

How to approach Hematuria

How to approach Proteinuria

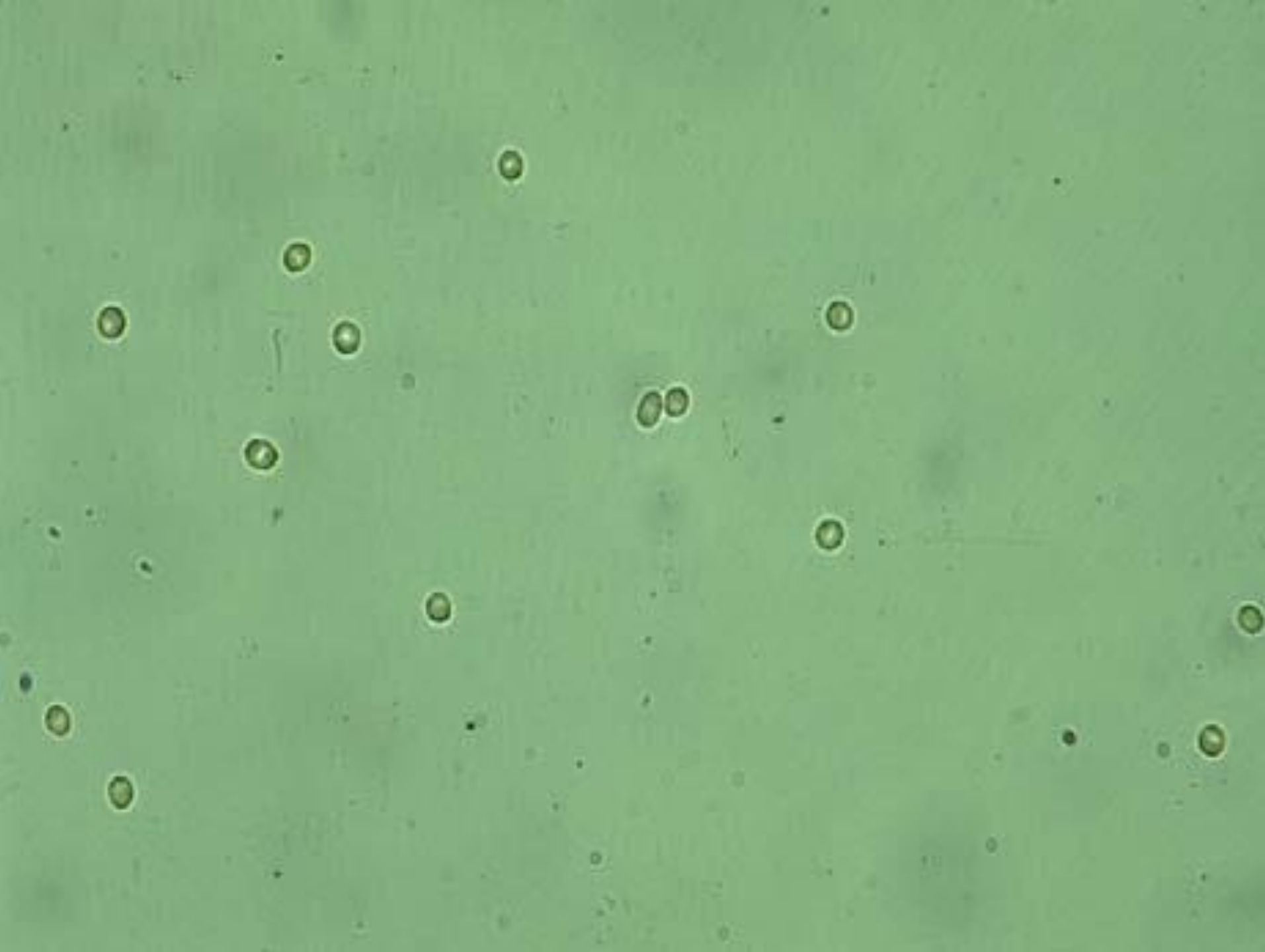
Glomerulonephritis Overview

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- **Definition of Hematuria:**

Presence of at least 3 RBCs per high power field (HPF) in a spun urine

HPF: 400x magnification level





Microscopic Hematuria: Non-visible, detected by microscopy.

Macroscopic Hematuria = Gross hematuria

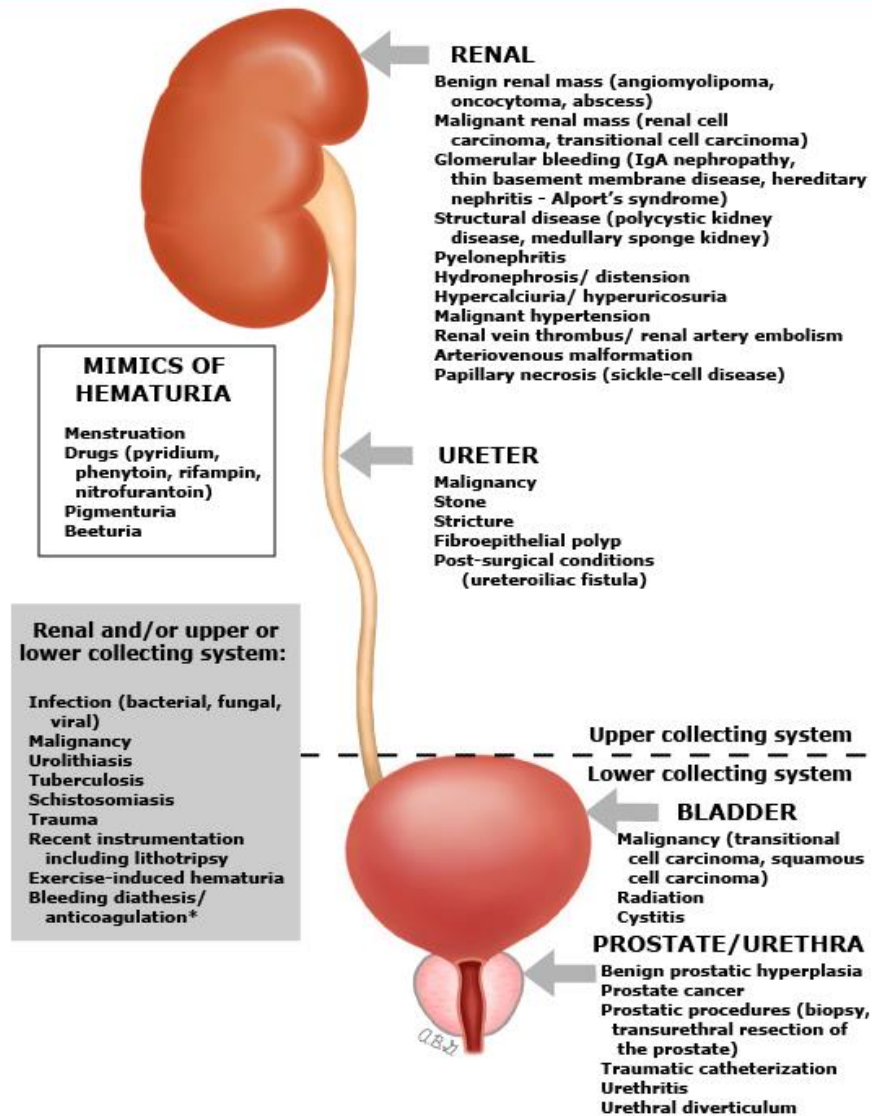
Not every dark urine means Hematuria:

Conditions where the urine becomes dark and positive for heme on dipstick but negative for RBCs on microscopy (+ve dipstick but no hematuria):

- Intravascular hemolysis (Hemoglobin)
- Rhabdomyolysis (Myoglobin).

Negative dipstick exclude hematuria.

Causes of hematuria



* Hematuria may not be attributed solely to alterations in coagulation or platelet function until competing causes have been ruled out.

Courtesy of Michael Kurtz, MD.

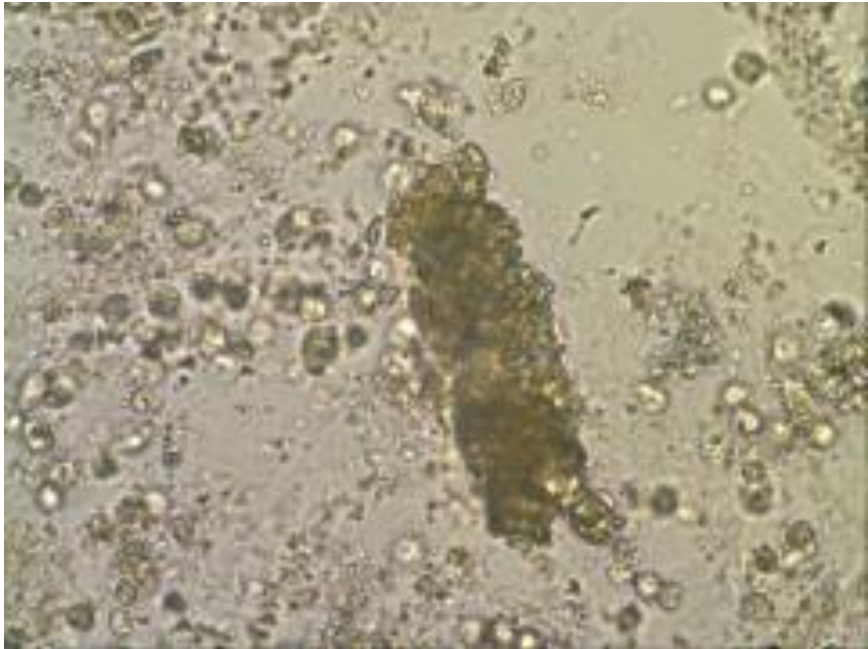
Main causes of Hematuria:

- Glomerular

Non- Glomerular:

- Stones
- Tumors
- Infections
- Trauma

- In **Interstitial nephritis**: Urinalysis typically show WBCs, RBCs and WBC casts.
- **Acute tubular necrosis**: Characterized by Heme granular cast (muddy brown cast) on urinalysis.
Typically there are **no** RBCs however presence of some won't exclude the possibility of ATN.



Gross Hematuria:

Distinguishing extraglomerular from glomerular hematuria

	Extraglomerular	Glomerular
Color (if macroscopic)	Red or pink	Red, smoky brown, or "Coca-Cola"
Clots	May be present	Absent
Proteinuria	<500 mg/day	May be >500 mg/day
RBC morphology	Normal	Some RBCs are dysmorphic
RBC casts	Absent	May be present

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RBC Cast



RBC cast



- Commonest type of glomerulonephritis that can present with gross hematuria:

IgA nephropathy

Post infectious glomerulonephritis

Both can be triggered by URTI

Both can cause nephritis: AKI, HTN

The onset of hematuria in relation to the URTI is important:

In IgA: it is synpharyngitic (within 4 days after URTI symptoms) while in post infectious is usually 1 week– 2 weeks.

The definitive way of differentiation is renal biopsy.

- **Commonest Causes of Isolated glomerular microscopic hematuria (without proteinuria or renal impairment):**

IgA nephropathy

Thin basement membrane (benign familial hematuria)

Alport's syndrome

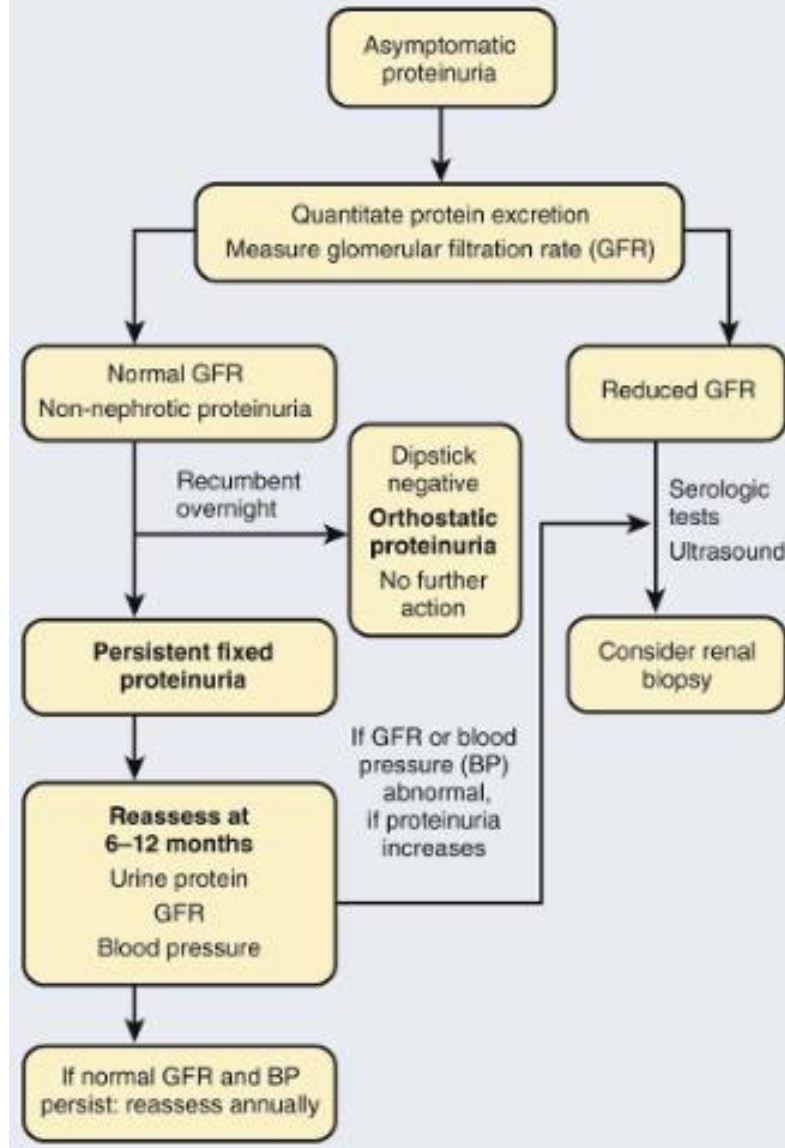
- **Indication for biopsy in microscopic hematuria:**

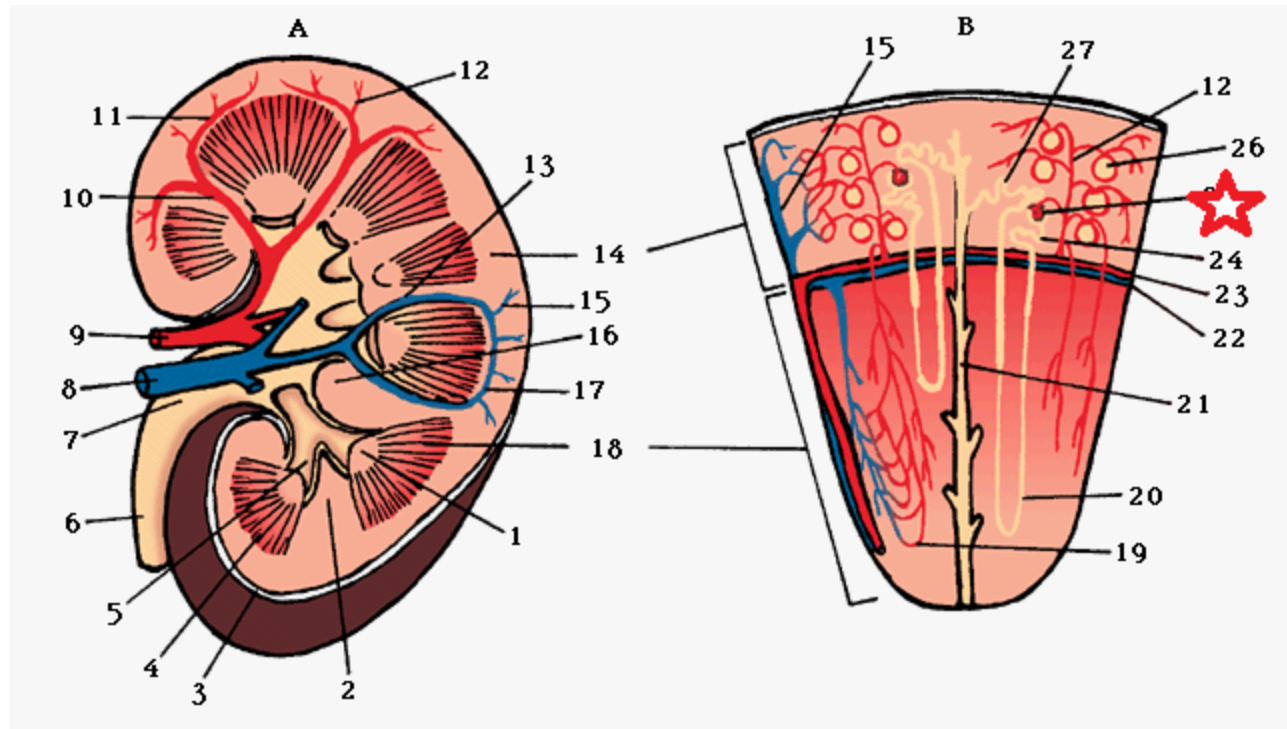
renal impairment or

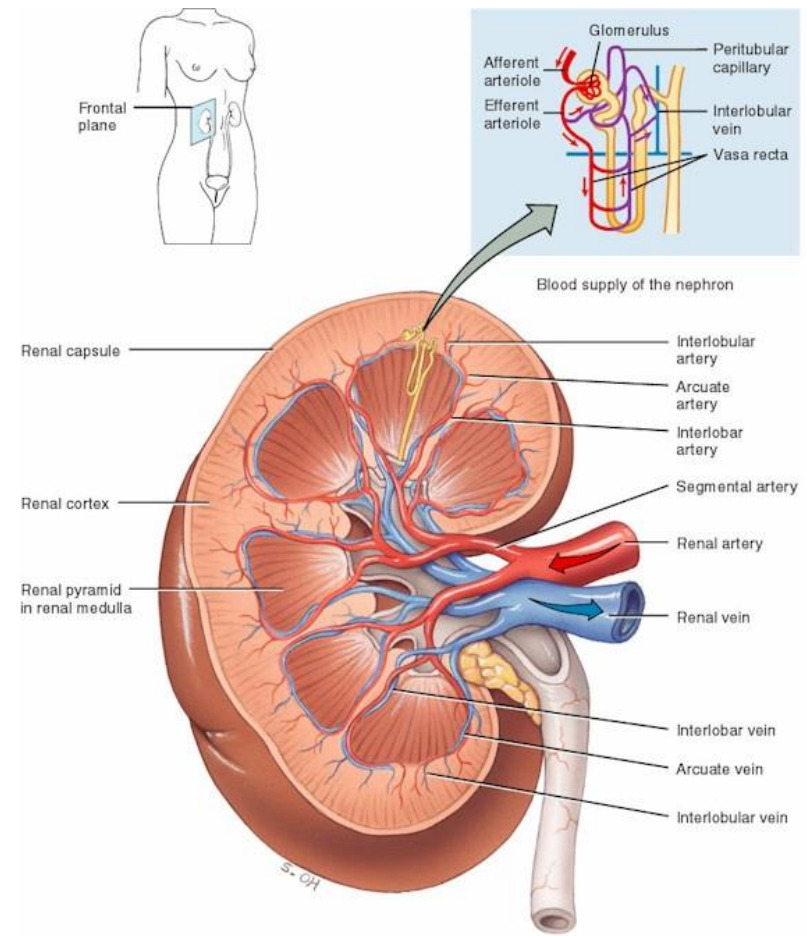
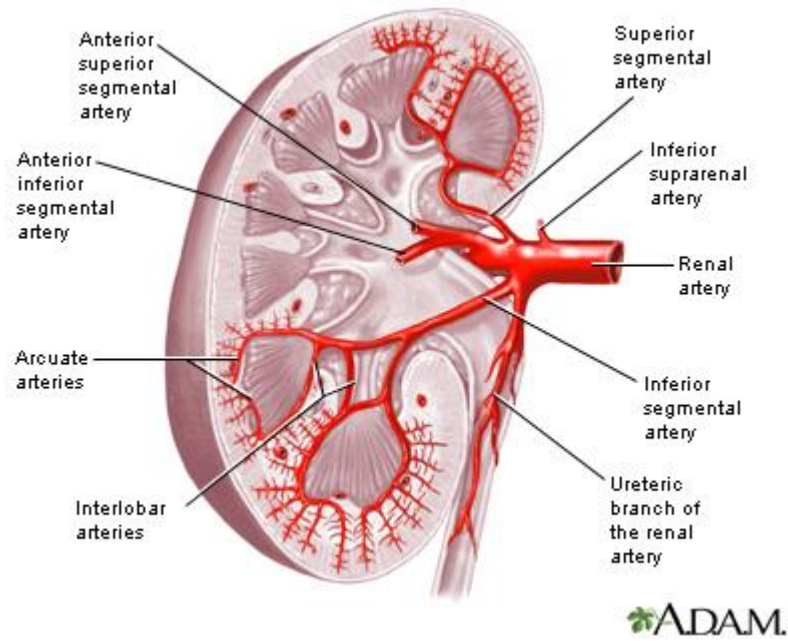
Presence of proteinuria > 1 g/day or

HTN

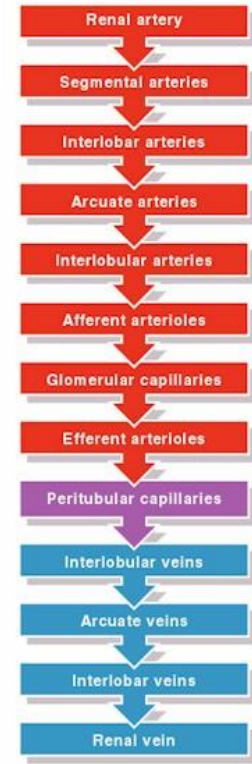
Evaluation of Isolated Asymptomatic Proteinuria



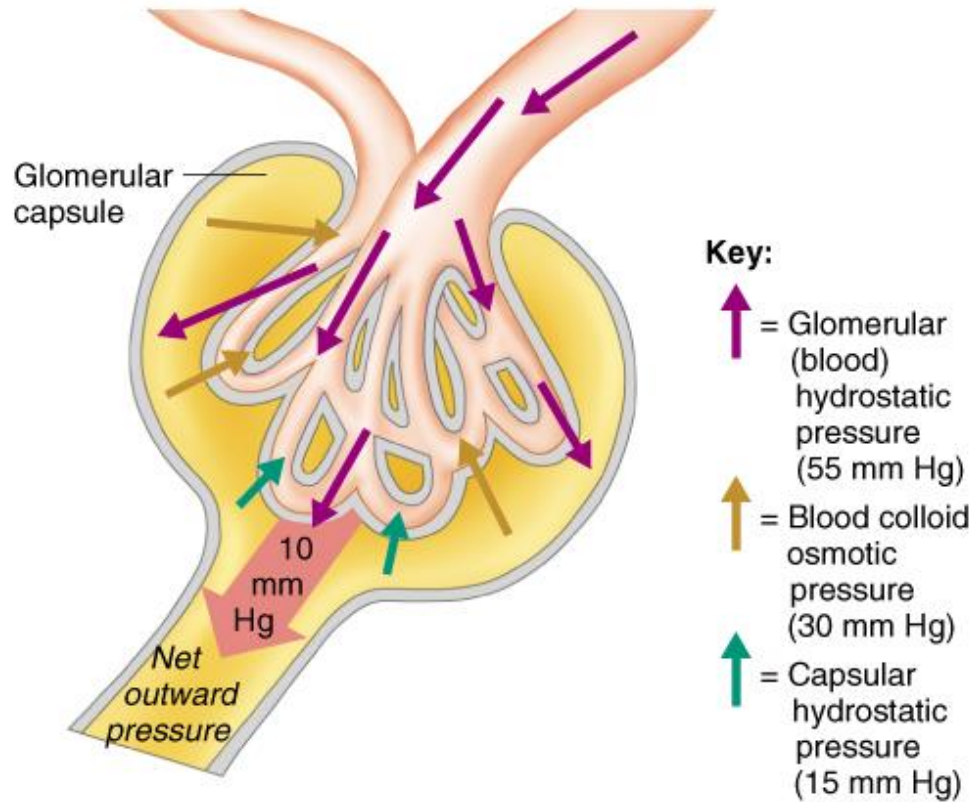




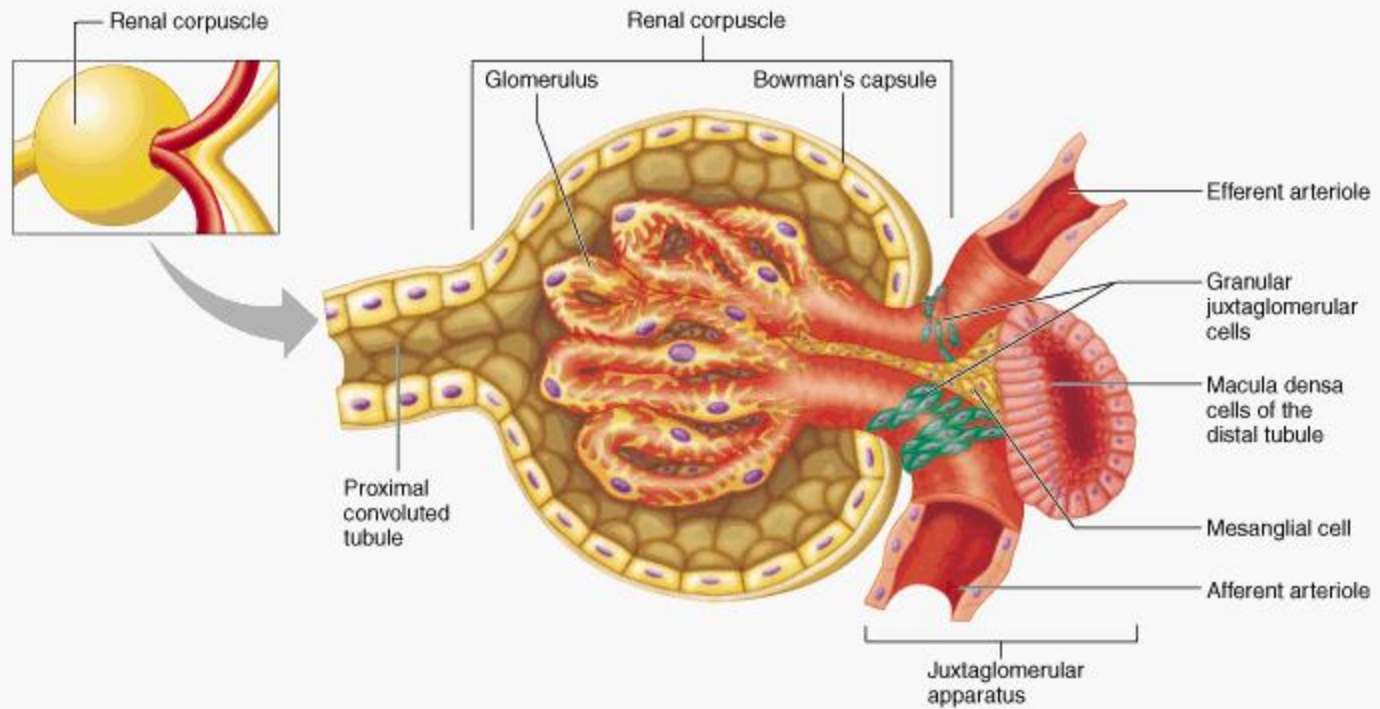
(a) Frontal section of right kidney



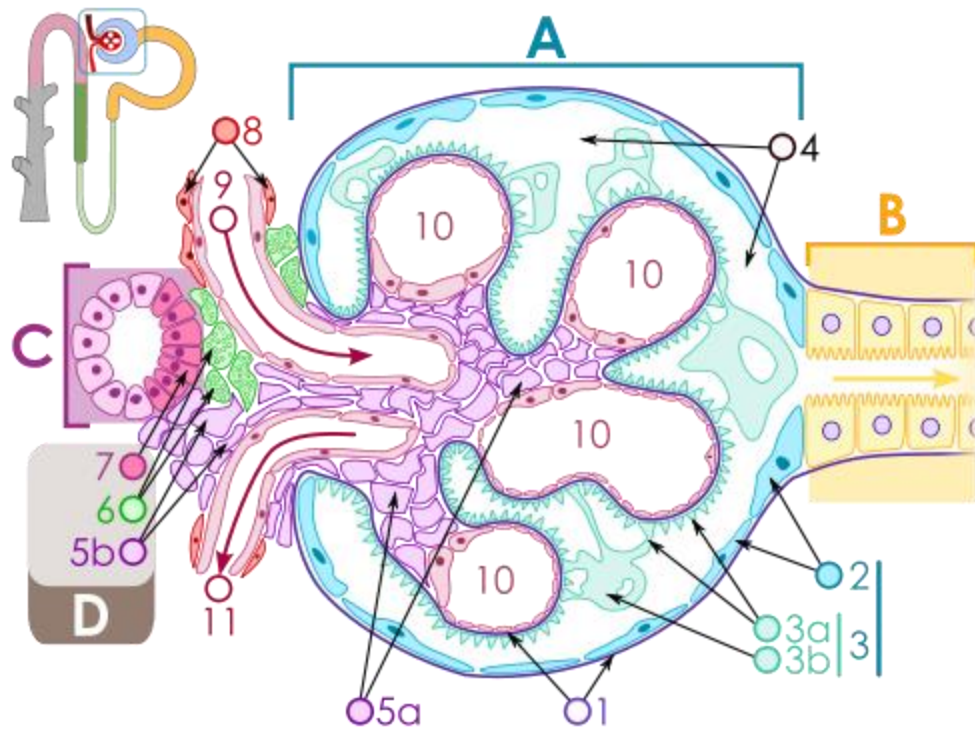
(b) Path of blood flow

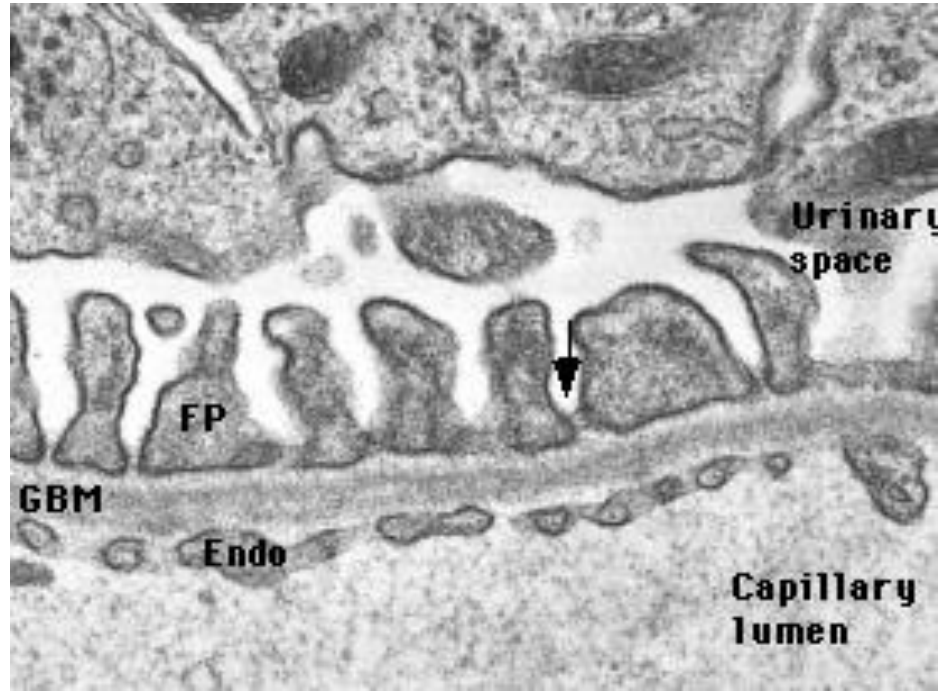


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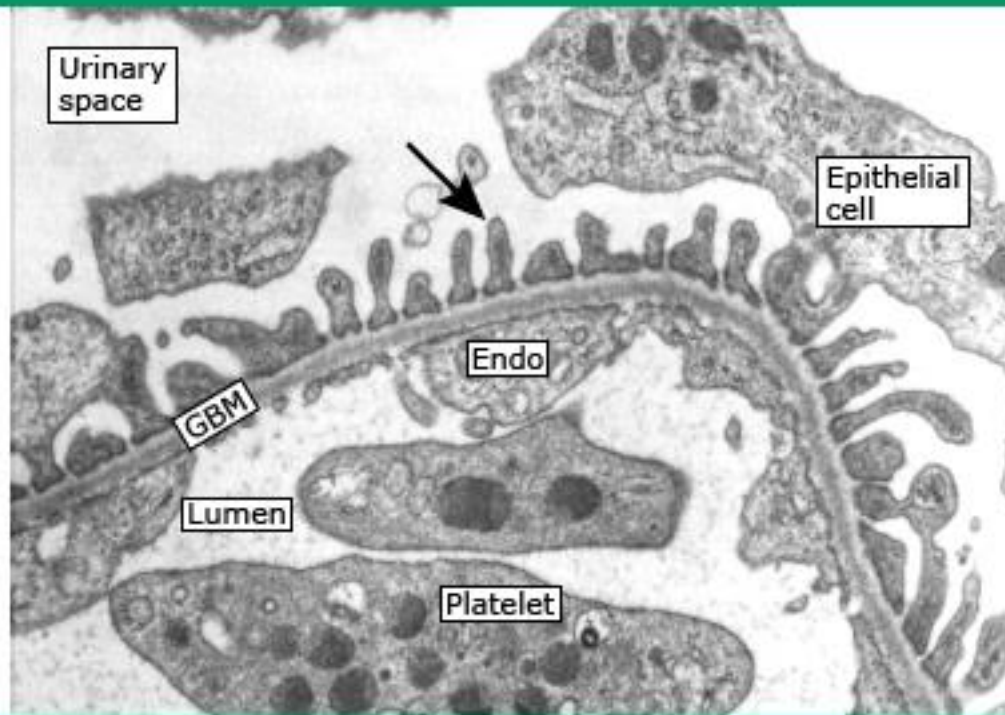


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Electron micrograph of a normal glomerulus



Electron micrograph of a normal glomerular capillary loop showing the fenestrated endothelial cell (Endo), the glomerular basement membrane (GBM), and the epithelial cells with its interdigitating foot processes (arrow). The GBM is thin, and no electron-dense deposits are present. Two normal platelets are seen in the capillary lumen.

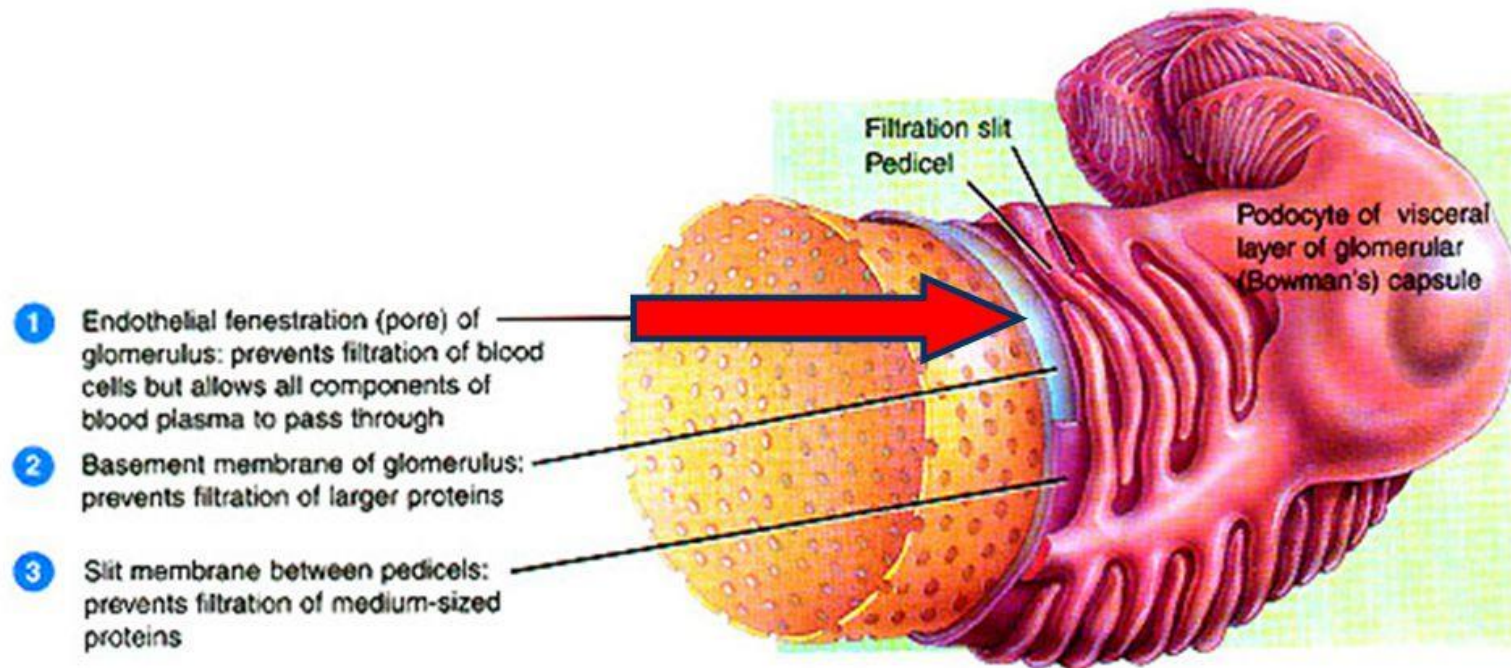
Courtesy of Helmut G Rennke, MD.

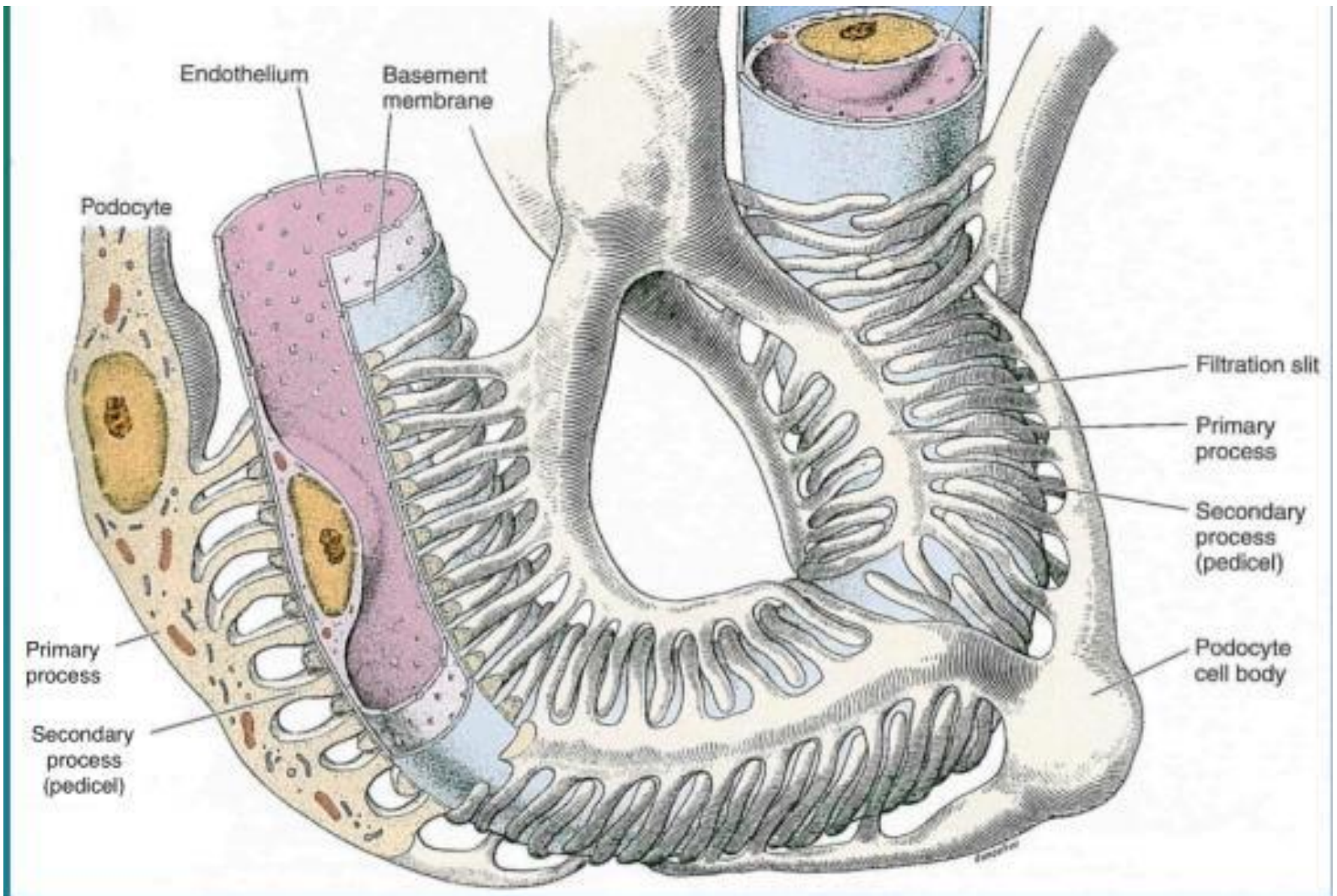
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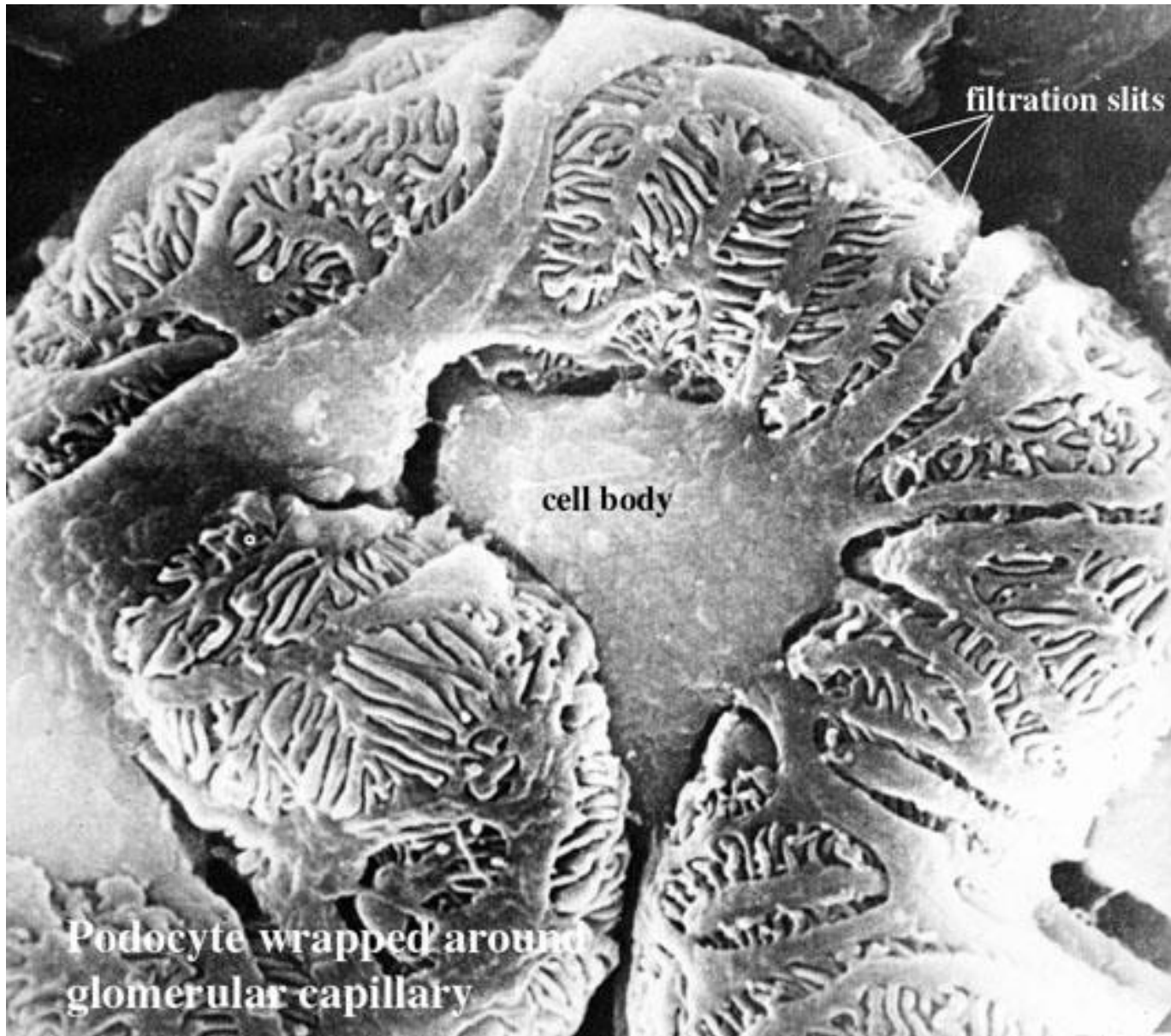
Renal Corpuscle Histology

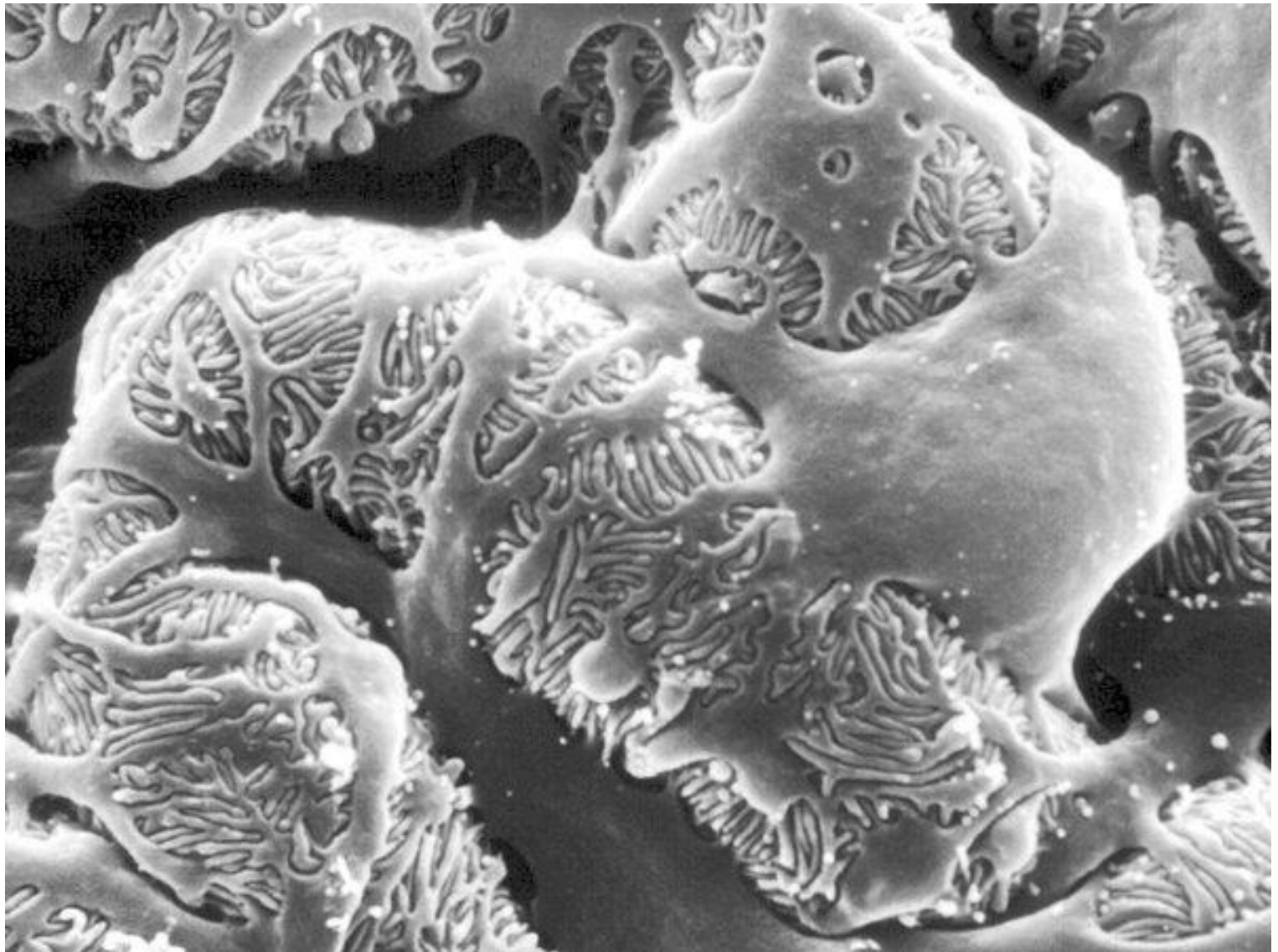
2) Basement membrane of glomerulus

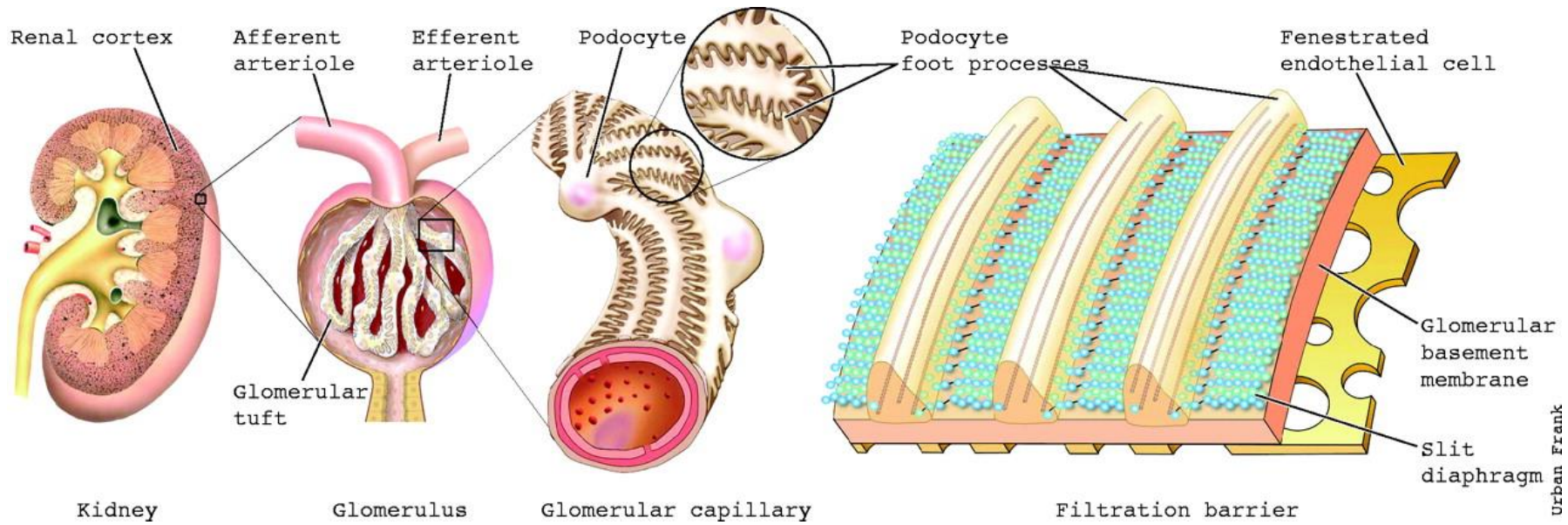
- Between endothelium and visceral layer of glom capsule
- Prevents large protein movement



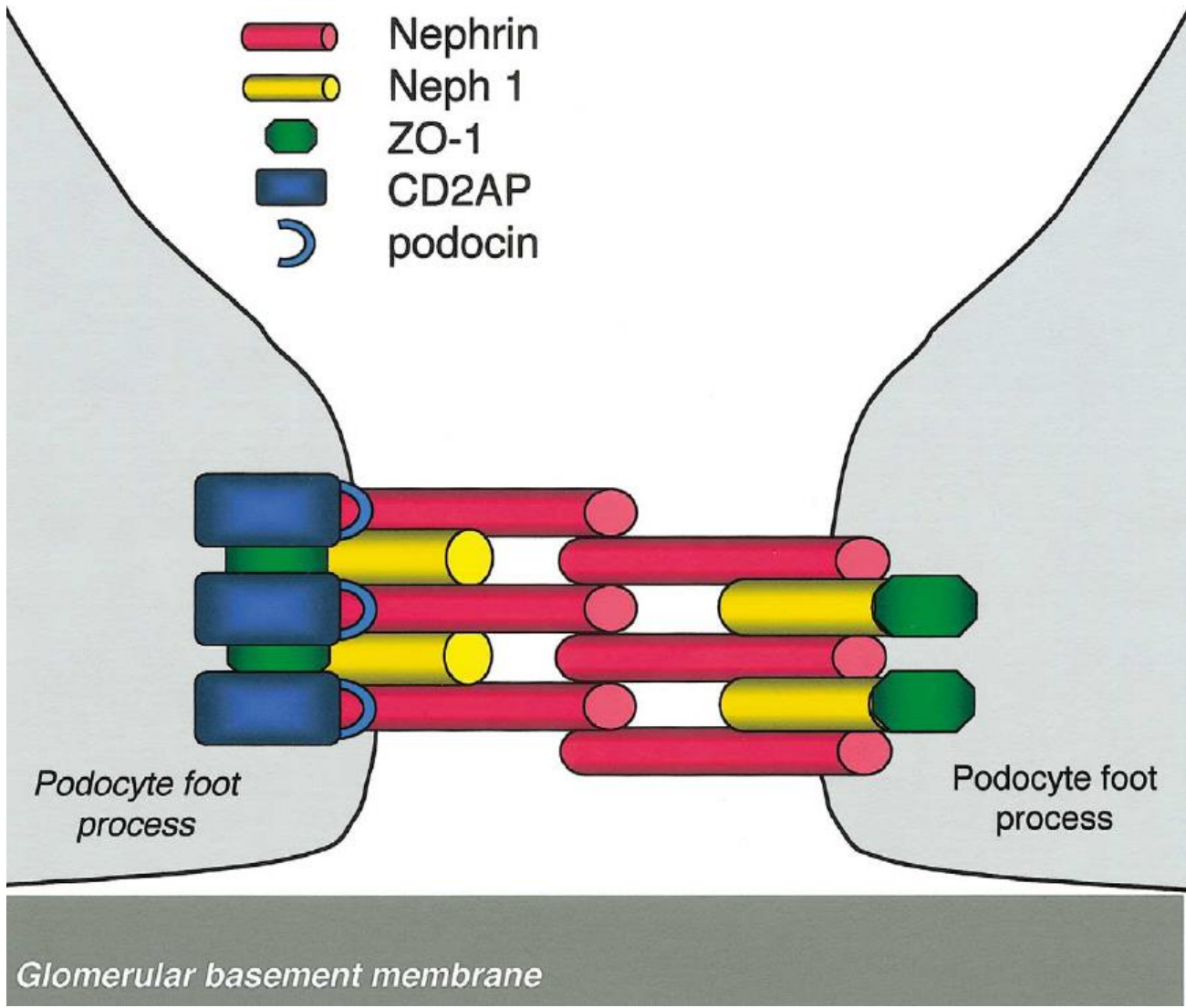








Urban Frank



- **Glomerulonephritis Diseases could be primary or secondary to variety of conditions:**

Examples:

- Membranous nephropathy could be primary (idiopathic) or secondary to HBV or to Lupus.
- Minimal change disease could be primary or secondary to Hodgkin lymphoma or NSAID use.

In primary we treat them with immunosuppressive agents while in secondary we treat the underlying diseases.

Differentiation Between Nephrotic Syndrome and Nephritic Syndrome

Typical Features	Nephrotic	Nephritic
Onset	Insidious	Abrupt
Edema	++++	++
Blood pressure	Normal	Raised
Jugular venous pressure	Normal/low	Raised
Proteinuria	++++	++
Hematuria	May/may not occur	+++
Red cell casts	Absent	Present
Serum albumin	Low	Normal/slightly reduced

Common Glomerular Diseases Presenting as Nephritic Syndrome

Disease	Associations	Serologic Tests Helpful in Diagnosis
Poststreptococcal glomerulonephritis	Pharyngitis, impetigo	ASO titer, streptozyme antibody
Other postinfectious disease		
Endocarditis	Cardiac murmur	Blood cultures, C3 ↓
Abscess	—	Blood cultures, C3, C4 normal or increased
Shunt	Treated hydrocephalus	Blood cultures, C3 ↓
IgA nephropathy	Upper respiratory or gastrointestinal infection	Serum IgA ↑
Systemic lupus	Other multisystem features of lupus	Antinuclear antibody, anti-double-stranded DNA antibody, C3 ↓, C4 ↓

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 \pm 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

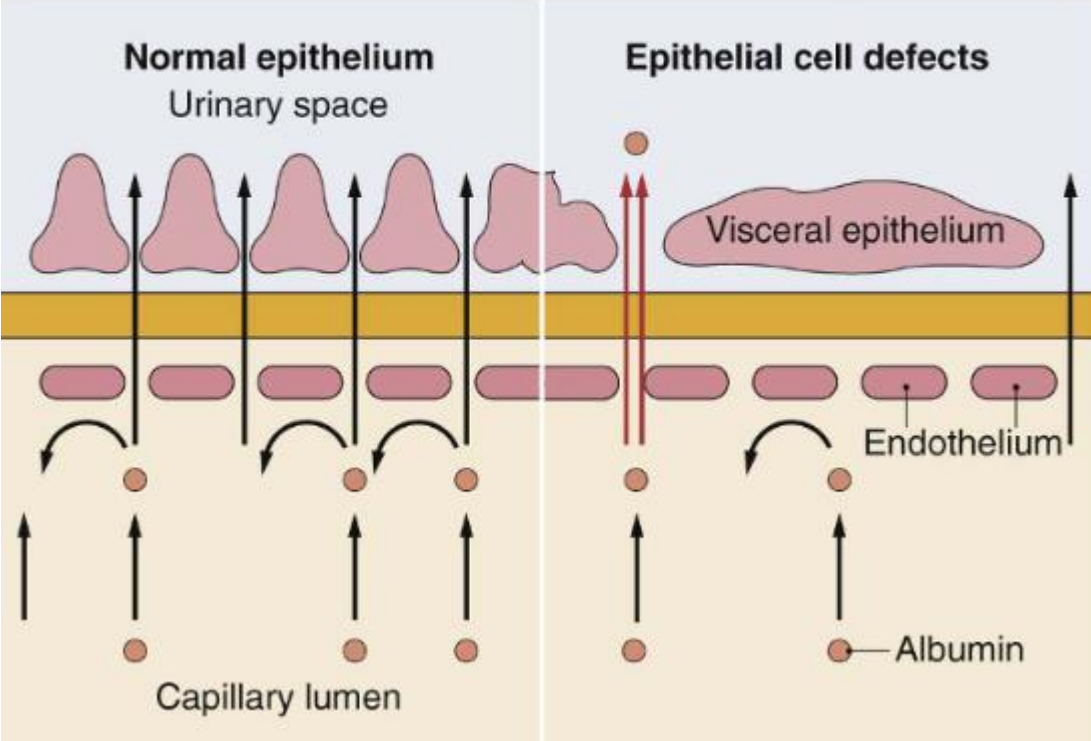
Rapidly progressive glomerulonephritis

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 insufficiency
Proteinuria often >3 g/day
Shrunken smooth kidneys

Mechanisms of Proteinuria

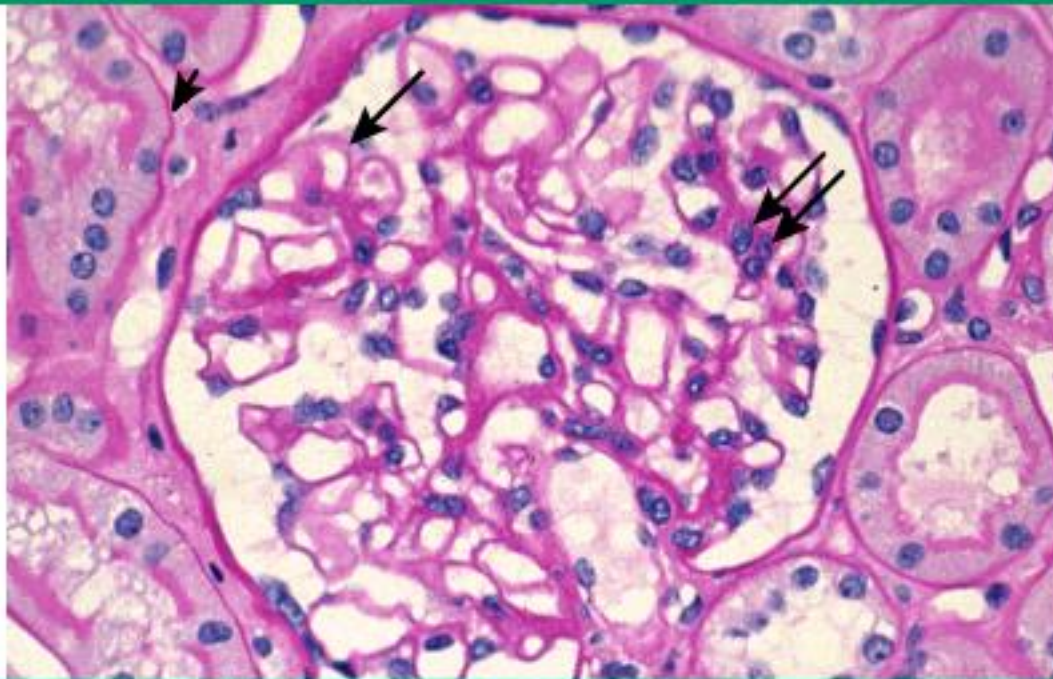


Common Glomerular Diseases Presenting as Nephrotic Syndrome in Adults

Disease	Associations	Serologic Tests Helpful in Diagnosis
Minimal change disease (MCD)	Allergy, atopy, NSAIDs, Hodgkin's disease	None
Focal segmental glomerulosclerosis (FSGS)	African Americans HIV infection Heroin, pamidronate	— HIV antibody —
Membranous nephropathy (MN)	Drugs: gold, penicillamine, NSAIDs Infections: hepatitis B, C; malaria Lupus nephritis Malignancy: breast, lung, gastrointestinal tract	— Hepatitis B surface antigen, anti-hepatitis C virus antibody Anti-DNA antibody —
Membranoproliferative glomerulonephritis (MPGN) (type I)	C4 nephritic factor	C3 ↓, C4 ↓
Membranoproliferative glomerulonephritis (MPGN) (type II) (Dense deposit disease)	C3 nephritic factor	C3 ↓, C4 normal
Cryoglobulinemic membranoproliferative glomerulonephritis	Hepatitis C	Anti-hepatitis C virus antibody, rheumatoid factor, C3 ↓, C4 ↓, CH50 ↓
Amyloid	Myeloma Rheumatoid arthritis, bronchiectasis, Crohn's disease (and other chronic inflammatory conditions), familial Mediterranean fever	Serum protein electrophoresis, urine immunoelectrophoresis —
Diabetic nephropathy	Other diabetic microangiopathy	None

- Pathological Classification of Glomerulonephritis diseases:
 - Proliferative
 - Non-proliferative

Normal glomerulus

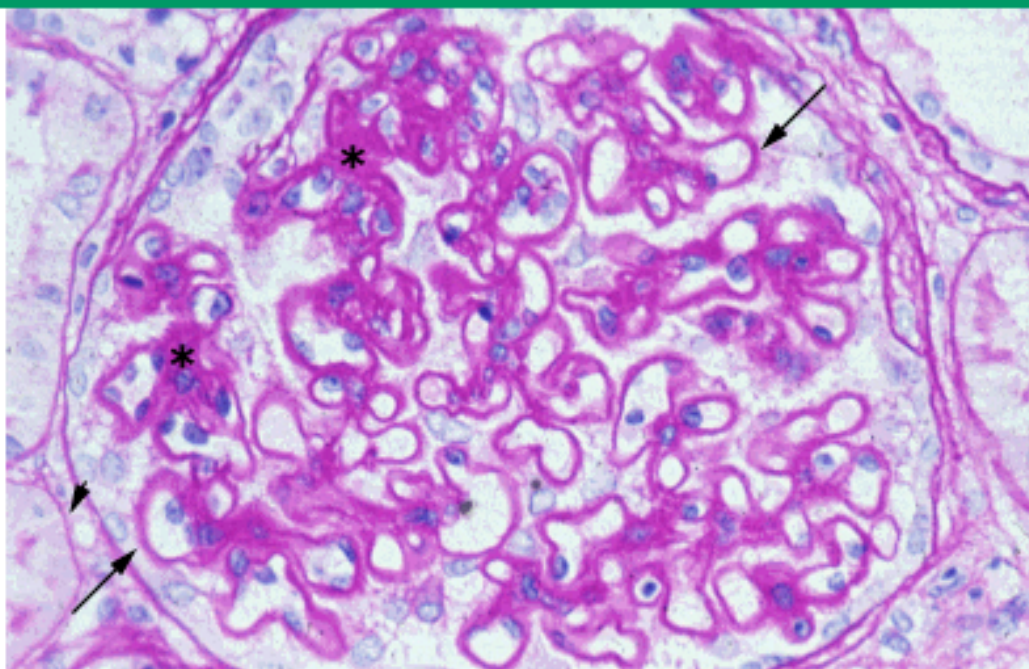


Light micrograph of a normal glomerulus. There are only 1 or 2 cells per capillary tuft, the capillary lumens are open, the thickness of the glomerular capillary wall (long arrow) is similar to that of the tubular basement membranes (short arrow), and the mesangial cells and mesangial matrix are located in the central or stalk regions of the tuft (arrows).

Courtesy of Helmut G Rennke, MD.

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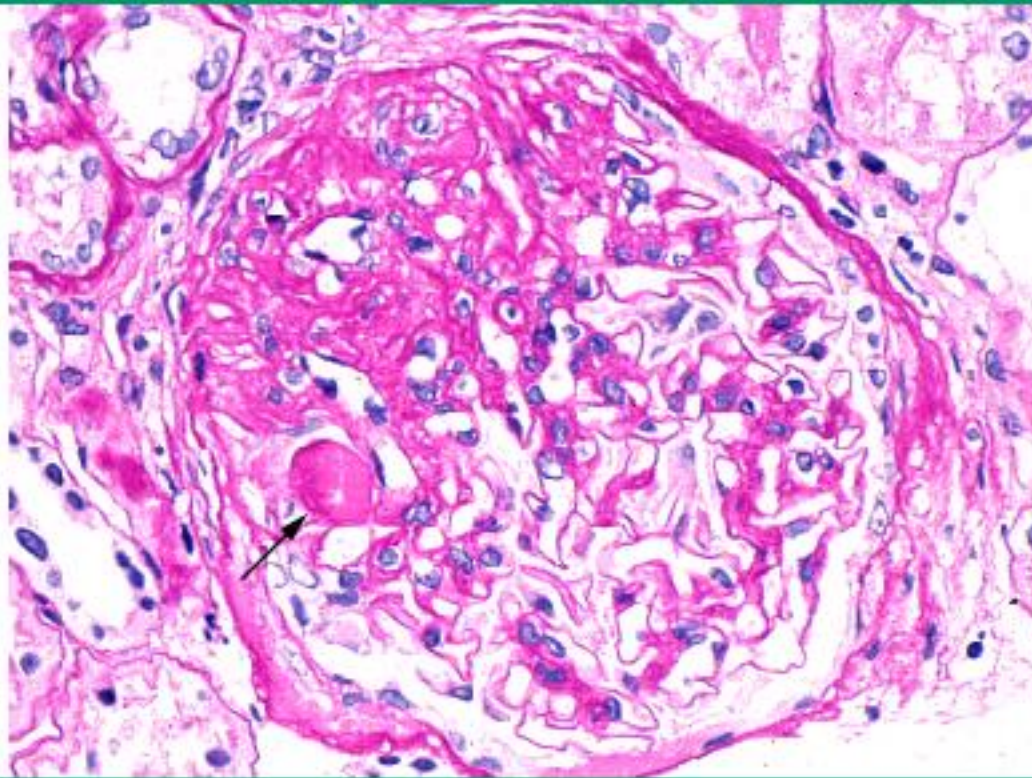
Light micrograph showing membranous nephropathy



Light micrograph of membranous nephropathy, showing diffuse thickening of the glomerular basement membrane (long arrows) with essentially normal cellularity. Note how the thickness of the glomerular capillary walls is much greater than that of the adjacent tubular basement membranes (short arrow). There are also areas of mesangial expansion (asterisks). Immunofluorescence microscopy (showing granular IgG deposition) and electron microscopy (showing subepithelial deposits) are generally required to confirm the diagnosis.

Courtesy of Helmut Rennke, MD.

Moderate FGS

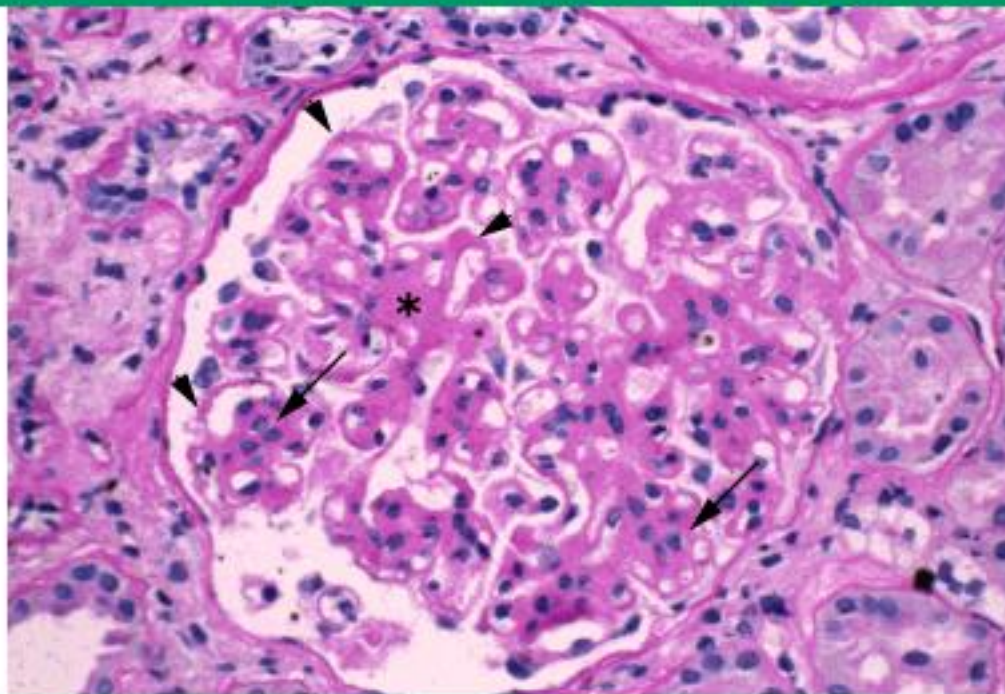


Light micrograph in focal segmental glomerulosclerosis shows a moderately large segmental area of sclerosis with capillary collapse on the upper left side of the glomerular tuft; the lower right segment is relatively normal. Focal deposition of hyaline material (arrow) is also seen.

Courtesy of Helmut Rennke, MD.

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Membranoproliferative glomerulonephritis

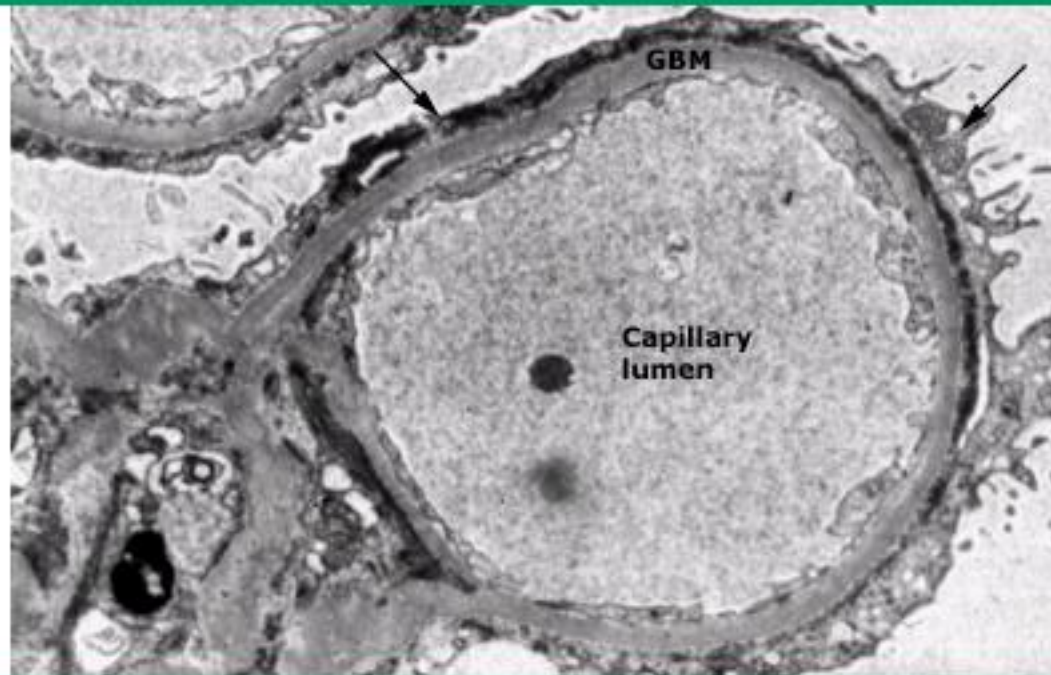


Light micrograph in membranoproliferative glomerulonephritis showing a lobular appearance of the glomerular tuft with focal areas of increased glomerular cellularity (large arrows), mesangial expansion (*), narrowing of the capillary lumens, and diffuse thickening of the glomerular capillary walls (small arrows).

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Electron microscopy in minimal change disease

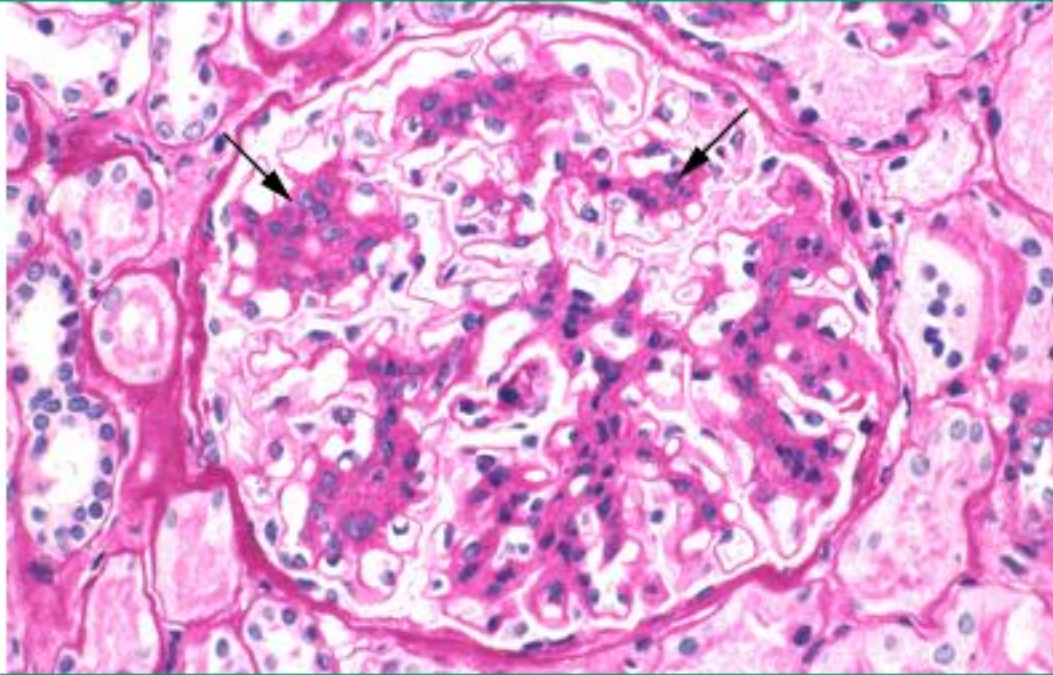


Electron micrograph in minimal change disease showing a normal glomerular basement membrane (GBM), no immune deposits, and the characteristic widespread fusion of the epithelial cell foot processes (arrows).

Courtesy of Helmut Rennke, MD.

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Light micrograph showing mesangial proliferative glomerulonephritis

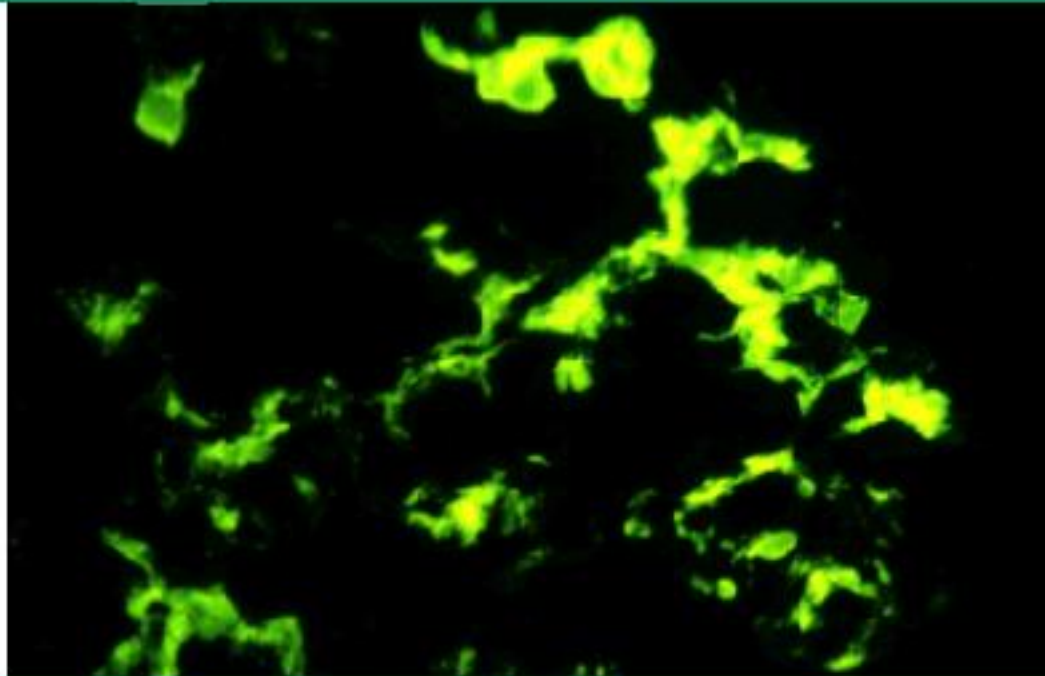


Light micrograph of a mesangial glomerulonephritis showing segmental areas of increased mesangial matrix and cellularity (arrows). This finding alone can be seen in many diseases, including IgA nephropathy and lupus nephritis.

Courtesy of Helmut G Rennke, MD.

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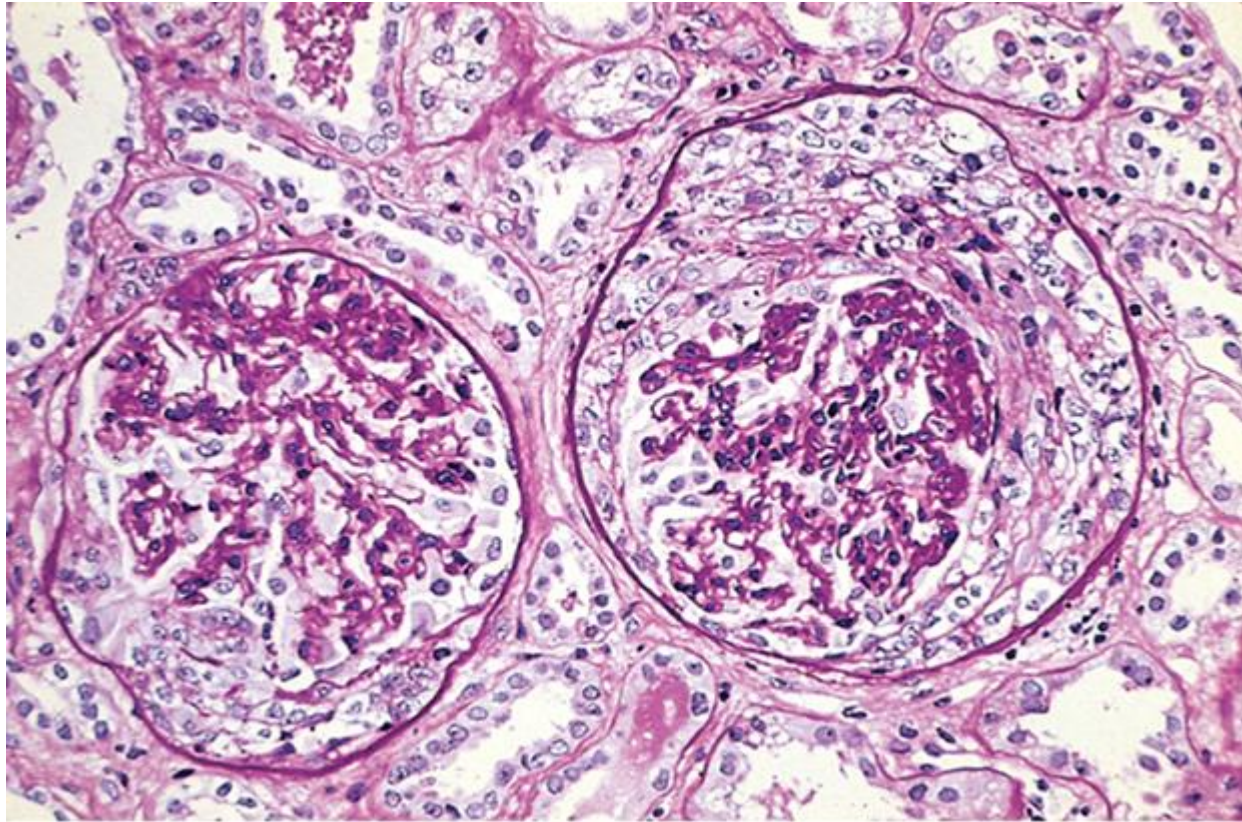
Immunofluorescence microscopy showing mesangial immunoglobulin A (IgA) deposits



Immunofluorescence microscopy demonstrating large, globular mesangial IgA deposits that are diagnostic of IgA nephropathy or Henoch-Schönlein purpura (IgA vasculitis). Note that the capillary walls are not outlined since the deposits are primarily limited to the mesangium.

Courtesy of Helmut Rennke, MD.

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Thank You

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