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Pathology GUS

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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** so the kidney can't get rid of the toxic waste products
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.

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*

The presence of RBCs in urine

Peripheral Edema/Puffy Eyes

The presence of RBCs in the urine will lead to the smoky color of it

"Smoky Urine"

2-Nephrotic syndrome

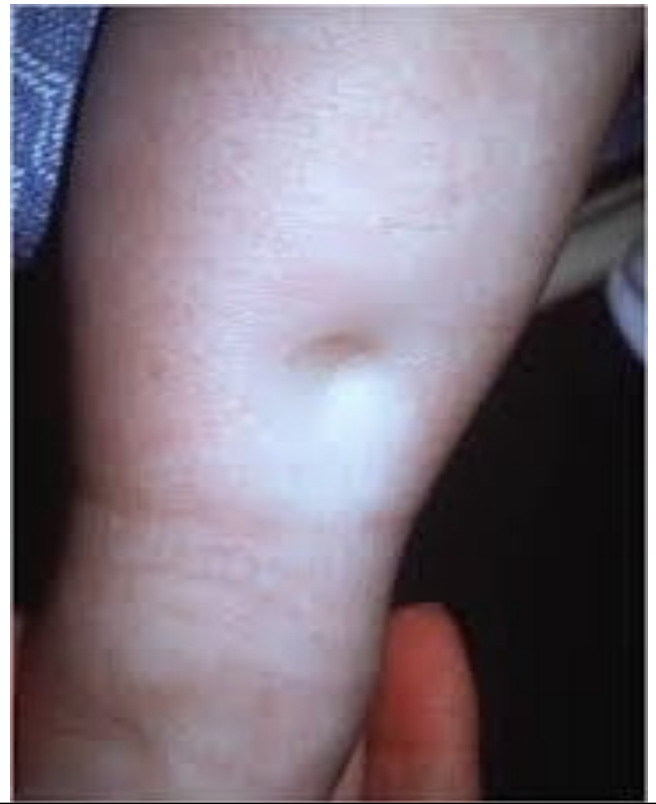
!!!Nephrotic Not nephritic!!!

- **a glomerular syndrome characterized by:**
  - **heavy proteinuria (excretion of >3.5 gm of protein/day in adults** (different number in children which is related to the body weight)**)**
  - **hypoalbuminemia** (low concentration of albumin in the blood)**.**
  - **severe edema**(puffy eyes, face, abdomen, upper and lower limbs) and it is the major clinical manifestation in the nephrotic syndrome).
  - **hyperlipidemia**(elevated concentration of lipid in the blood)**.**
  - **lipiduria (lipid in the urine).**

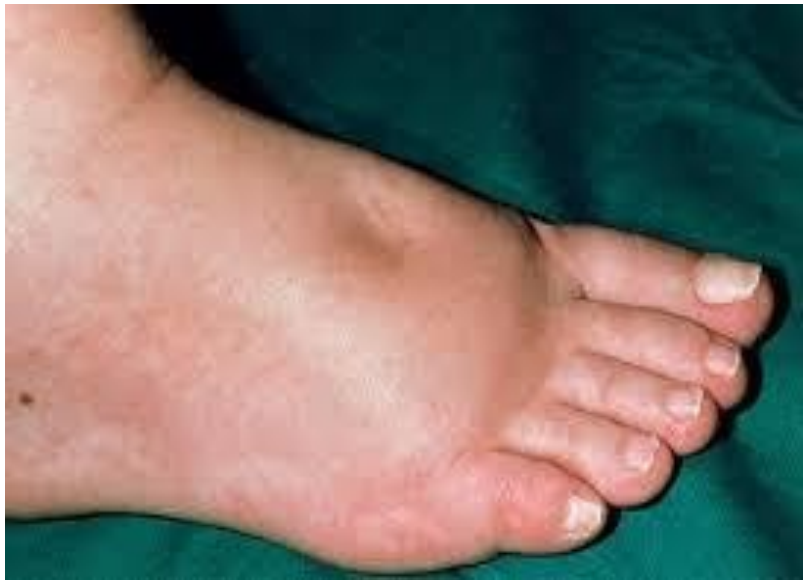
Nephrotic syndrome

Edema that involves the lips the face and the eyes causing puffy eyes of nephrotic syndrome

Pitting Edema in the upper limb



Pitting Edema in the lower limb



3-Asymptomatic hematuria or proteinuria:

A manifestation of mild glomerular abnormalities.

completely asymptomatic but by incidence, we might have a mild degree of hematuria or proteinuria during urine analysis, shouldn't be left without proper evaluation of the patients because it might be a manifestation of some mild glomerular disease that might progress to something more serious if not treated or evaluated correctly.

4- Rapidly progressive glomerulonephritis (crescentic GN)

- loss of renal function in a few days or weeks
- <u>It is manifested by :</u>
  - microscopic hematuria.
  - dysmorphic RBC and RBC casts in urine sediment.
  - mild-moderate proteinuria

5-Acute renal failure

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

- **<u>can result from :</u>**

1- sever glomerular injury

2-sever interstitial injury

3-significant 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

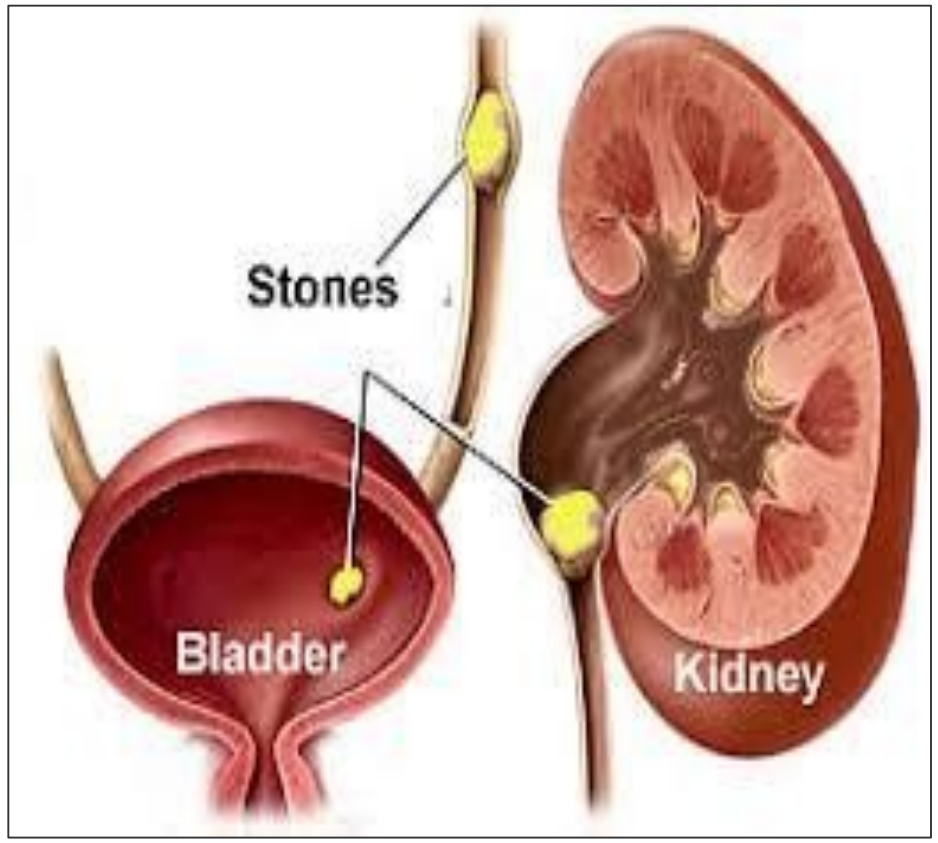
- **bacteriuria and pyuria (bacteria and WBCs in urine).**
- **symptomatic or asymptomatic.**

- **Types :** depends on the level of the infection and the magnitude of the involvement of the urinary tract.

1- *pyelonephritis* (kidney). Severe

2- *cystitis* (bladder).

8-Nephrolithiasis



- **= Renal stones** anywhere in the urinary tract
- **manifested by:**

1-renal colic

2-hematuria

3-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

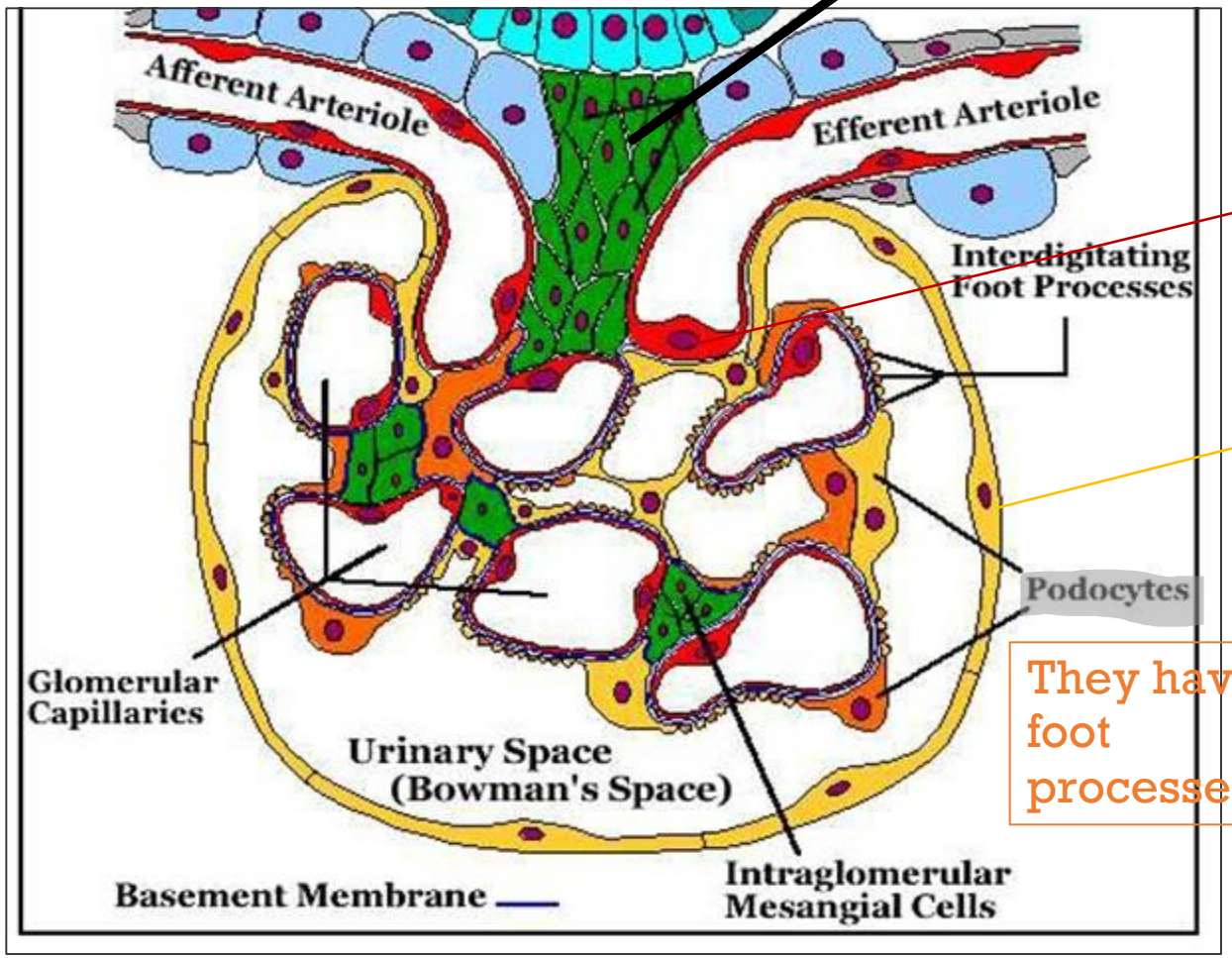
Bowman space (**urinary space**)= the cavity in which plasma ultra-filtrate first collects.

- 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

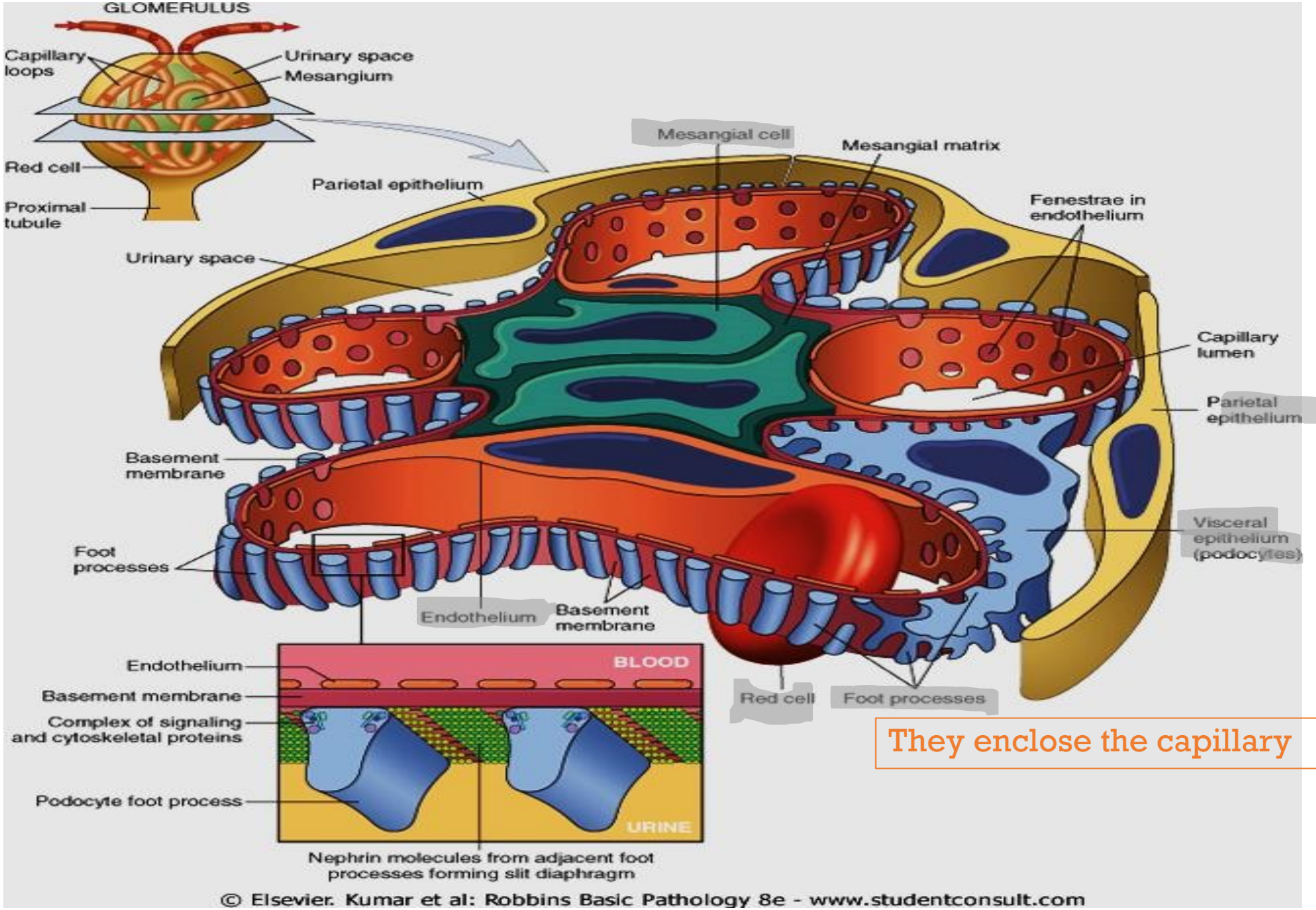
is an anastomosing capillary that begins with an afferent arteriole and ends with an efferent arteriole and its function is the filtration of the blood



Endothelial cells

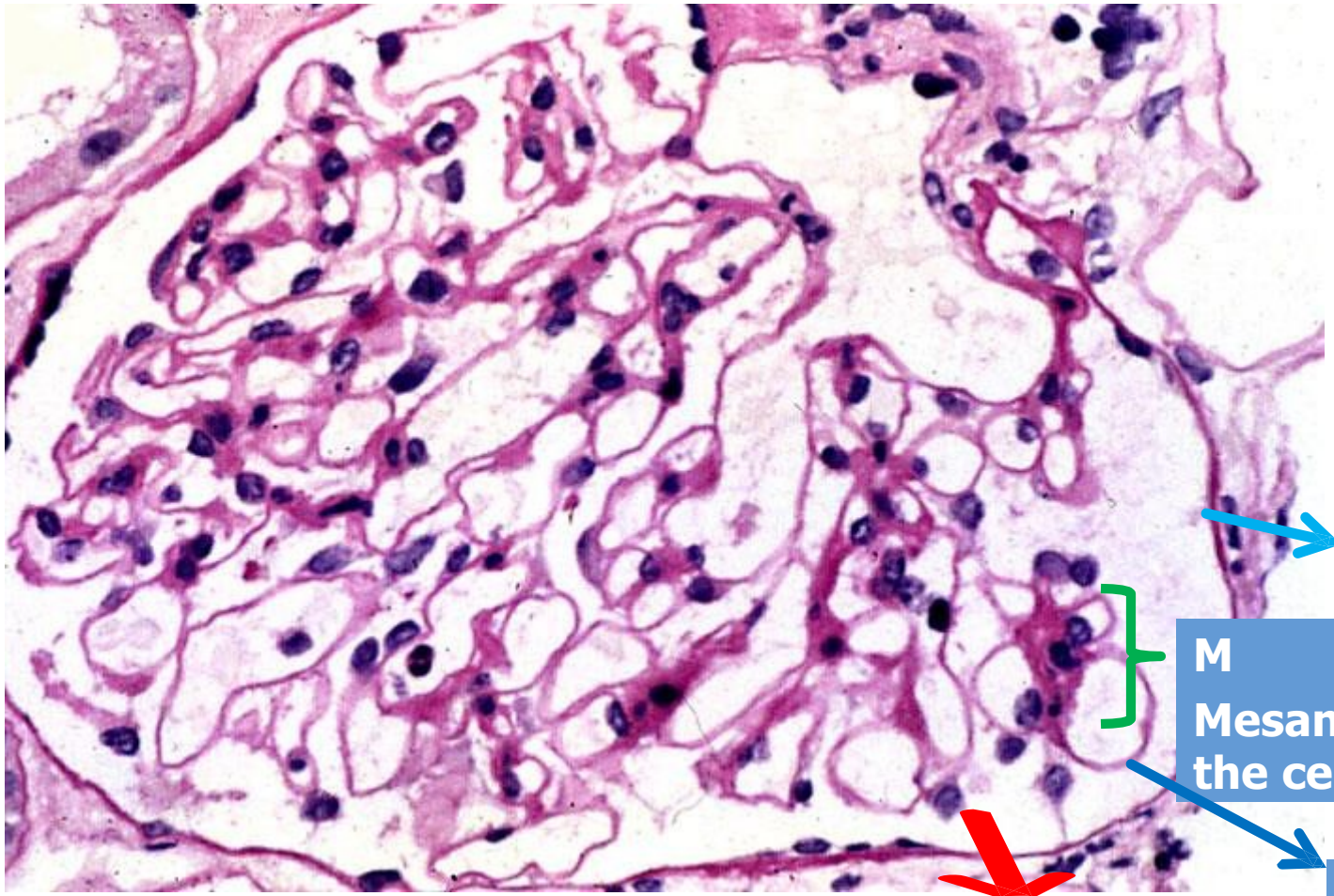
The parietal epithelial cells which form bowman's capsule

They have foot processes



They enclose the capillary

Normal glomerulus

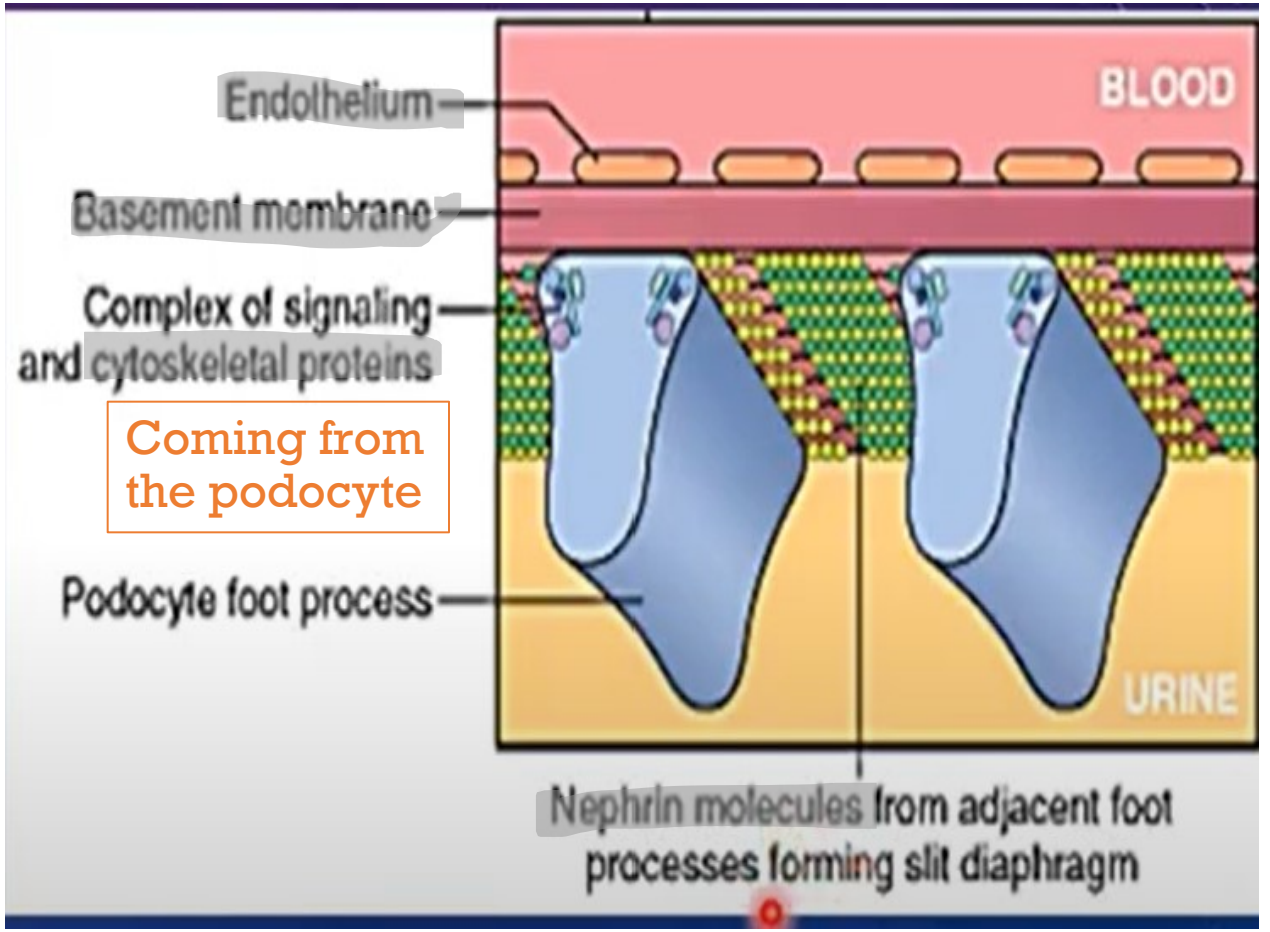


Glomerular filtration membrane/ unit

- **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 in large part of nephrin.**



Coming from the podocyte

Very important for the permeability of the basement membrane

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 anionic)**

- So :

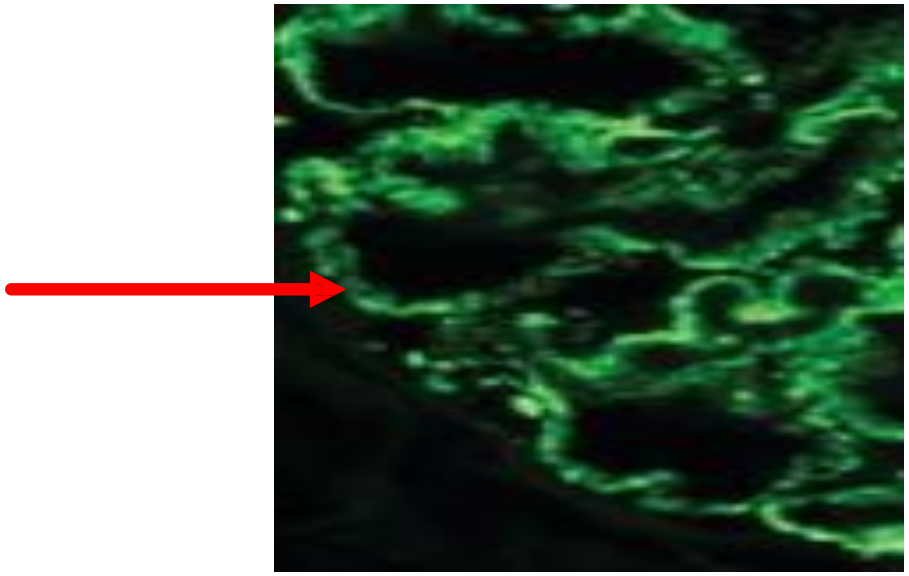
1 **the larger the less permeable**

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

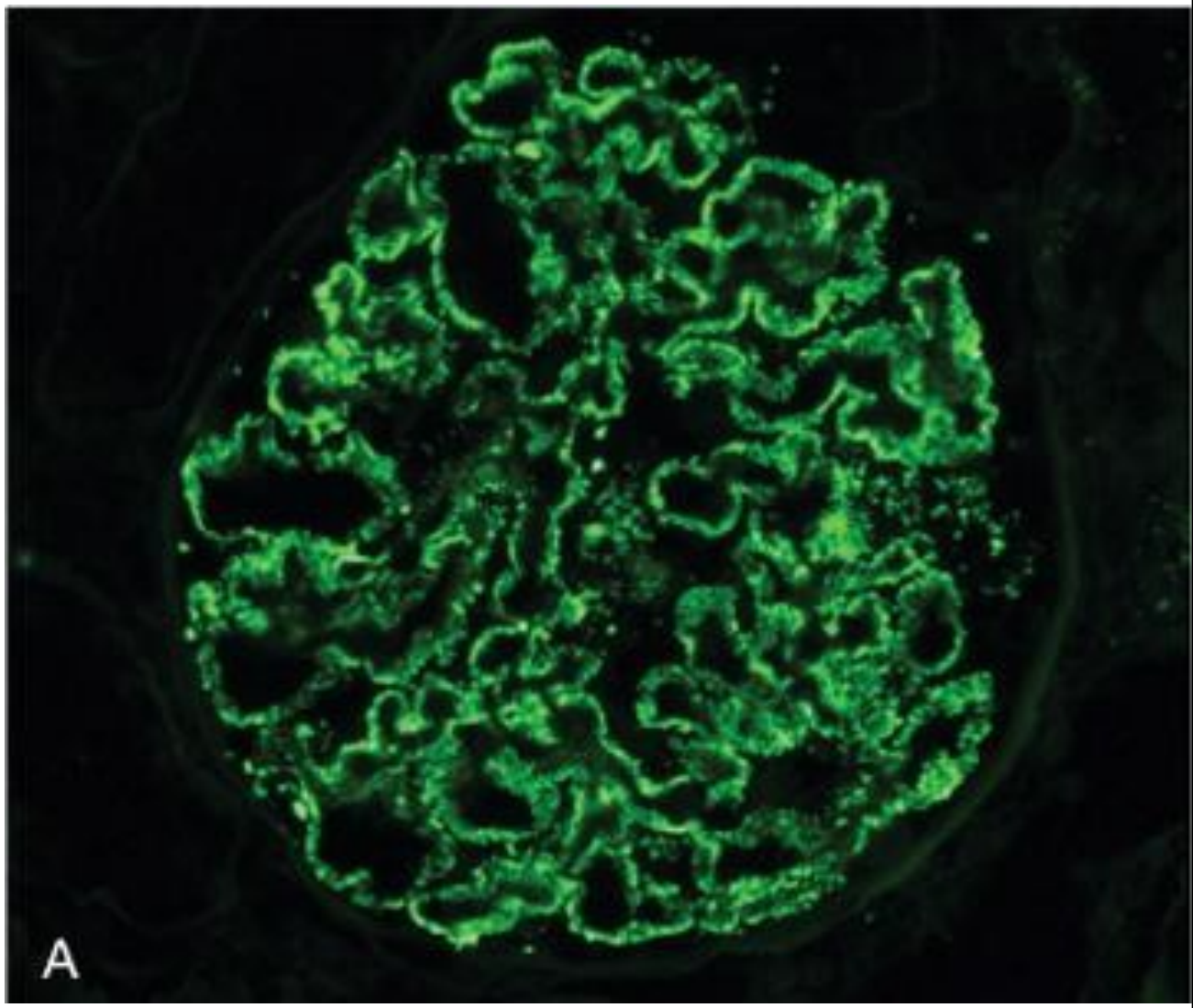
Fluorescein-labeled antibodies used for the antigens that should be routinely examined include immunoglobulins (primarily IgG, IgM, and IgA), complement components (primarily C3, C1q, and C4), fibrin, and kappa and lambda light chains.



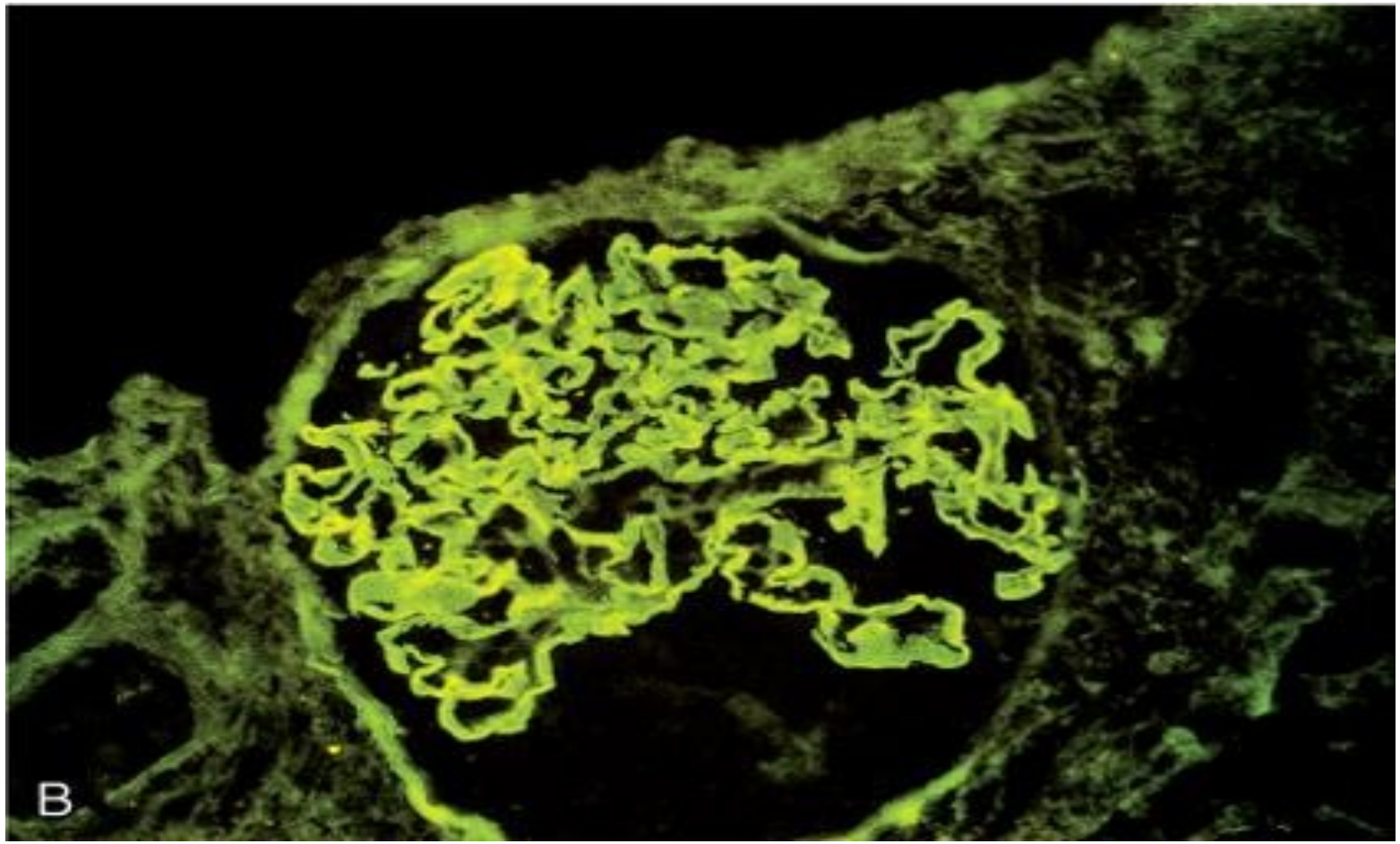
https://en.wikipedia.org/wiki/Immunofluorescence#/media/File:Immunofluores cence.jpg

Immunofluorescence microscopy

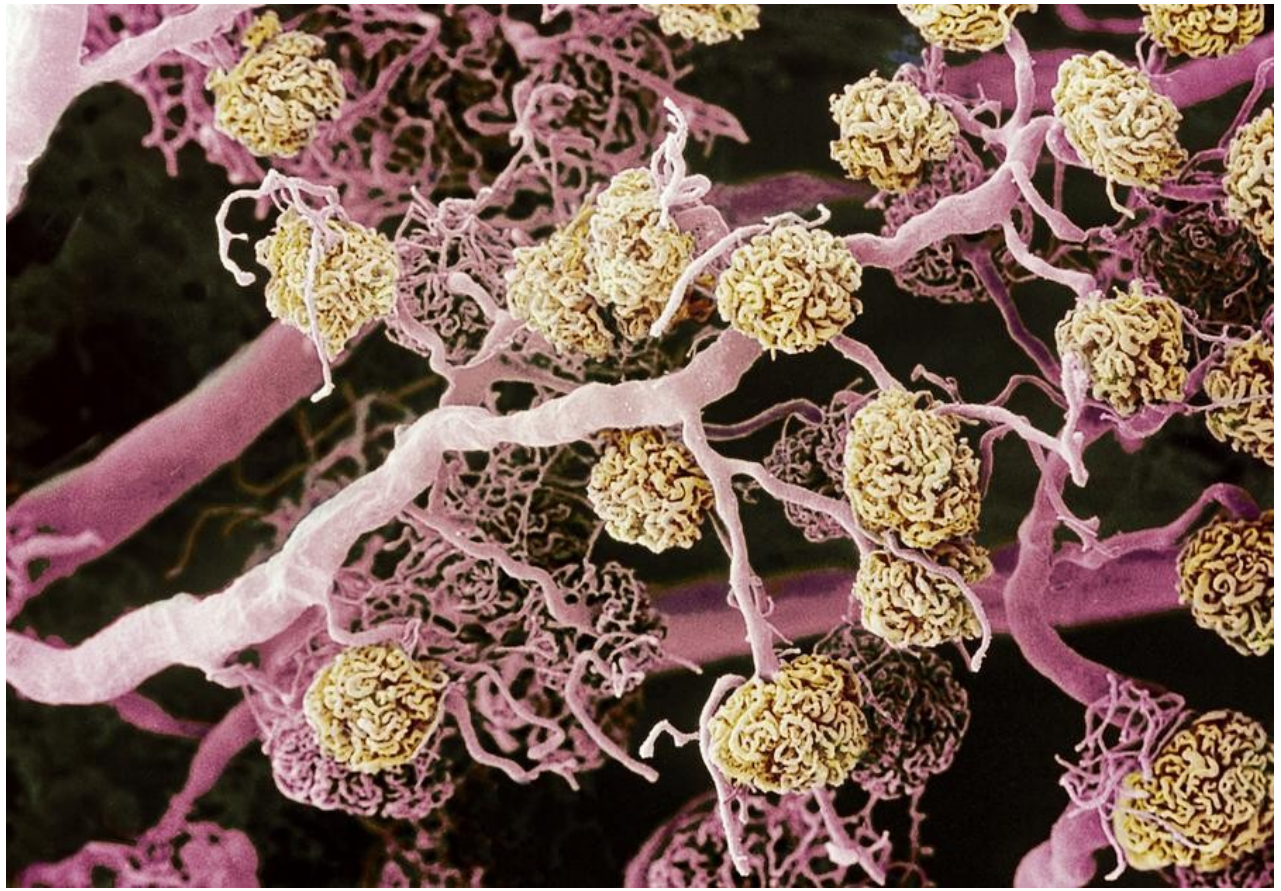
granular pattern of deposition will be in the form of small or larger dotes



immunofluorescence linear deposition of immune complexes

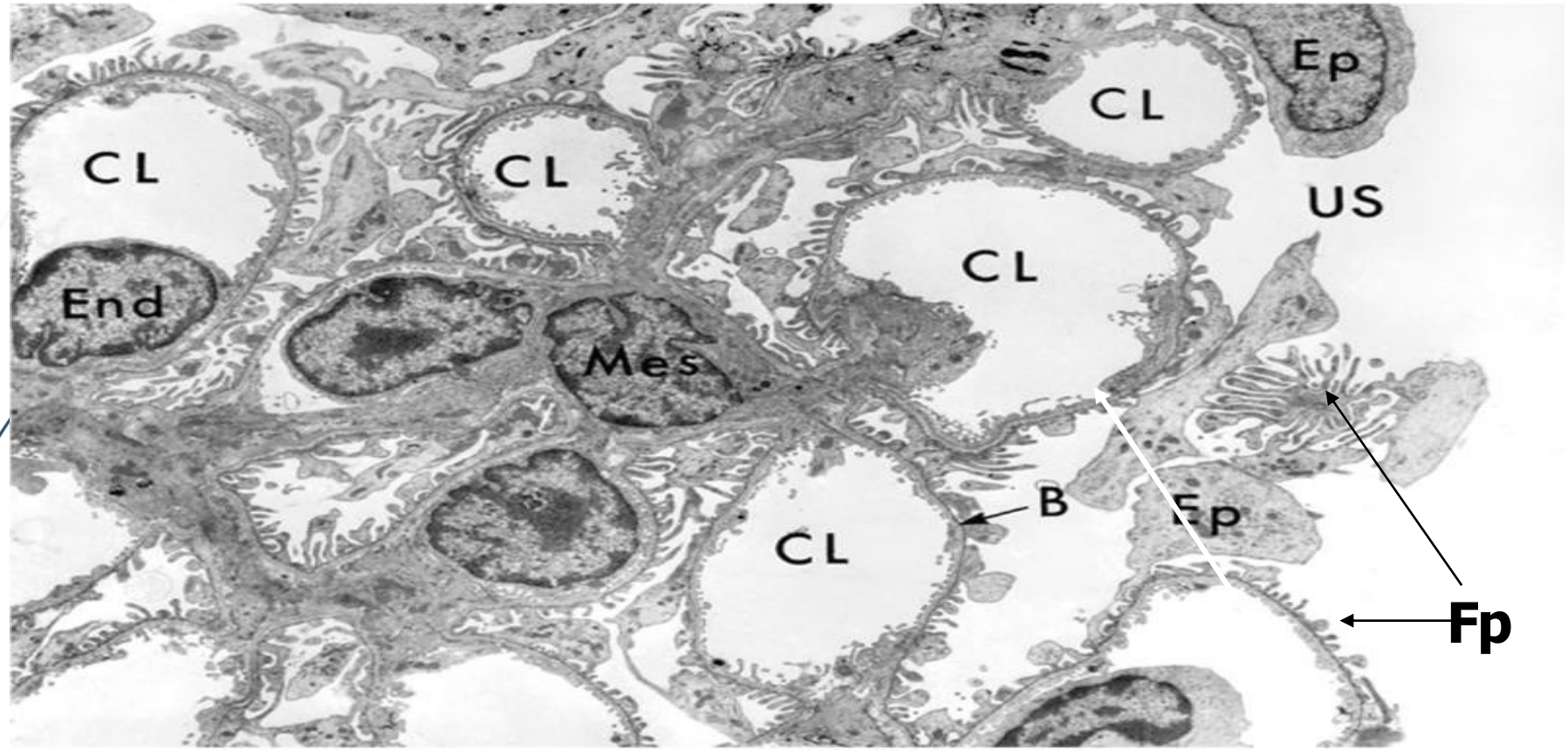


Electron Microscopy



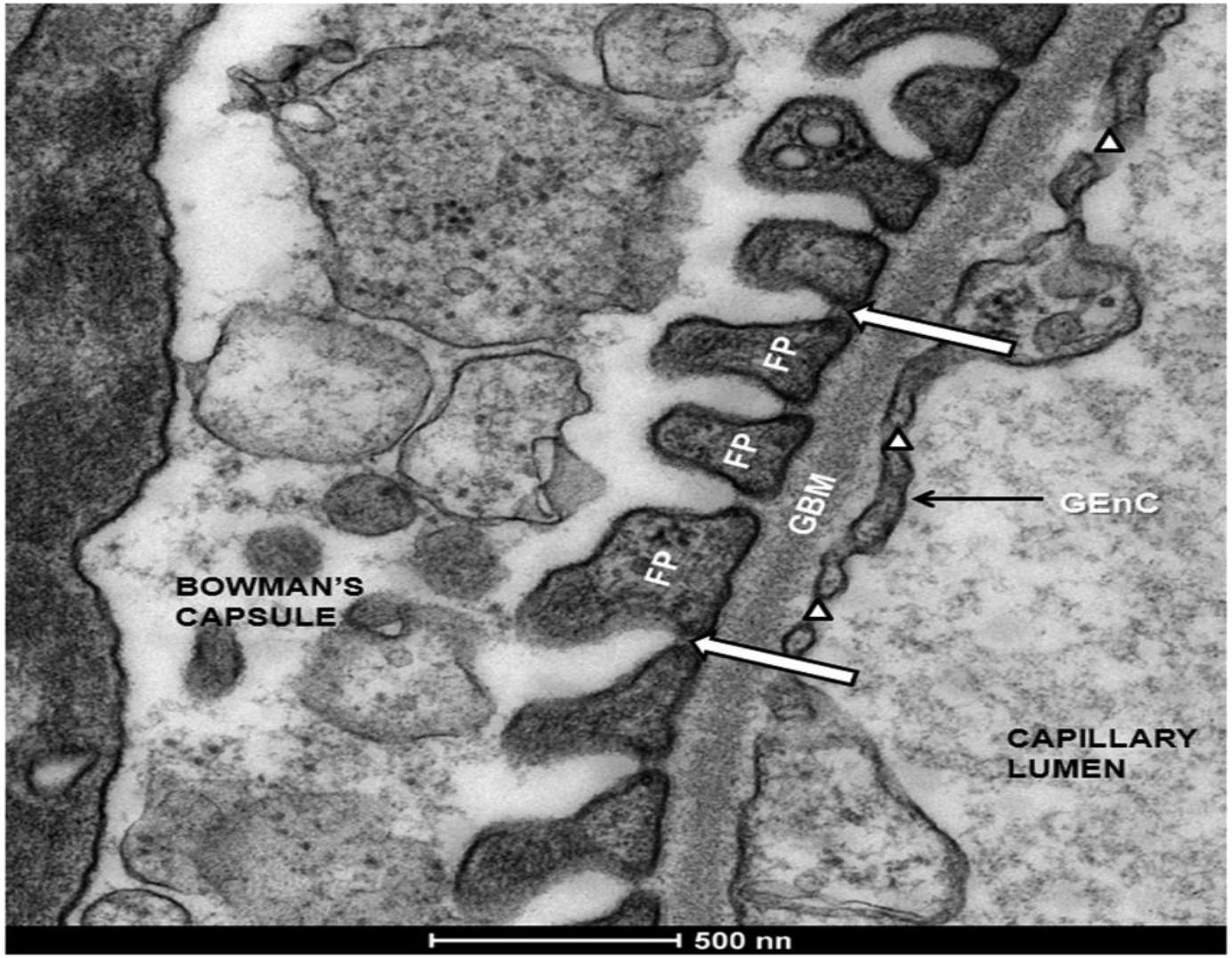
EM- normal GLOMERULUS

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:

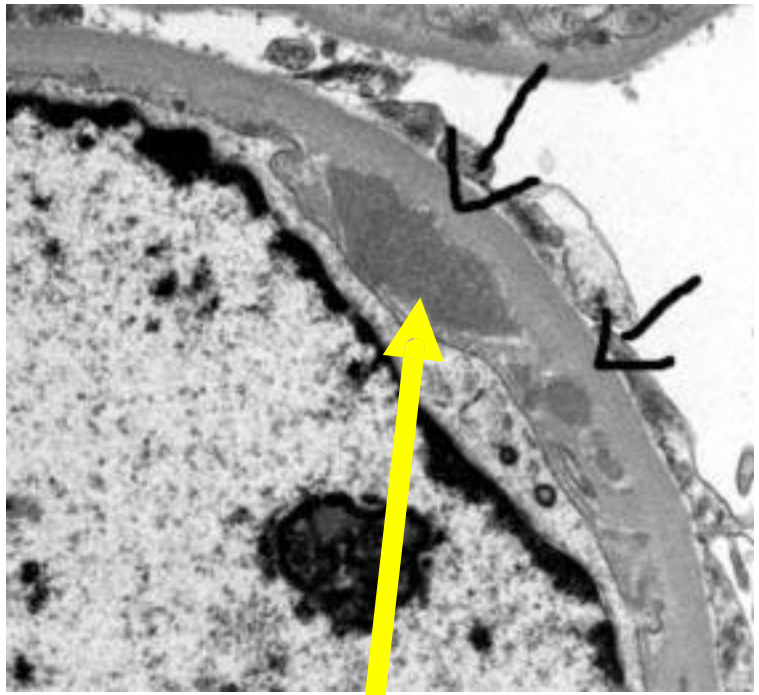
- **reveals the immune complexes as electron-dense deposits or clumps that lie at one of three sites:**

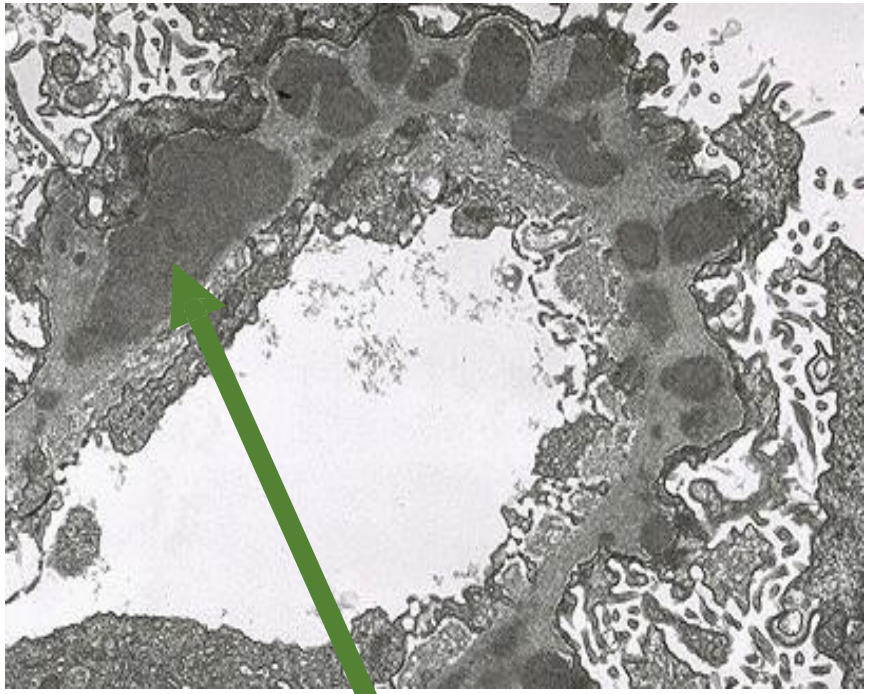
1 - in the mesangium.

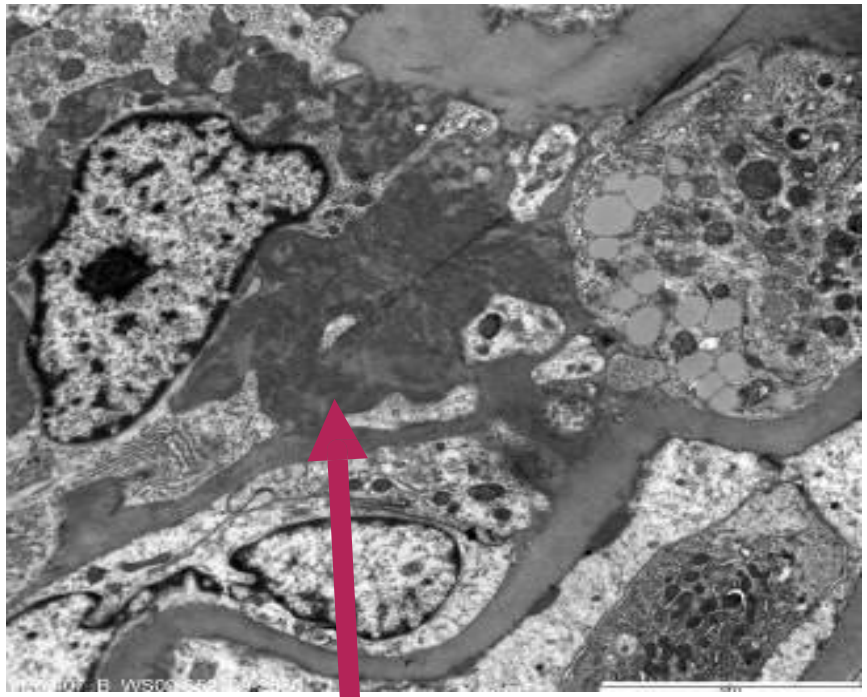
2 - between the endothelial cells and the GBM (subendothelial deposits).

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

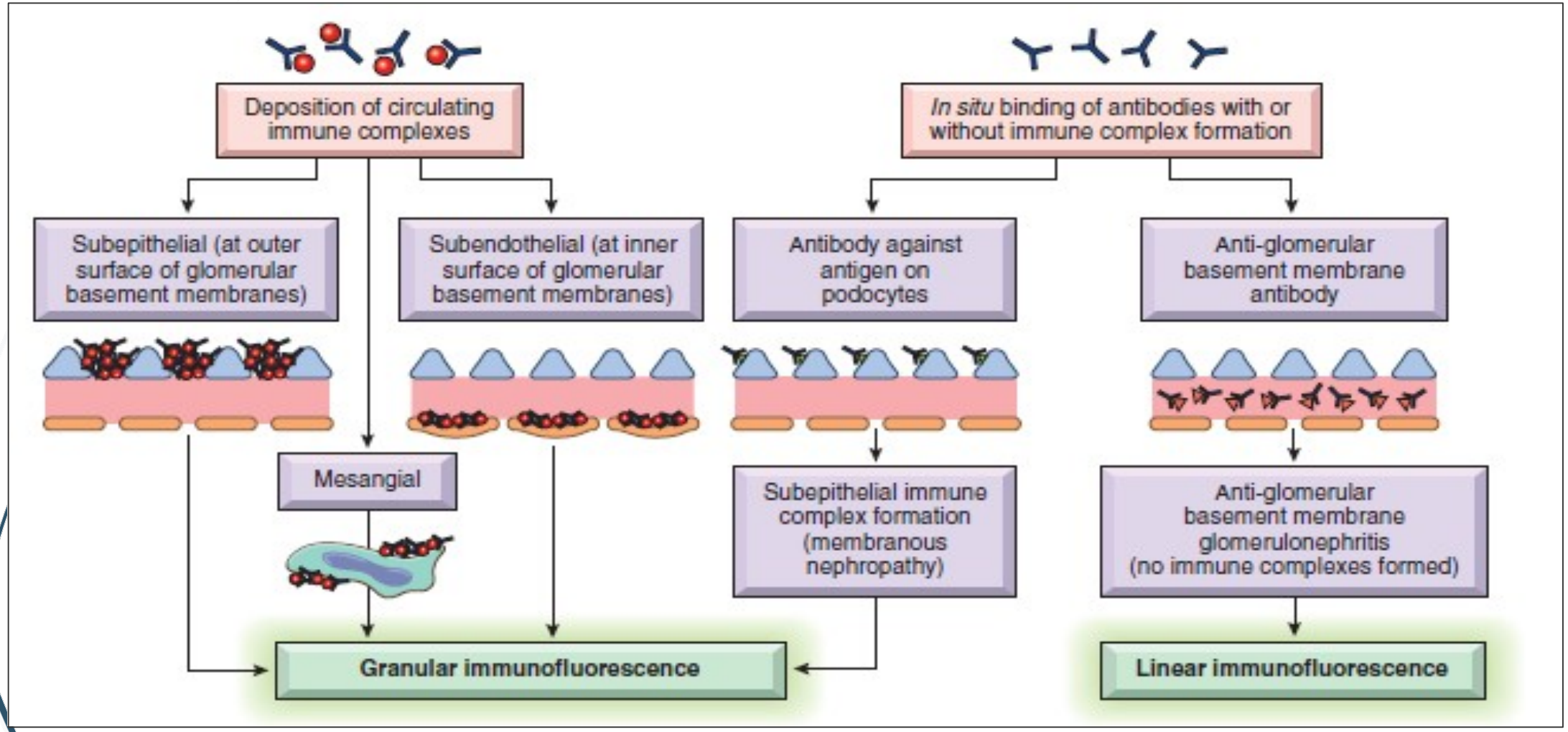
(1)deposition of soluble circulating Ag-Ab complexes in glomerulus.

(2)Abs reacting in situ within the glomerulus.

(3)Abs directed against glomerular cell components.

Antibody-mediated glomerular injury

Imp



Pathogenesis of Glomerular Diseases

2- Non-immune Mechanisms of Glomerular Injury

1) Podocyte Injury: anything that leads to a direct or mechanical injury of the 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)

Pathogenesis of Glomerular Diseases

2) Nephron Loss: anything that leads to progressive loss of functional parts ,include many things like complete loss of the whole kidney and some other diseases

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