# Genito-Urinary Pathology 2024


**Dr.Ghada Nazar Al-Jussani**

**Assistant professor**

**MBCHB.,FRCPATH (UK)**

**Fellowship of royal college of pathologist**

**Jordanian board in pathology**

**Iraqi Board in pathology (PhD)**

**European board in pathology**

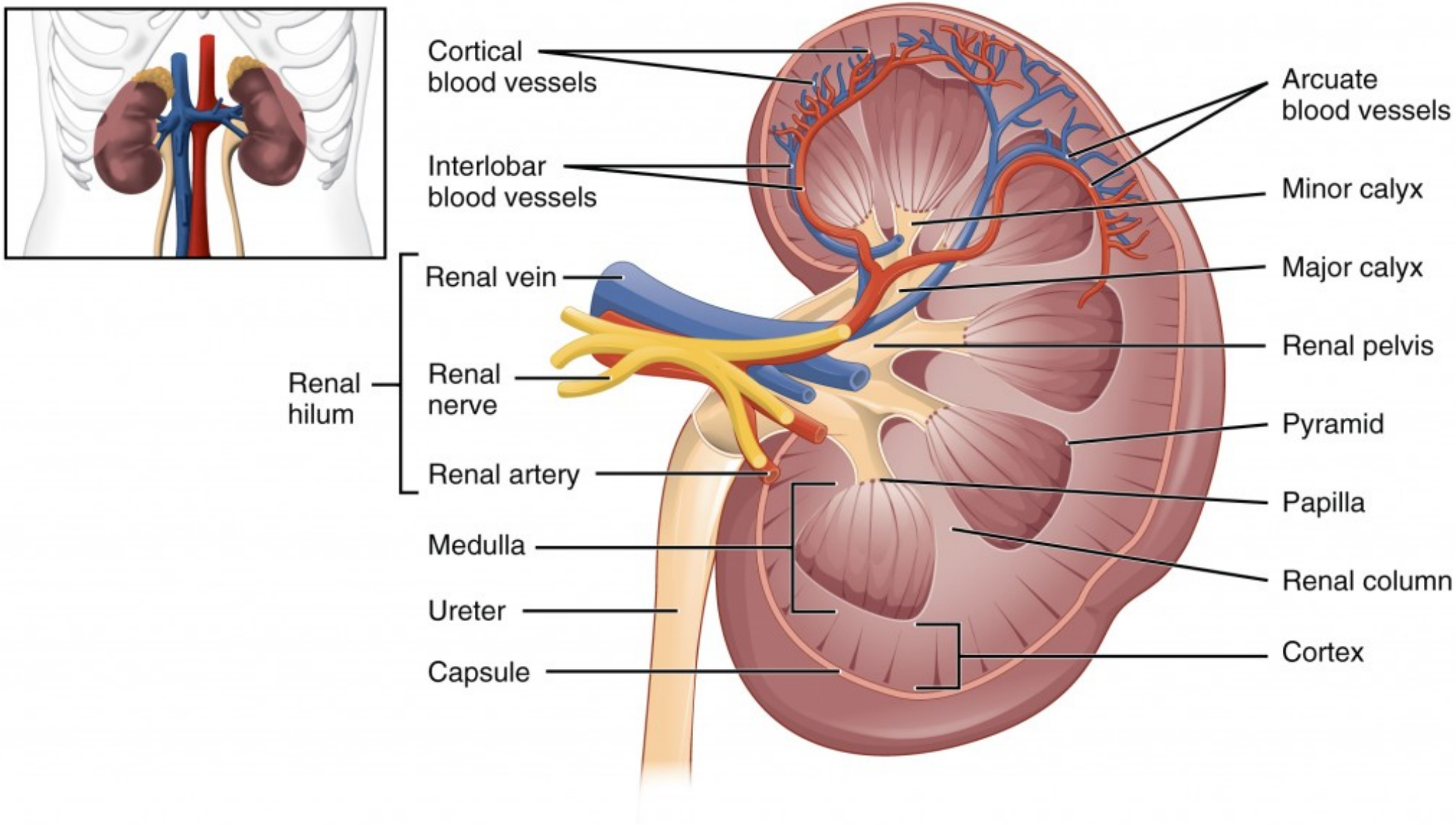
**International fellow College of American pathologist**

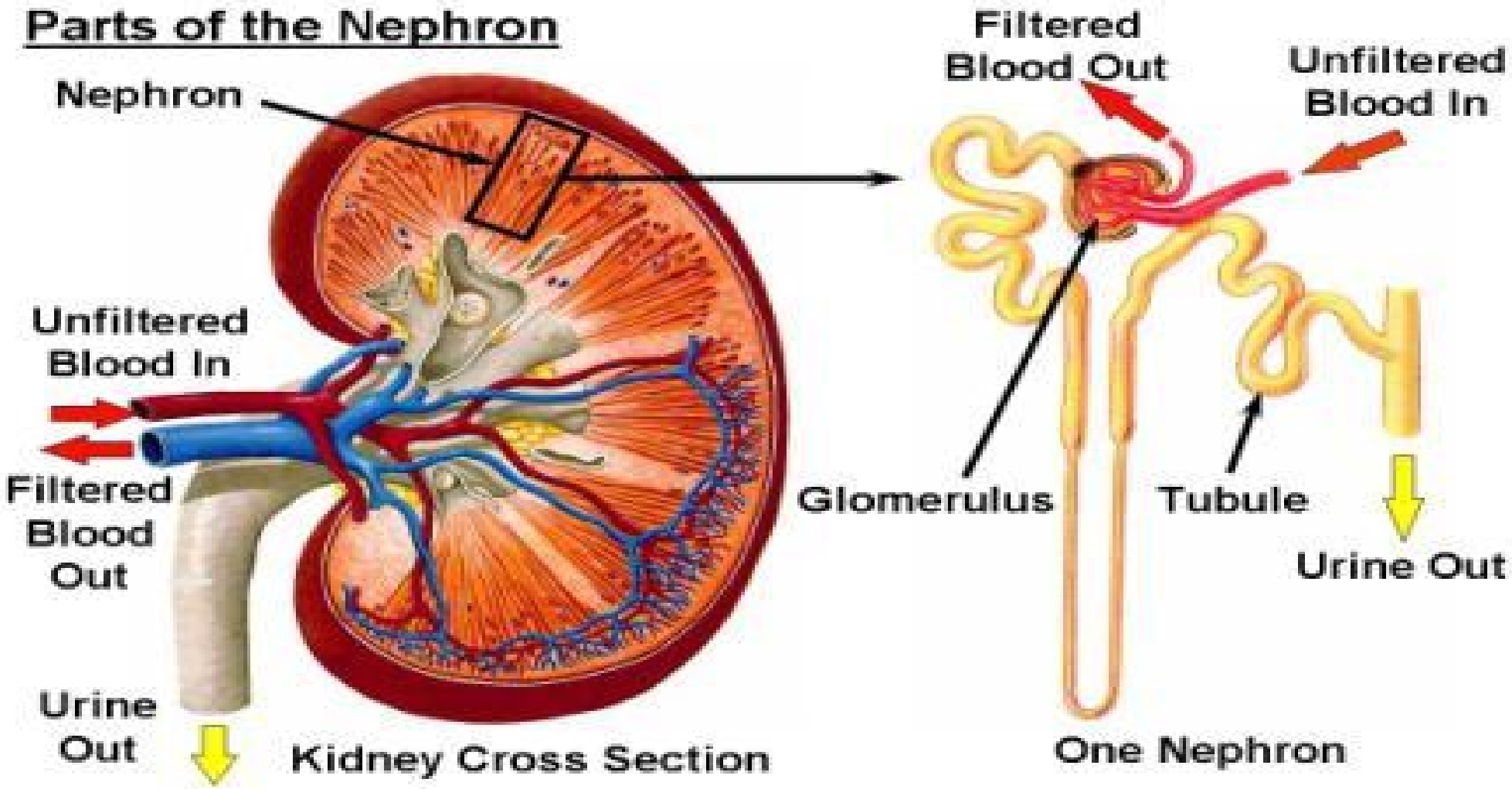
**Medical college ,Hashemite University**

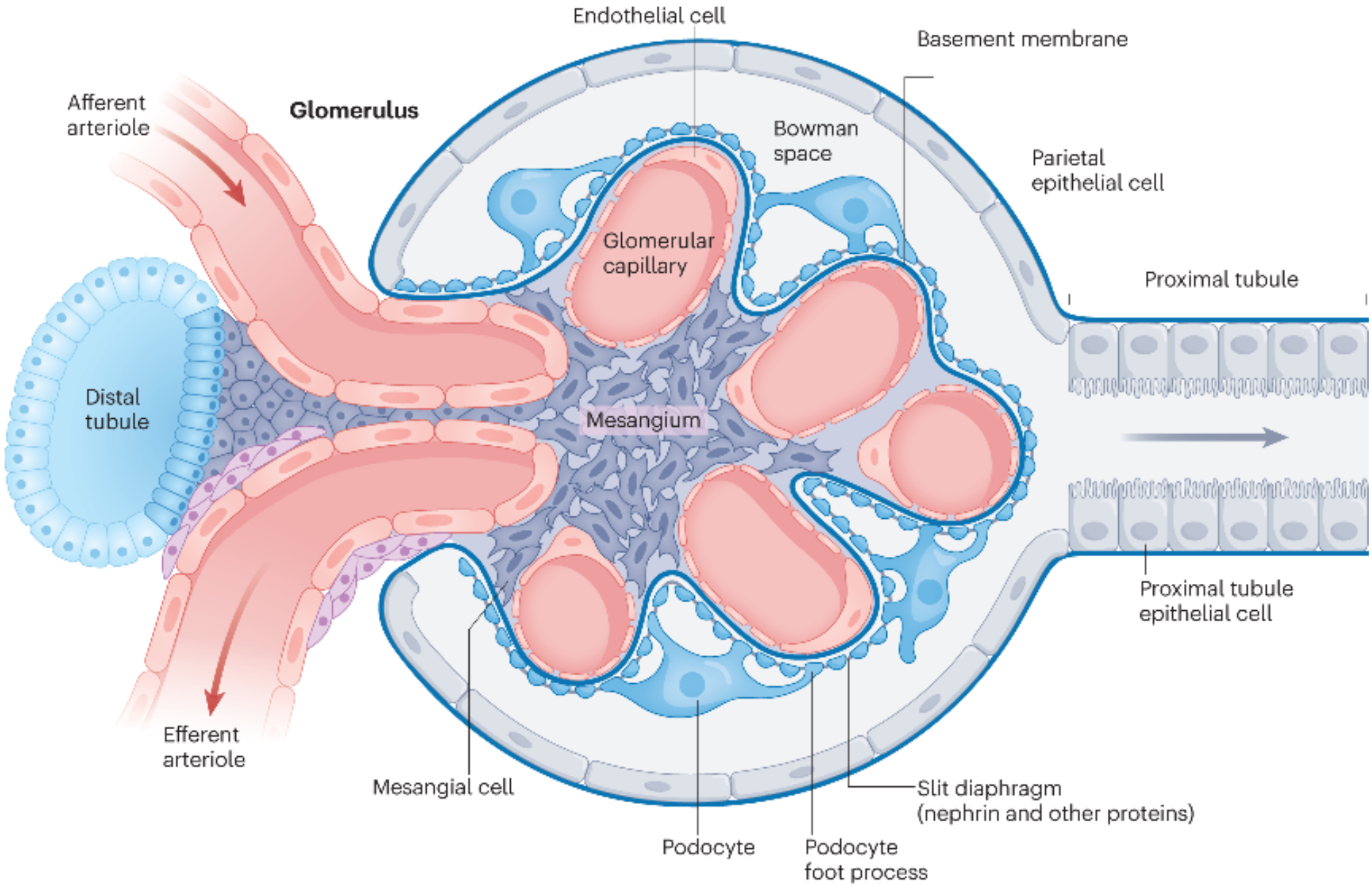
# Objectives

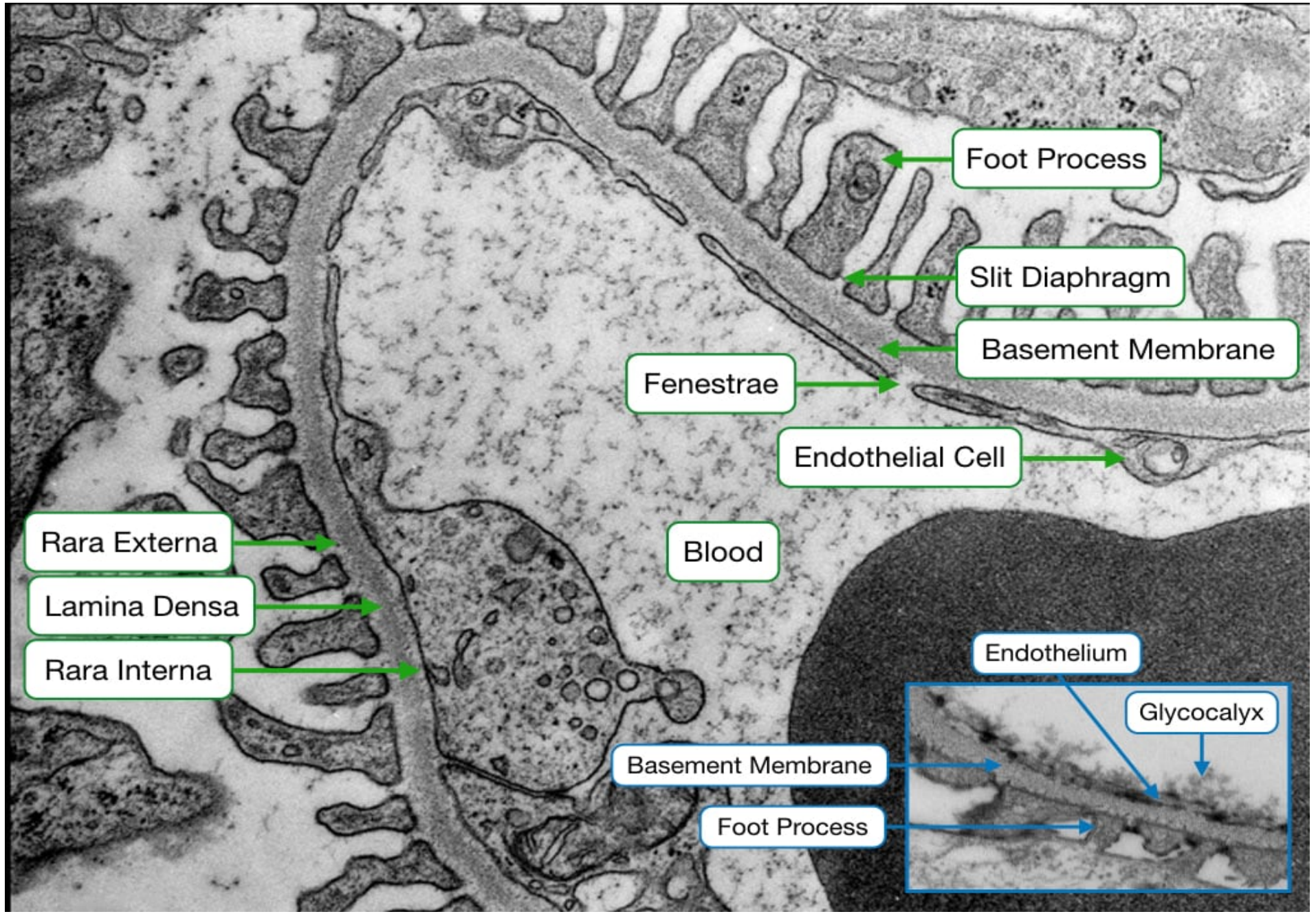
- Clinical manifestation of kidney disease
- understand the terminology of Renal diseases
- Discussion of Glomerular disease
- Nephrotic syndrome
- Nephritic syndrome
- Disease of blood vessels
- Urinary tract infection
- Analgesic nephropathy
- Acute Tubular Necrosis
- Hemolytic Uremic Syndrome
- Urolithiasis and hydronephrosis
- Renal Tumours RCC
- Bladder Tumours

# Normal Kidney structure




Parts of the Nephron
Nephron
Unfiltered Blood In
Filtered Blood Out
Urine Out
Kidney Cross Section
Filtered Blood Out
Unfiltered Blood In
Glomerulus
Tubule
Urine Out
One Nephron


Endothelial cell
Basement membrane
Afferent arteriole
Glomerulus
Bowman space
Parietal epithelial cell
Glomerular capillary
Proximal tubule
Distal tubule
Mesangium
Proximal tubule epithelial cell
Efferent arteriole
Mesangial cell
Slit diaphragm (nephrin and other proteins)
Podocyte
Podocyte foot process


Foot Process
Slit Diaphragm
Basement Membrane
Fenestrae
Endothelial Cell
Blood
Rara Externa
Lamina Densa
Rara Interna
Endothelium
Glycocalyx
Basement Membrane
Foot Process

- **Kidney diseases** can be divided into those affecting the 4 basic components:

**(1) Glomeruli**

**(2) Tubules**

**(3) Blood vessels**

**(4) Interstitium.**

- **B**ecause some components seem to be more vulnerable to specific forms of renal injury; **e.g. glomerular(G)** diseases are often **immunologically mediated**; whereas **tubular & interstitial** disorders are more likely to be caused by **toxic or infectious agents**,

- **The clinical manifestations of renal disease can be grouped into 8 major syndromes:**

Some are peculiar to diseases of G; others are present in diseases that affect any one of the 4 components. These are:

**(1) Acute nephritic syndrome is** a G syndrome characterized by acute onset of gross hematuria (RBCs in urine), **mild to moderate proteinuria, edema, azotemia,& hypertension**; it is the classic presentation of acute post streptococcal GN.

**(2) The nephrotic syndrome is** a G syndrome characterized by **heavy proteinuria (excretion of >3.5 grams of protein/day in adults), hypoalbuminemia, severe edema, hyperlipidemia, & lipiduria(lipid in the urine).**

**(3) Asymptomatic hematuria or proteinuria, or** both, is usually a manifestation of subtle (mild) G abnormalities.

**(4) Rapidly progressive GN** manifested by microscopic hematuria,
dysmorphic RBC & RBC casts in the urine & mild-to-moderate proteinuria, resulting in loss of renal function in a few days or weeks

**(5) Acute renal failure(RF) or (Acute Kidney Injury)**is dominated by **oliguria or anuria** (no urine flow),

**(7) Urinary tract infection(UTI)**characterized by **bacteriuria& pyuria**(bacteria & leukocytes in the urine respectively)).

The infection may be symptomatic or asymptomatic, & it may affect the kidney (pyelonephritis)or the bladder (cystitis).

**(8) Nephrolithiasis(renal stones)** is manifested by **renal colic, hematuria, & recurrent stone formation.**

UT obstruction**&** renal tumors represent specific anatomic lesions that often have varied manifestations.

# Clinical Presentations of Glomerular Disease

**Asymptomatic**

Proteinuria 150 mg to 3 g per day

Hematuria >2 red blood cells per high-power field in spun urine or $>10 \times 10^6$ cells/liter (red blood cells usually dysmorphic)

**Macroscopic hematuria**

Brown/red painless hematuria (no clots); typically coincides with intercurrent infection

Asymptomatic hematuria ± proteinuria between attacks

**Nephrotic syndrome**

Proteinuria: adult >3.5 g/day; child >40 mg/h per $m^2$

Hypoalbuminemia <3.5 g/dl

Edema

Hypercholesterolemia

Lipiduria

**Nephritic syndrome**

Oliguria

Hematuria: red cell casts

Proteinuria: usually <3 g/day

Edema

Hypertension

Abrupt onset, usually self-limiting

**Rapidly progressive glomerulonephritis**

Renal failure over days/weeks

Proteinuria: usually < 3 g/day

Hematuria: red cell casts

Blood pressure often normal

May have other features of vasculitis

**Chronic glomerulonephritis**

Hypertension

Renal impairment

Proteinuria often > 3 g/day

Shrunken smooth kidneys

# Glomerular Disease

- One of the most common causes of **chronic kidney disease** and is major problems encountered in nephrology; and **chronic GN** is one of the most common causes of chronic kidney disease in humans.
- Glomerulonephritis (GN) is serious disorder that can lead to end-stage renal disease (ESRD), other serious morbidity, or death.
- GN is particular topic in nephrology with many clinical variants
- Could be asymptomatic or full blown
- Patients may come with abnormal urinalysis as the only presentation.
- Little is know about the epidemiology of GN, since no large scale examination of GN incidence and prevalence is available.

- The glomerulus normally consists of an anastomosing **network of capillaries,** invested by two layers of epithelium.
- The visceral epithelium (**podocytes**) is an intrinsic part of the capillary wall, whereas the **parietal** epithelium lines **Bowman space**(urinary space), the cavity in which plasma ultrafiltrate first collects.
- The G capillary wall is the filtration unit & consists of the following structures :

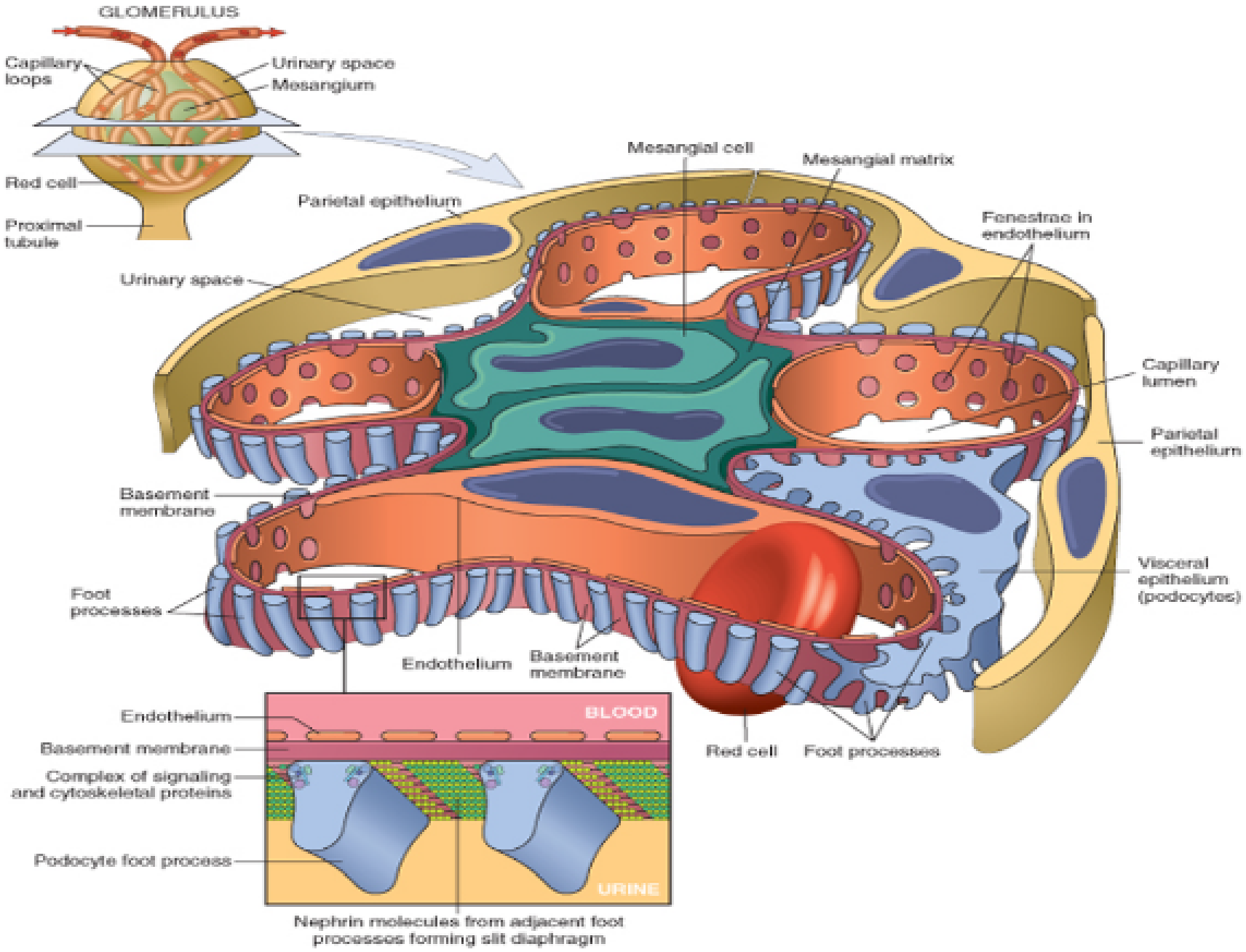
(I) A thin layer of fenestrated endothelial cells (EC).

(II) A glomerular basement membrane(GBM) with a thick, electron-dense central layer, the lamina densa,& thinner, electron-lucent peripheral layers, the lamina rara interna & lamina rara externa.

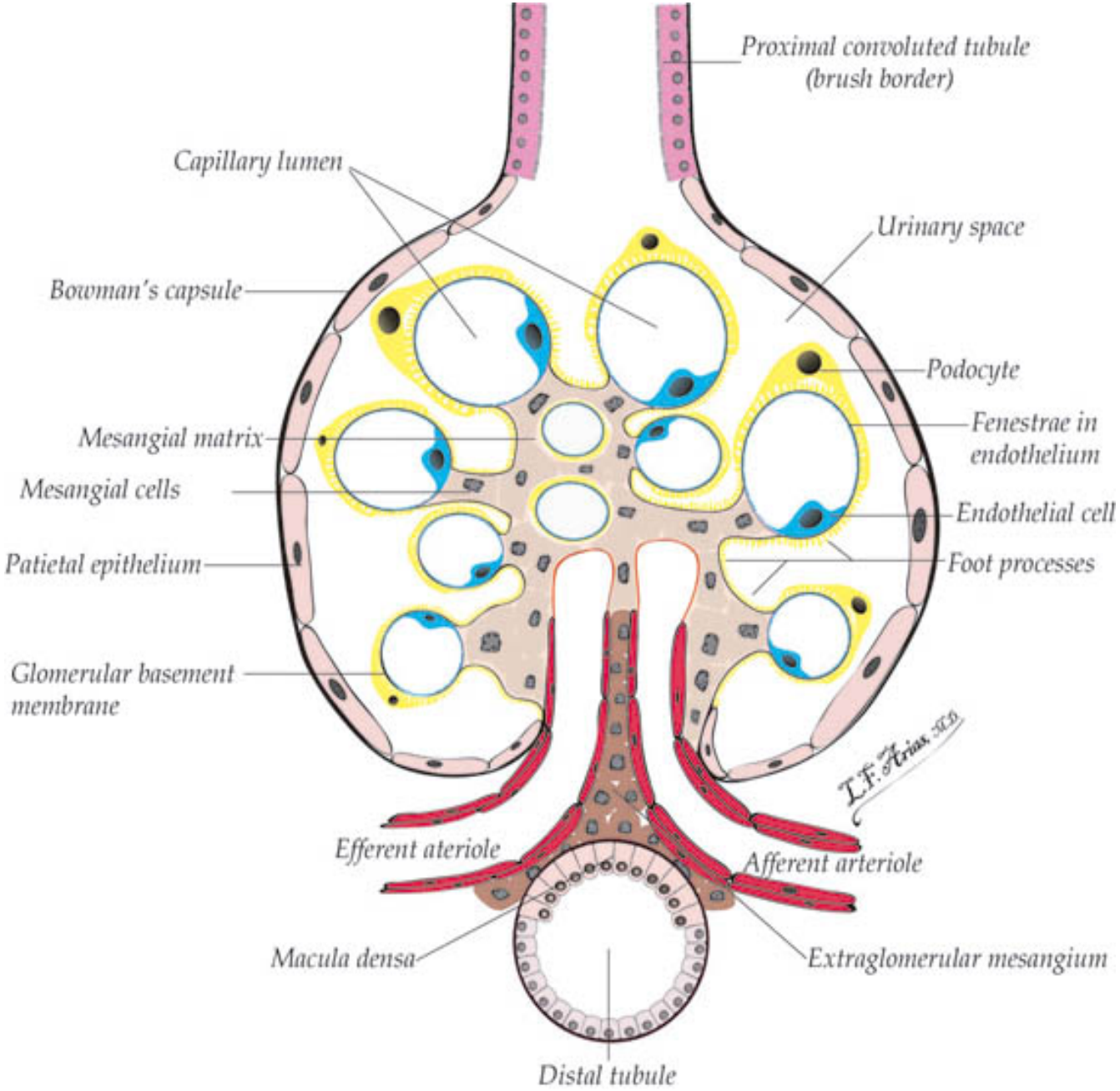
- The GBM consists of collagen (mostly type IV), laminin, proteoglycans, fibronectin, & several other glycoproteins.

(III) The visceral epithelial cells(podocytes),structurally complex cells that possess interdigitating foot processes embedded in & adherent to the lamina rara externa of the GBM.

- **The entire G tuft is supported by mesangial cells (of mesenchymal origin) lying between the capillaries**
- The major characteristics of GF are an extraordinarily **high permeability to water & small solutes**& an almost **complete impermeability to molecules of the size & molecular charge of albumin**(size: 3.6 nm.
- This **selective permeability**, called **glomerular barrier function**, discriminates among protein molecules depending on their size (the larger, the less permeable), their charge (the more cationic (+), the more permeable), & their configuration.



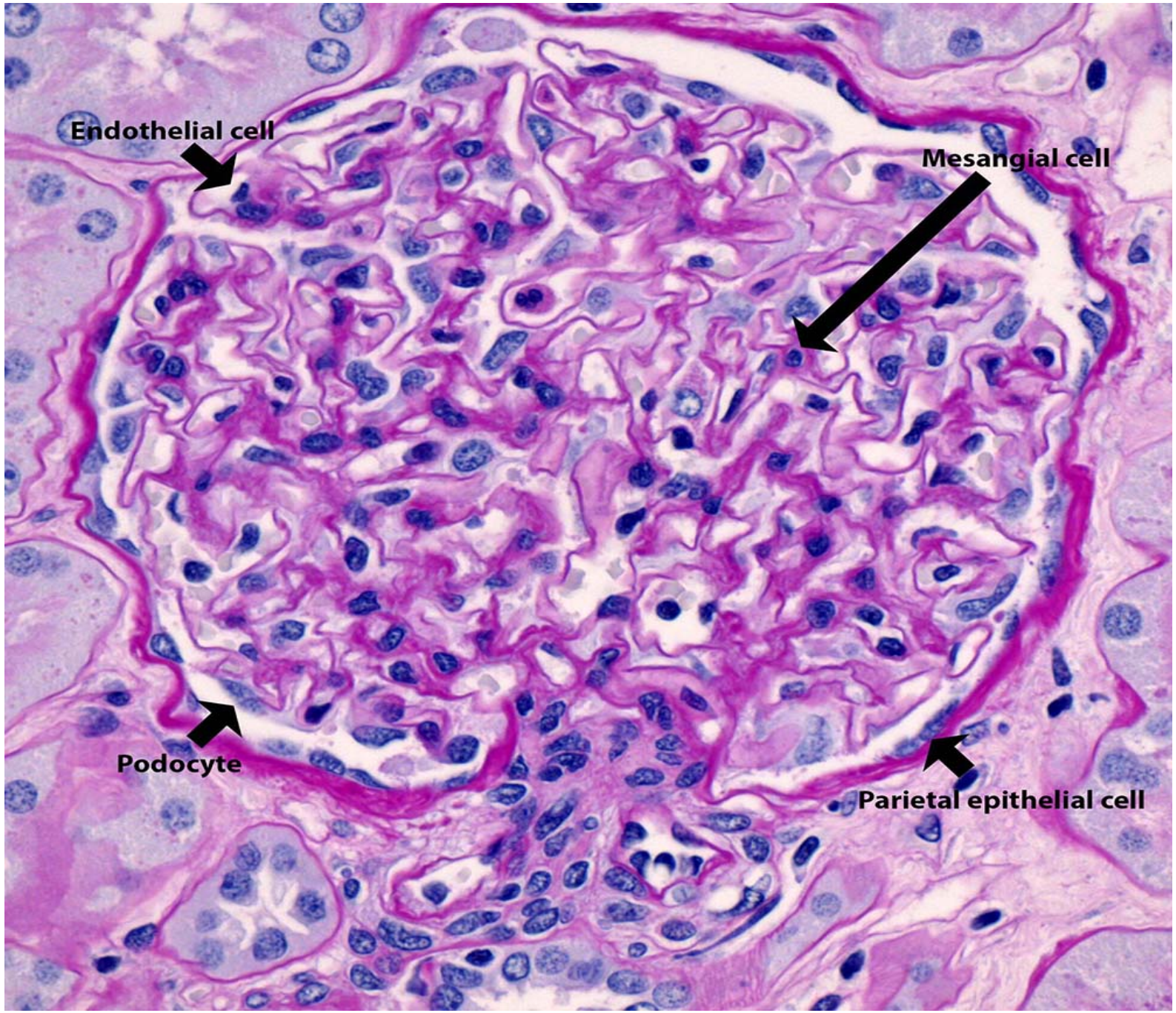

# Schematic diagram of a lobe of a normal glomerulus



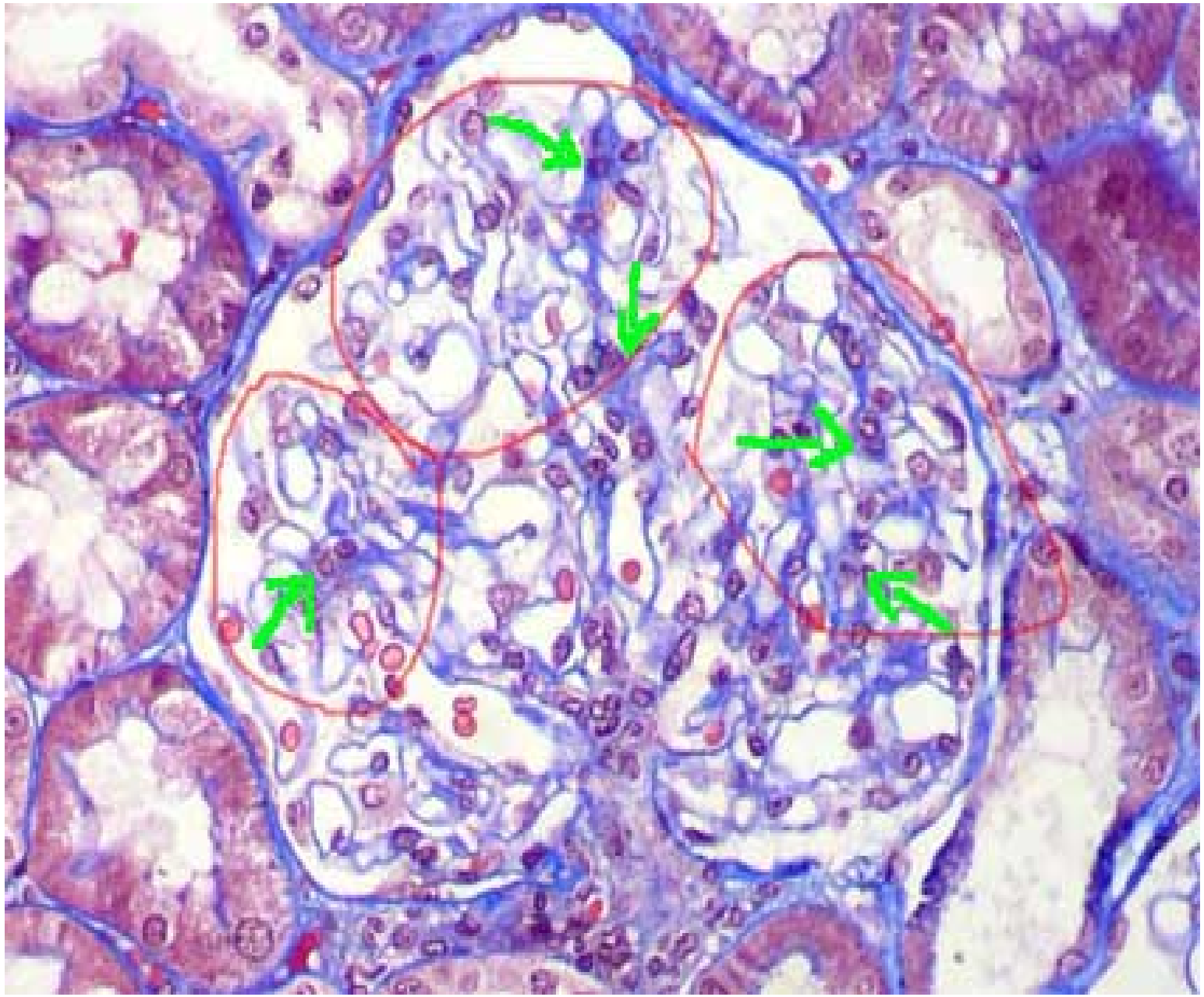

# Representative scheme of a normal glomerulus..

# Normal

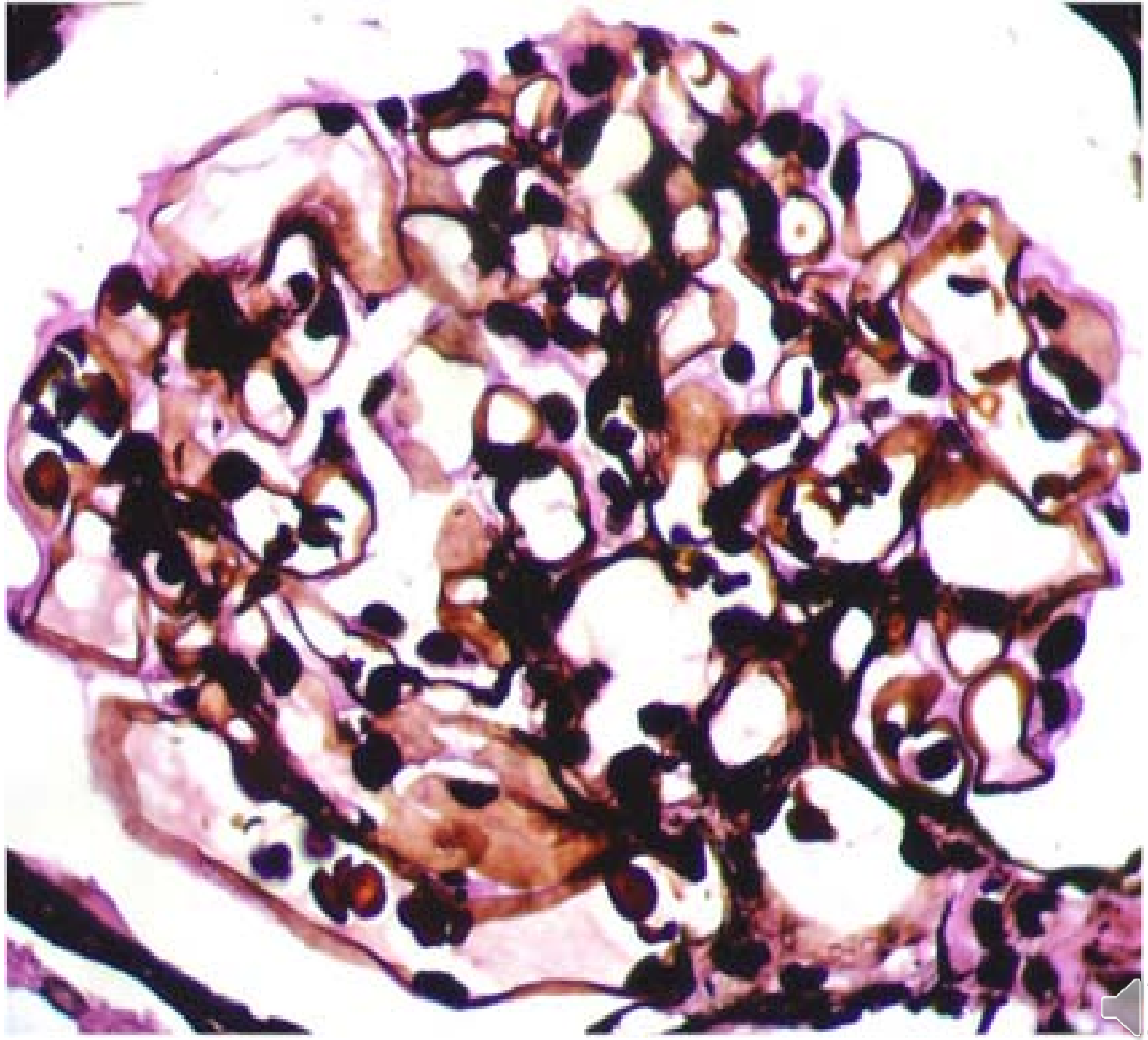
# Glomerulus



**The lobules appear highlighted in red; in normal glomeruli is difficult to determine with precision its limit.**
**Within each lobe there are several mesangial areas (some of them indicated with green arrows) in which there are not more than 2 or 3 nuclei of cells (Masson's trichrome, X300).**



**The mesangial matrix, like the basement membranes of capillaries, Bowman's capsule, and tubules are rich in type IV collagen, and has affinity by the methenamine-silver stain.**
**See the irregular characteristic aspect of mesangial matrix (in black) in a normal glomerulus (Methenamine-silver, X.400).**



Glomeruli may be injured by diverse mechanisms, which are either :

- Primary G diseases, those in which the kidney is the only or predominant organ involved.

- Secondary G diseases in which the G may be injured in the course of a number of systemic diseases(hereditary , metabolic , vascular etc )

# Glomerular Diseases

## (I) Primary Glomerular Diseases

- Minimal-change disease (MCD)
- Focal and segmental glomerulosclerosis (FSGS)
- Membranous GN = Membranous nephropathy (MN)
- Membranoproliferative GN (MPGN)
- Acute postinfectious GN
- IgA nephropathy
- Chronic GN

## (II) Glomerulopathies Secondary to Systemic Diseases

- Lupus (SLE) nephritis
- Diabetic nephropathy
- Goodpasture syndrome
- Microscopic polyangiitis
- Wegener's granulomatosis
- Henoch-Schönlein purpura
- Thrombotic microangiopathy
- Amyloidosis
- Bacterial endocarditis-related GN
- GN secondary to extrarenal infection
- GN secondary to lymphoplasmacytic disorders

# Glomerular diseases

- Primary Glomerular diseases
  - Minor Glomerular abnormalities:

  Minimal Change disease
  - Focal and/or segmental lesions:

  Focal glomerulosclerosis

  Focal proliferative glomerulonephritis
  - Diffuse glomerulonephritis
  - Chronic GN (Irreversible and most common cause of CRF)

- Glomerulopathies in Systemic diseases
  - SLE
  - Diabetes mellitus
  - Goodpasture
  - Bacterial endocarditis
  - Amyloidosis
  - Vascular disorders
    - Hypertension
    - PAN
    - Wegener's granulomatosis
    - Henoch-Schönlein purpura.



# Pathogenesis of Glomerular disease

- **Usually immune mediated** via antibody deposition, cell mediated injury or activation of alternative complement pathway
- **Antibodies deposited** are either to **in situ antigen (intrinsic or planted) or are circulating immune complexes**

 **Intrinsic:** **Good pasture disease antigens are in basement membrane; Heymann nephritis antigens are on visceral epithelial cells; produce linear immunofluorescence patterns.**

 **Planted antigens** are deposited in basement membrane; may be exogenous **(drugs, infectious agents)** or endogenous **(DNA, immunoglobulin, immune complexes)**; their cationic proteins bind to glomerular anionic sites and produce granular lumpy staining by immunofluorescence

- **Circulating immune complexes** may be endogenous (DNA, tumors) or exogenous (infectious products); they usually localize within glomeruli and activate complement; deposits are usually mesangial or subendothelial and resolve by macrophage phagocytosis, unless there are repeated cycles of formation (Hepatitis B / C, lupus)
- **Cell mediated immune injury** is by sensitized nephritogenic T cells
- **Progression** to end stage renal disease occurs when the glomerular filtration rate (GFR) is **30 - 50%** of normal, due to compensatory hypertrophy of remaining glomeruli and systemic hypertension (inhibited by angiotensin converting enzyme inhibitors), eventually causing glomerulosclerosis

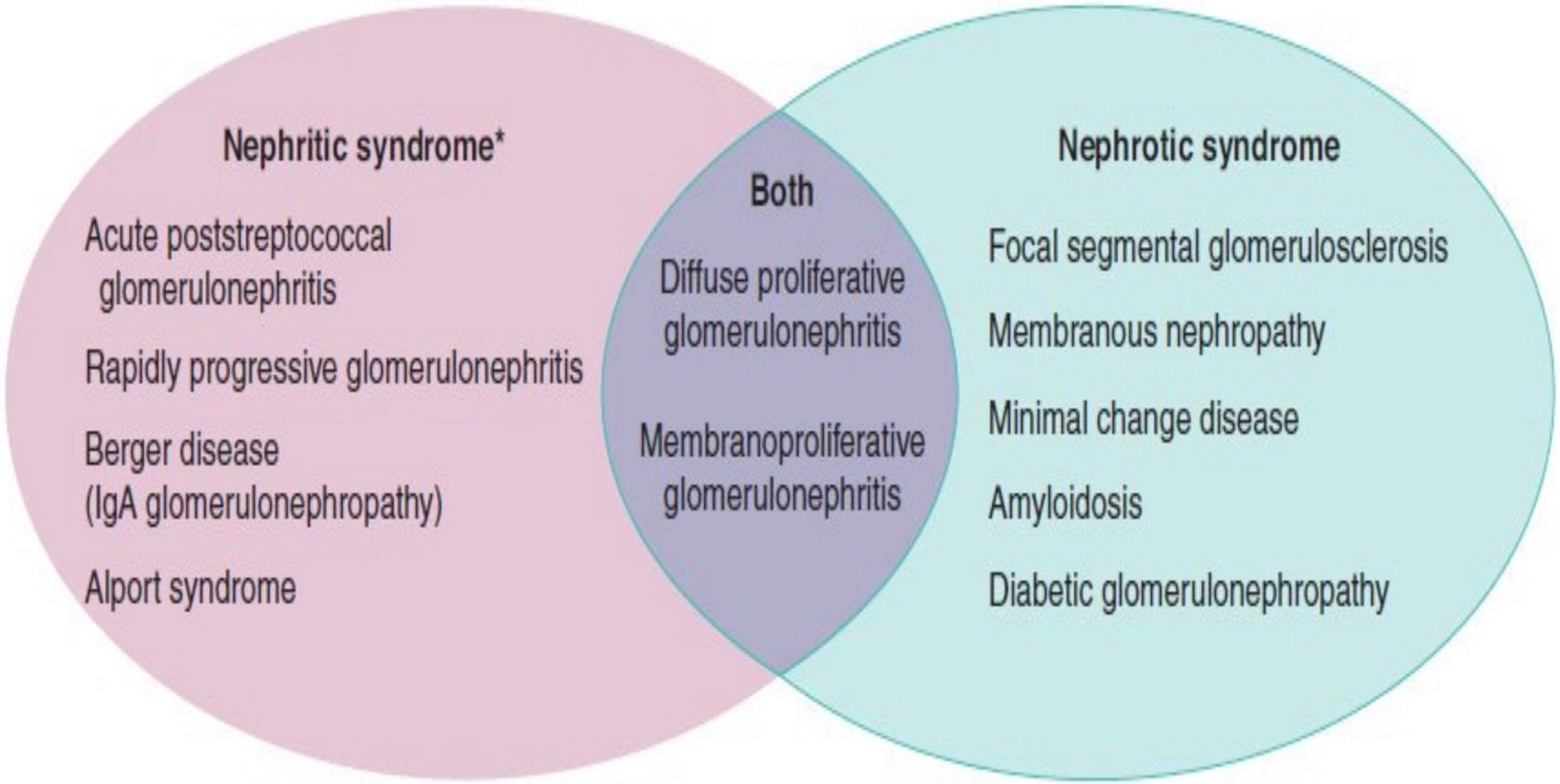
# Pathogenesis of Glomerular Diseases

- **Antibody-associated**
- **(1) injury resulting from deposition of soluble circulating Ag-Ab complexes in the glomerulus.**
- **(2) injury by Abs reacting in situ within the glomerulus.**
- **(3) Abs directed against glomerular cell components.**

## 1-Nephritis Caused by Circulating Immune Complexes

- **The antigen is not of glomerular origin.**
- **1- endogenous as in the GN associated with SLE.**
- **2- exogenous as in the GN that follows certain bacterial (streptococcal), viral (hepatitis B), parasitic (*Plasmodium falciparum* malaria), and spirochetal *(Treponema pallidum)* infections**

## Glomerular diseases




*Note that classic nephritic disorders can exhibit nephrotic features.