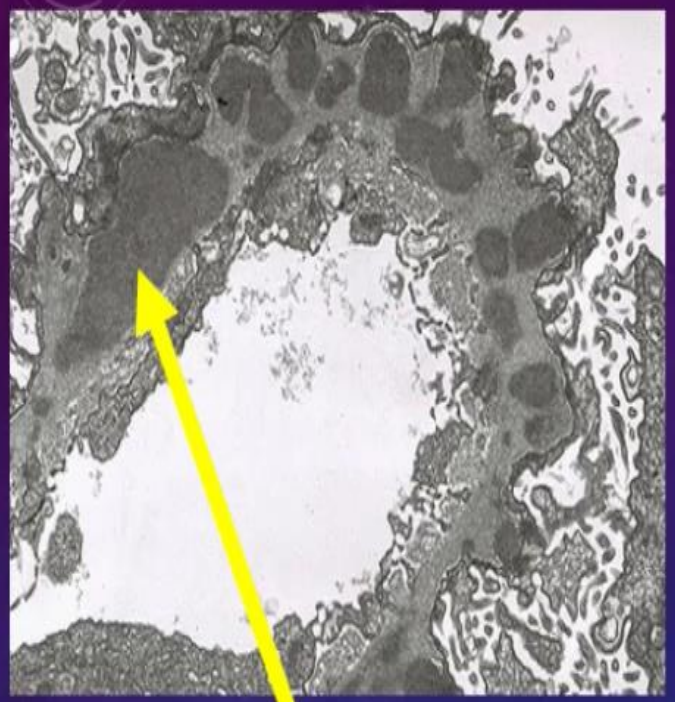
1 in the mesangium.

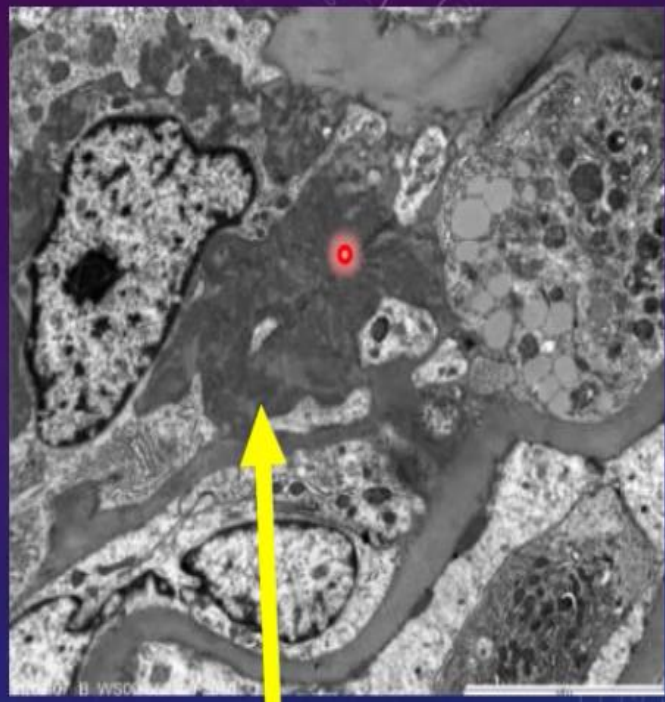
2 between the endothelial cells and the GBM (subendothelial deposits).

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

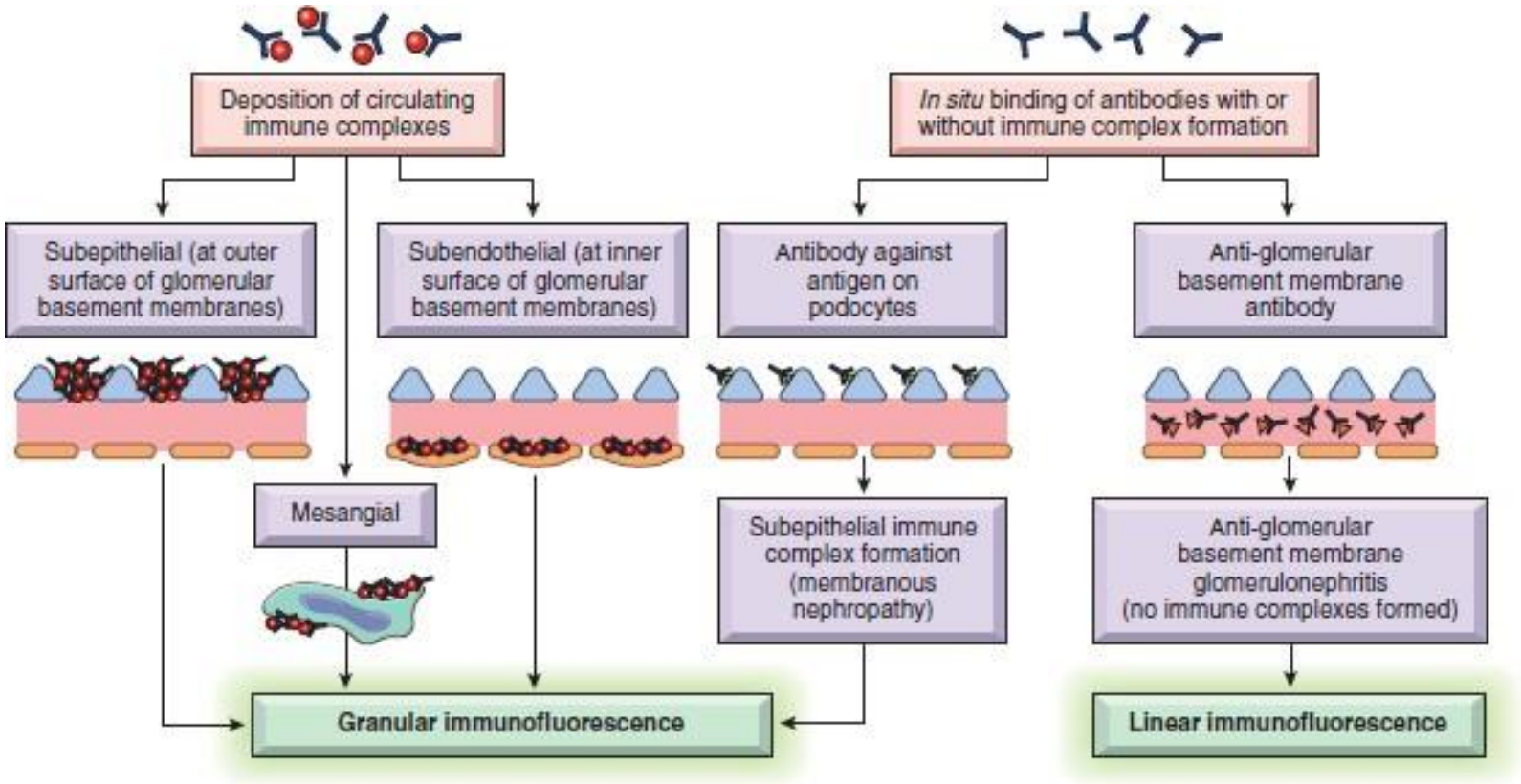
(1)deposition of soluble circulating Ag-Ab complexes in the glomerulus.

(2) Abs reacting in situ within the glomerulus.

(3)Abs directed against glomerular cell components.

Text in figure is imp

Antibody- mediated glomerular injury



Pathogenesis of Glomerular Diseases

2- Non-immune Mechanisms of Glomerular Injury

1) Podocyte Injury: Direct or mechanical injury of podocytes

- 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.