Overview of Glomerulonephritis

Approach to Hematuria

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Objectives

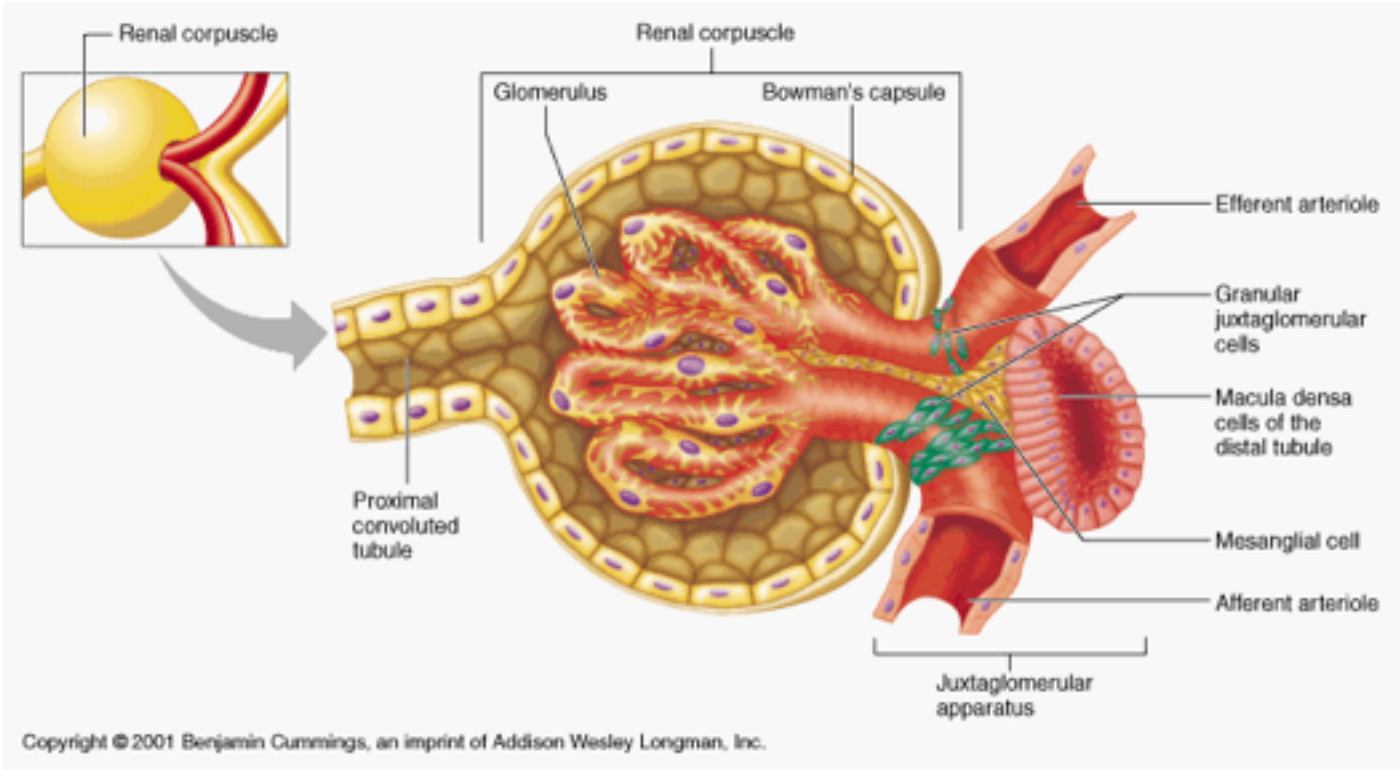
- To know the basics about the structure and functions of the glomerulus

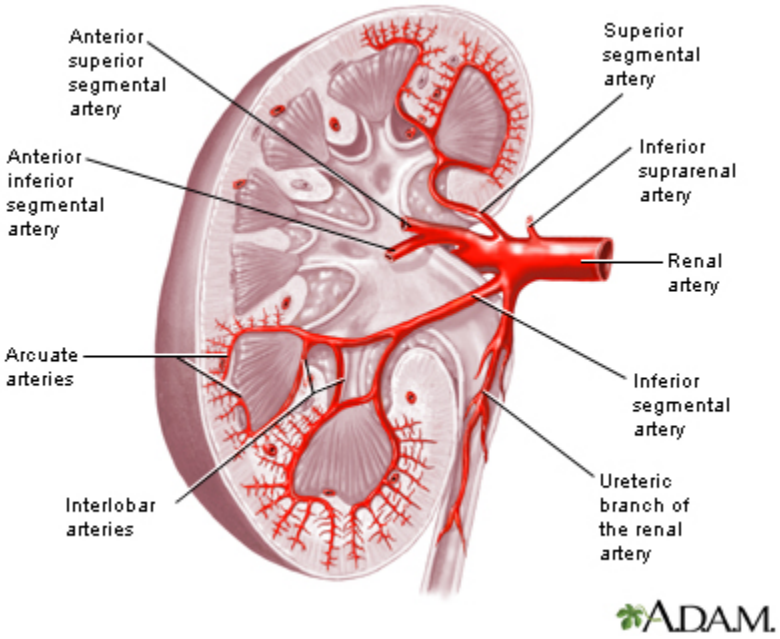
. To have an Idea how diseases are named in GN

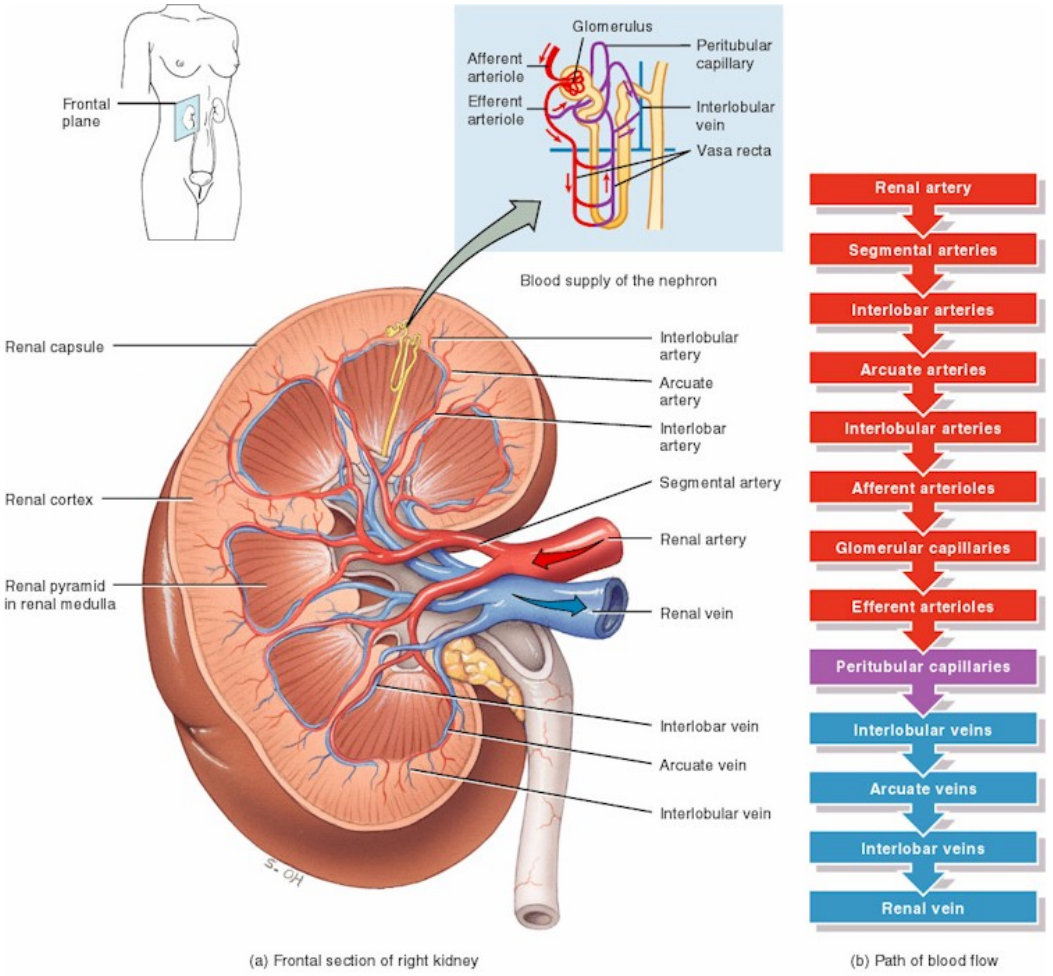
- To know some of the secondary causes of GN and realize its impact on the clinical management

- To know the initial screening workup for glomerulonephritis

- To know the different causes of hematuria and make your approach accordingly







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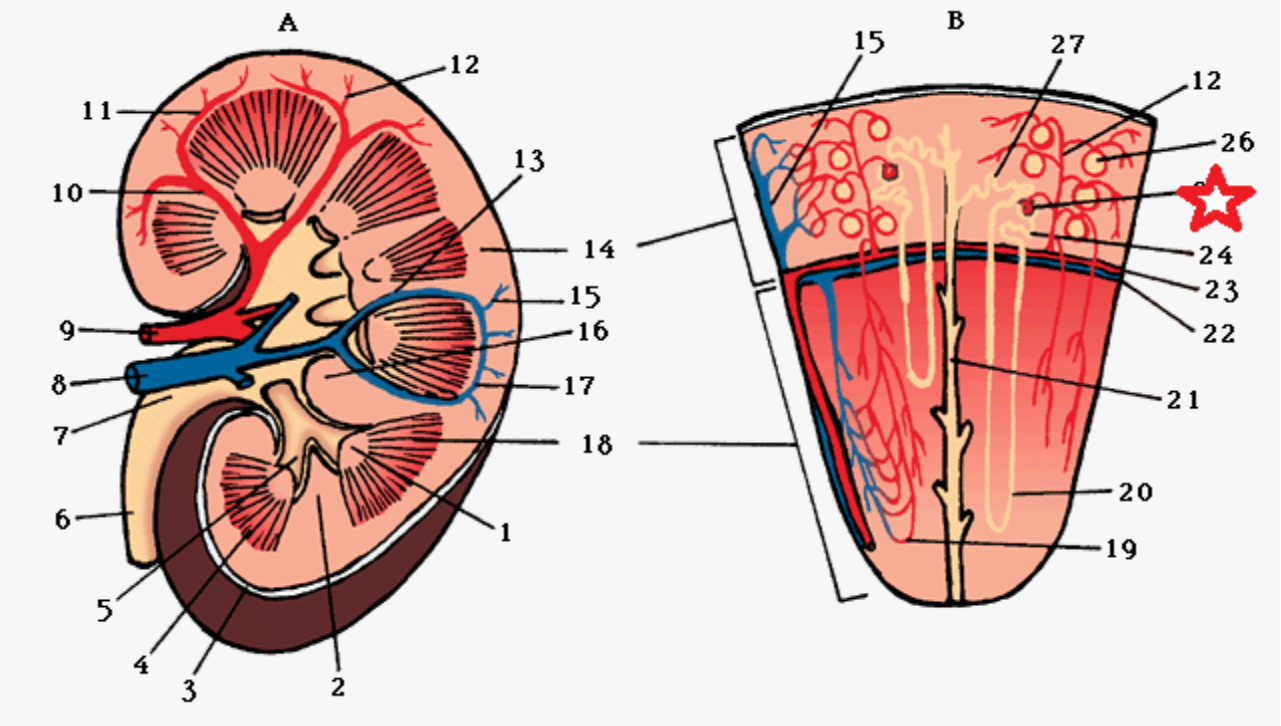
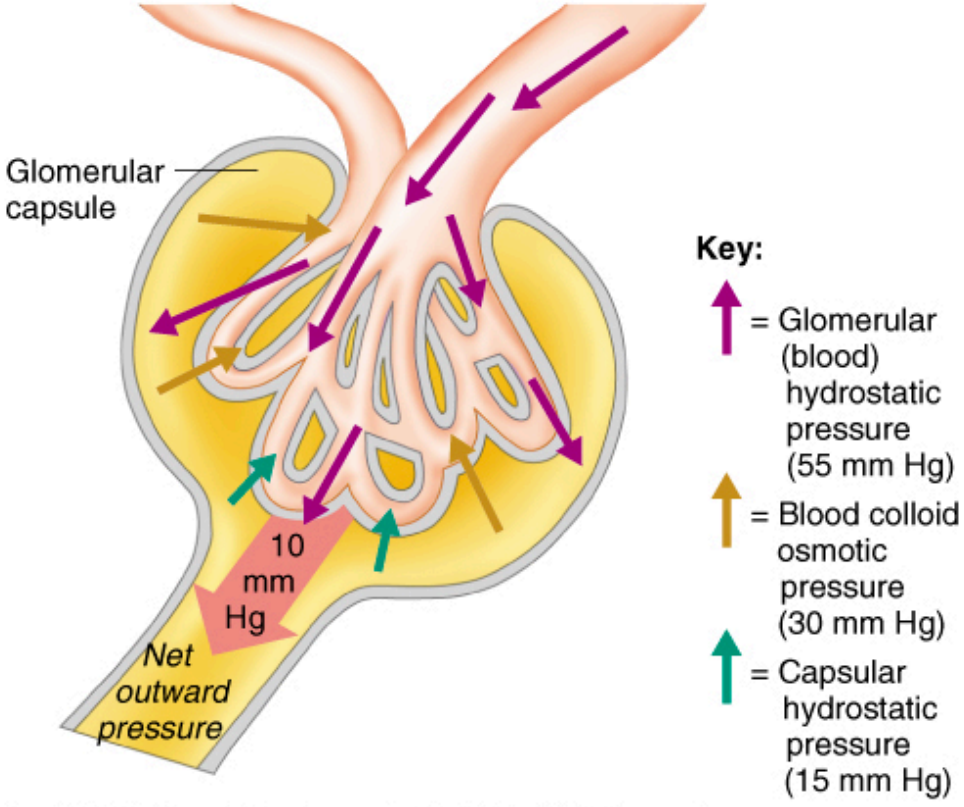
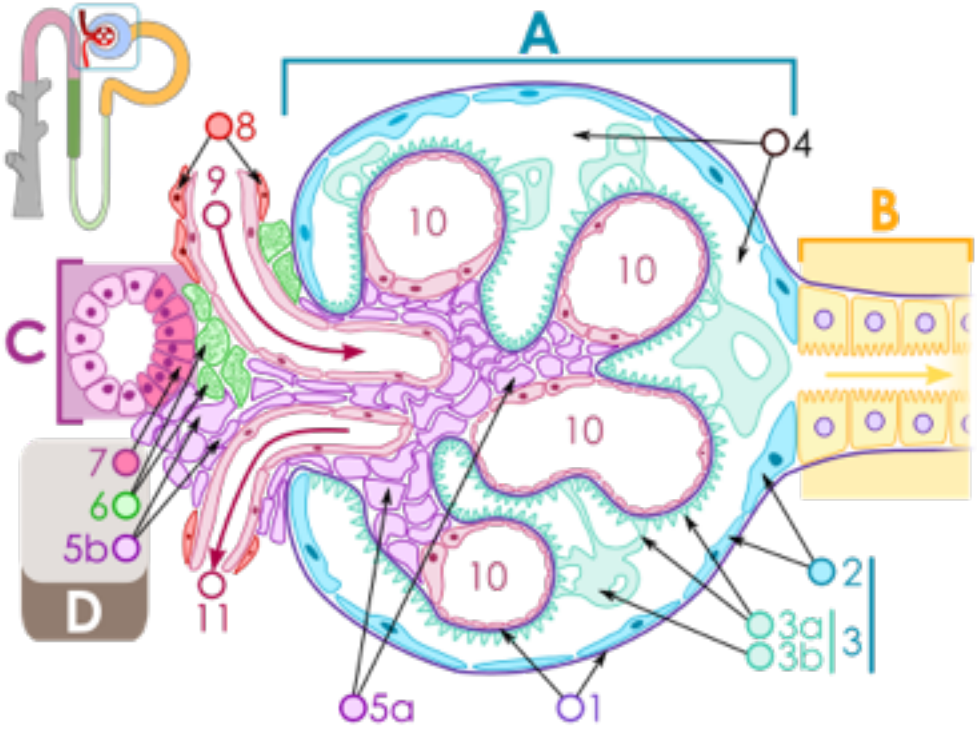
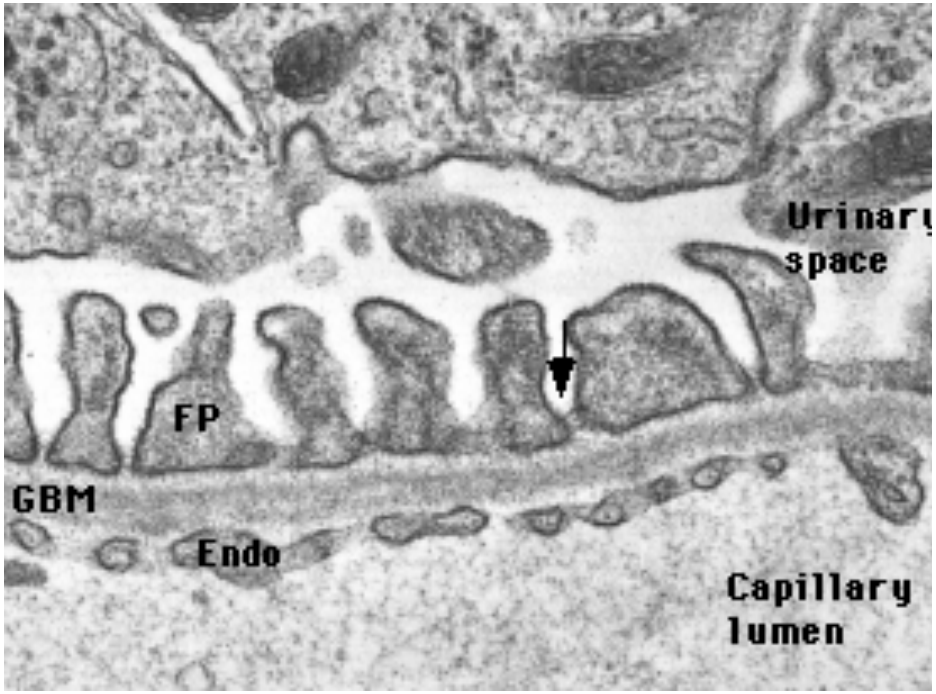
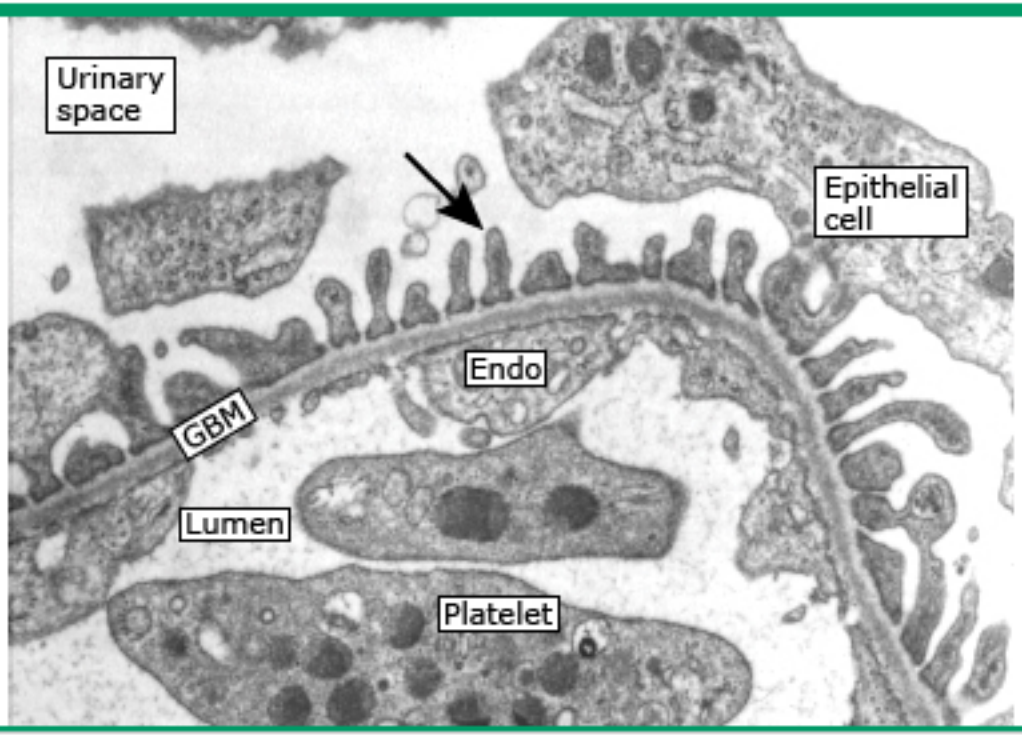








Electron micrograph of a normal glomerulus

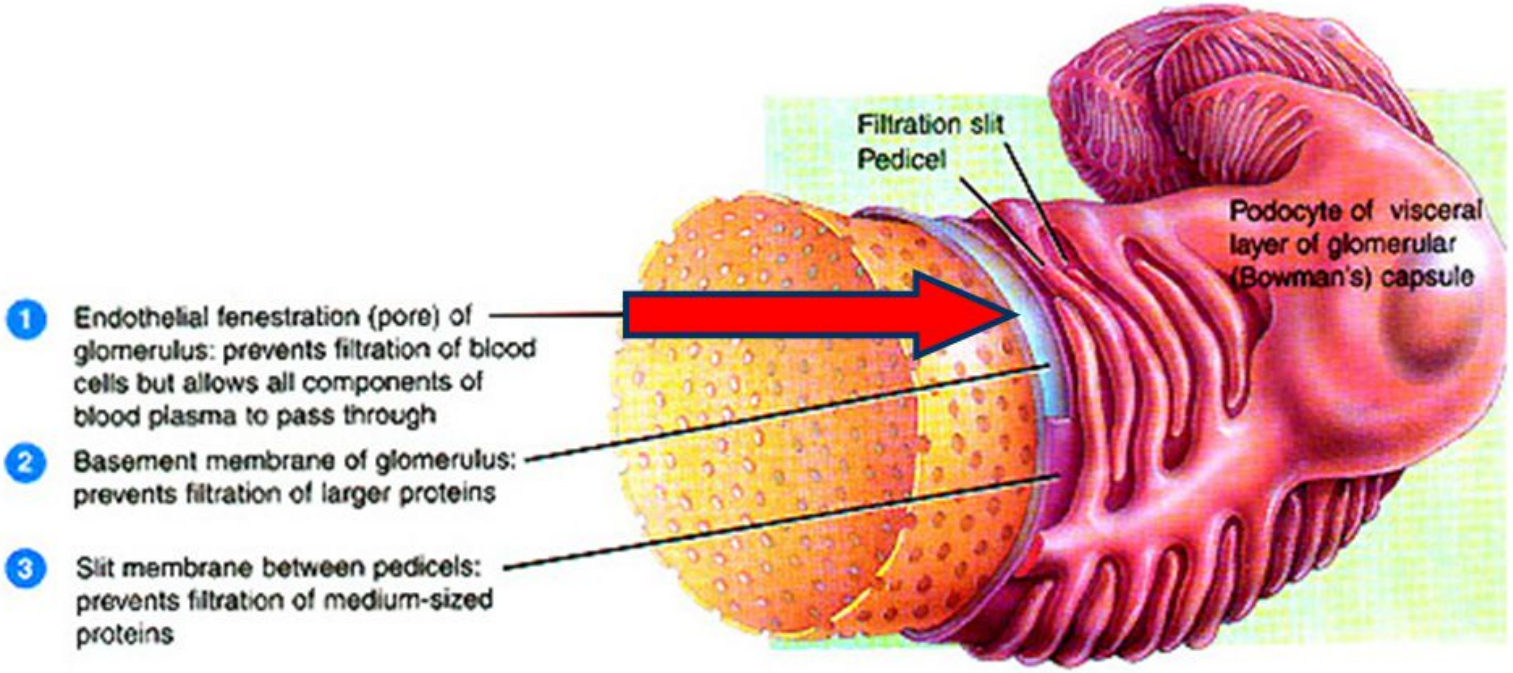


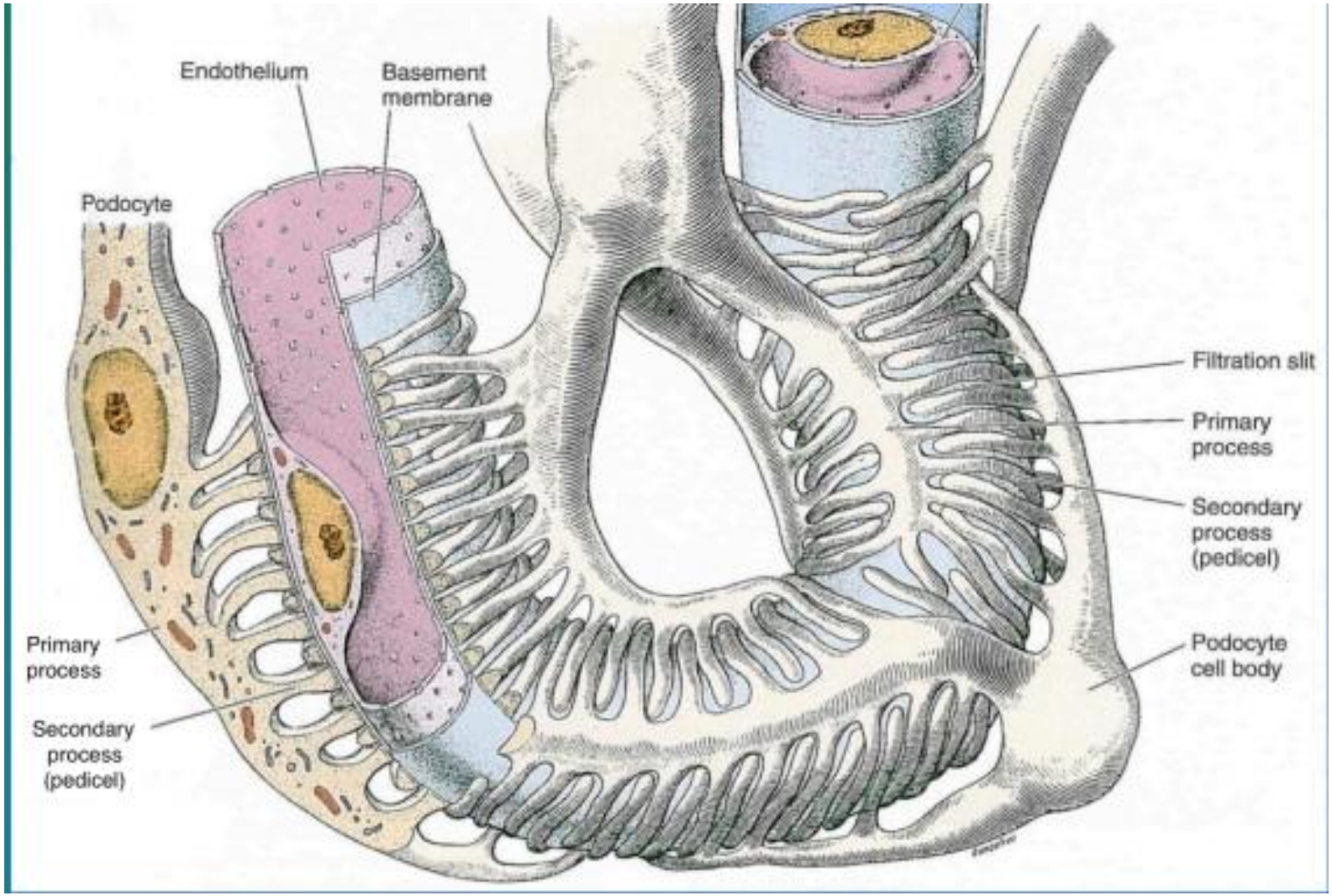
Electron micrograph of a normal glomerular capillary loop showing the fenestrated endothelial cell (Endo), the glomerular basement membrane (GBM), and the epithelial cells with its interdigitating foot processes (arrow). The GBM is thin, and no electron-dense deposits are present. Two normal platelets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

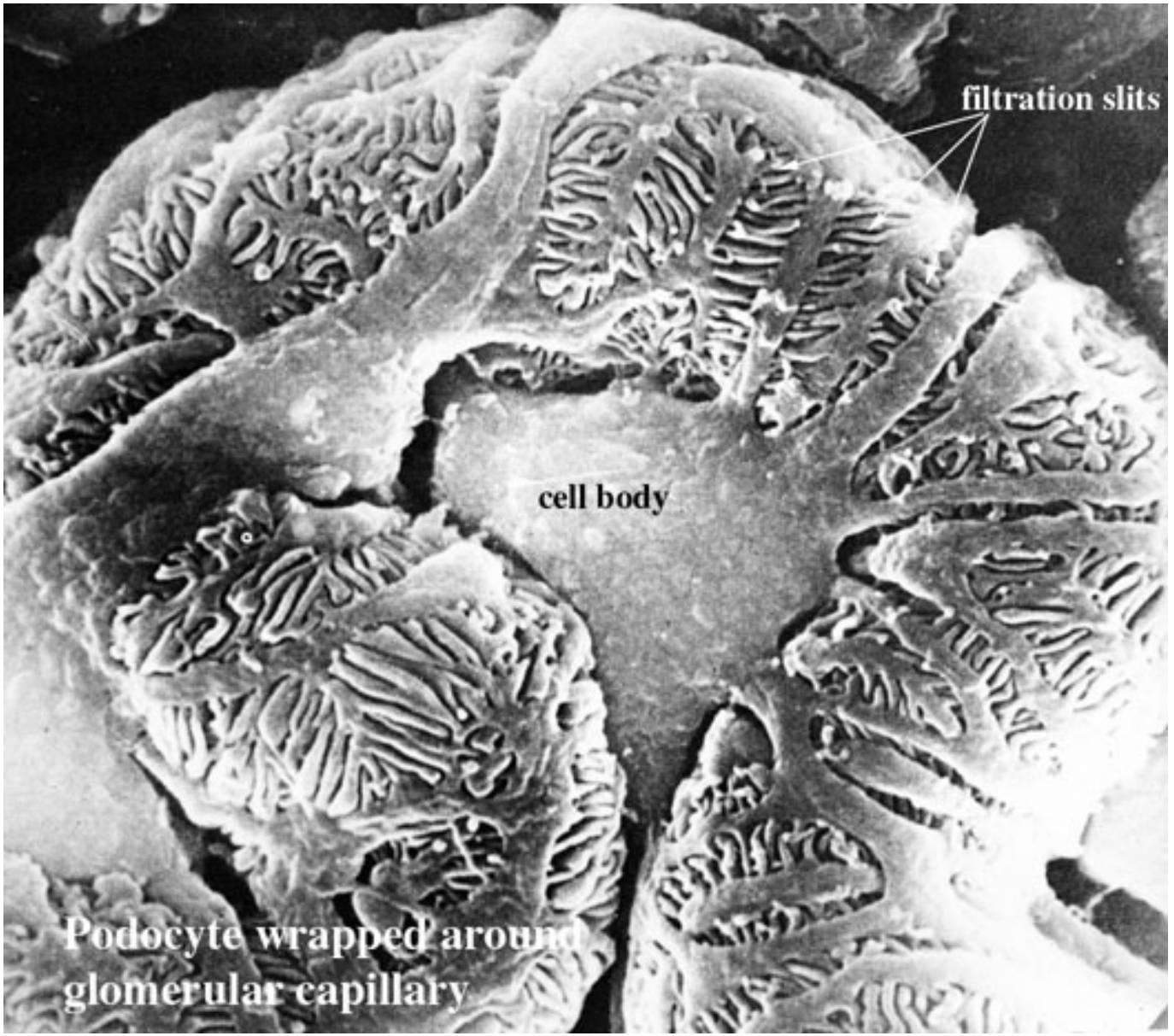
Courtesy of Helmut G Rennke, MD.

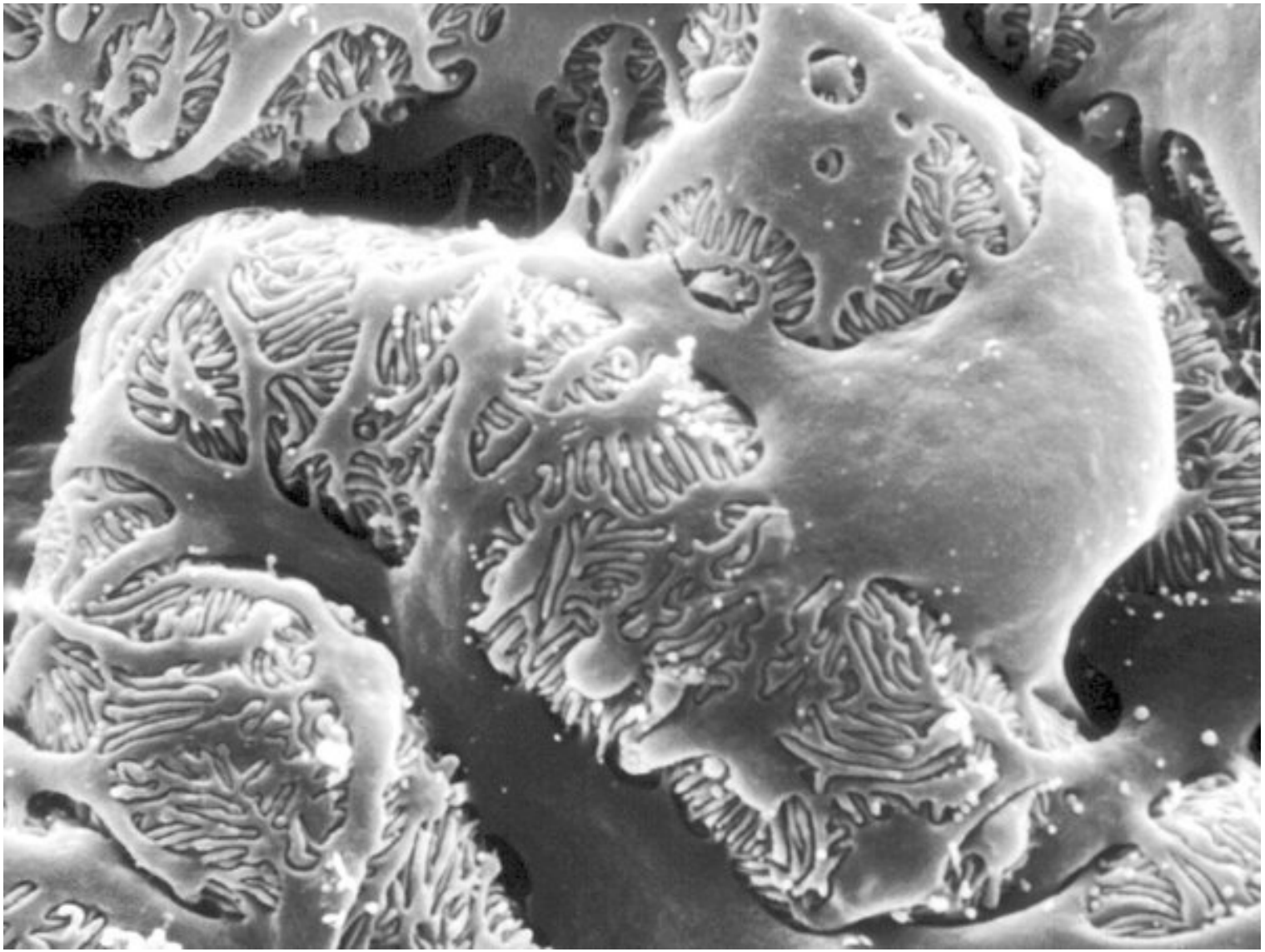
Renal Corpuscle Histology

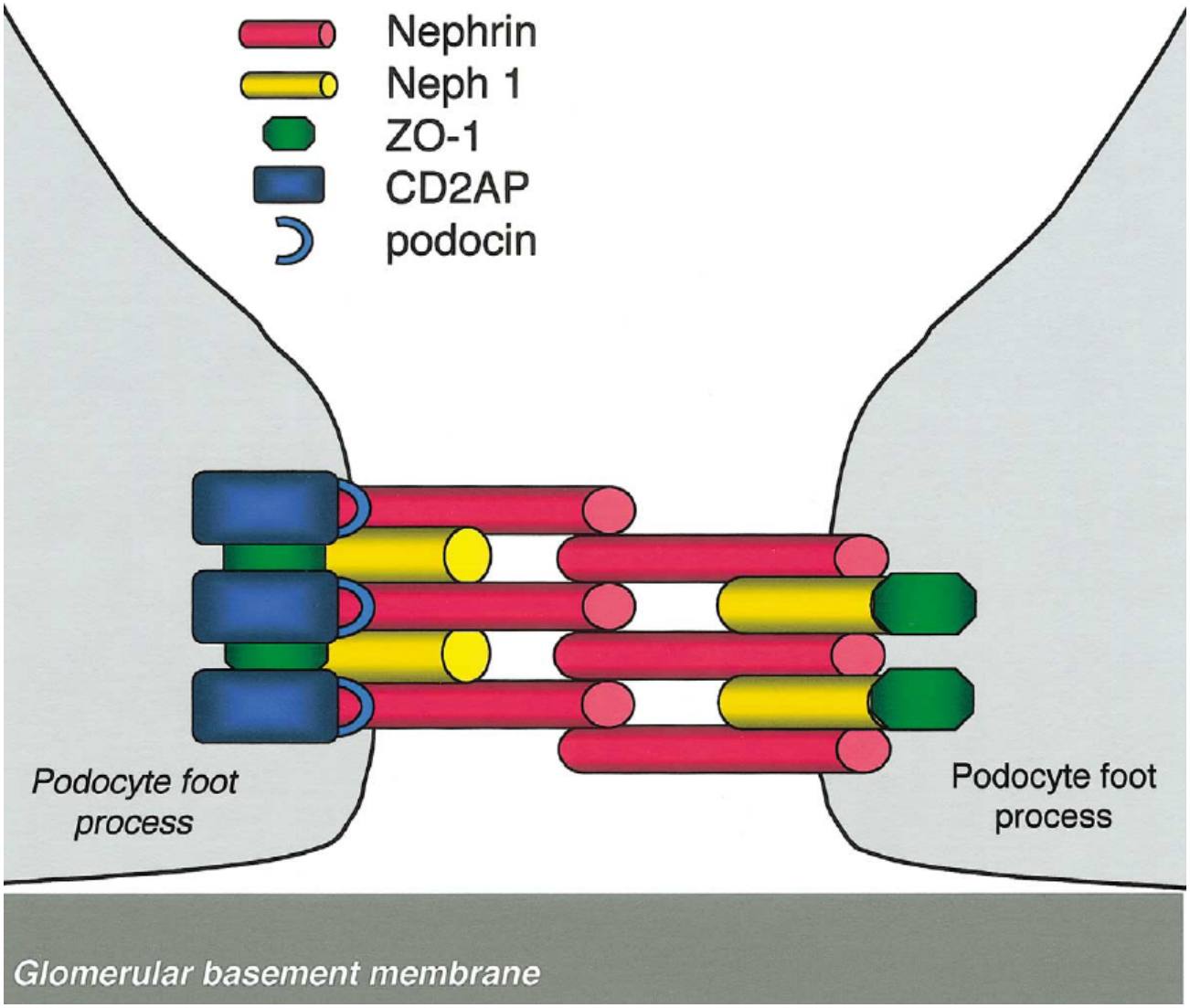
2) Basement membrane of glomerulus
   - Between endothelium and visceral layer of glom capsule
   - Prevents large protein movement

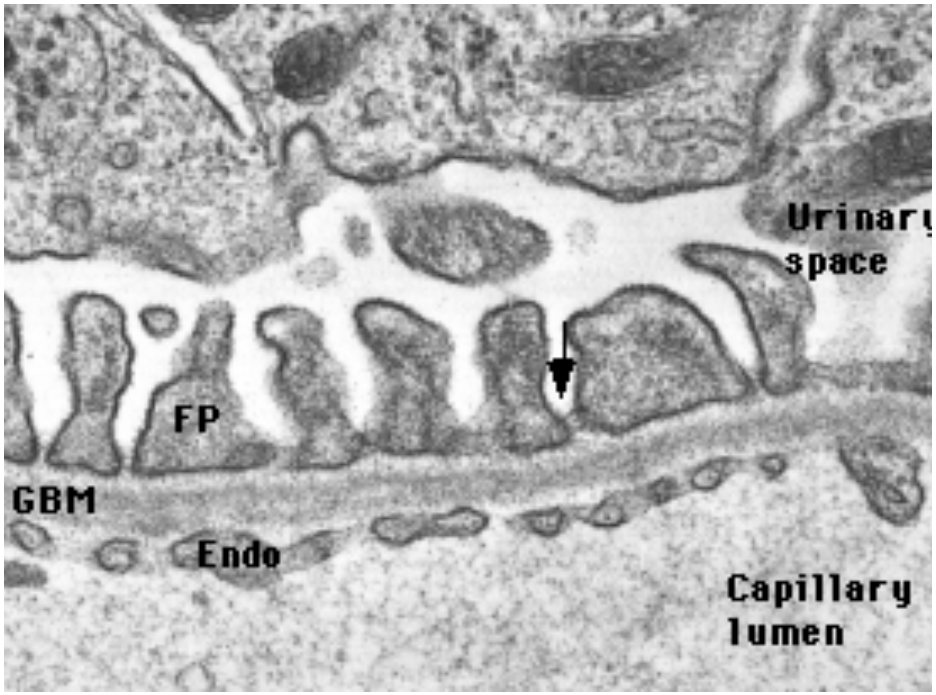












- What affect the trans-glomerular passage?
- 1- Molecular size
- 2- Charge
- 3- Shape

- *Which of the following are typical features of active glomerulonephritis:*

A- high creatinine, hypovolemia and proteinuria

B- High creatinine, hypervolemia, proteinuria & ↓ Mg

C- High creatinine, hypervolemia, microscopic hematuria and proteinuria

- *Is the statement below True or False?*

Mesangial cells maintain the structure and the function of the glomerulus

T

- *Is the statement below True or False?*

Slit diaphragm is composed of group of proteins that maintain the structure and the alignment of the endothelial cells

F

- *What are the layers of the glomerular capillary wall in order from inside to outside:*

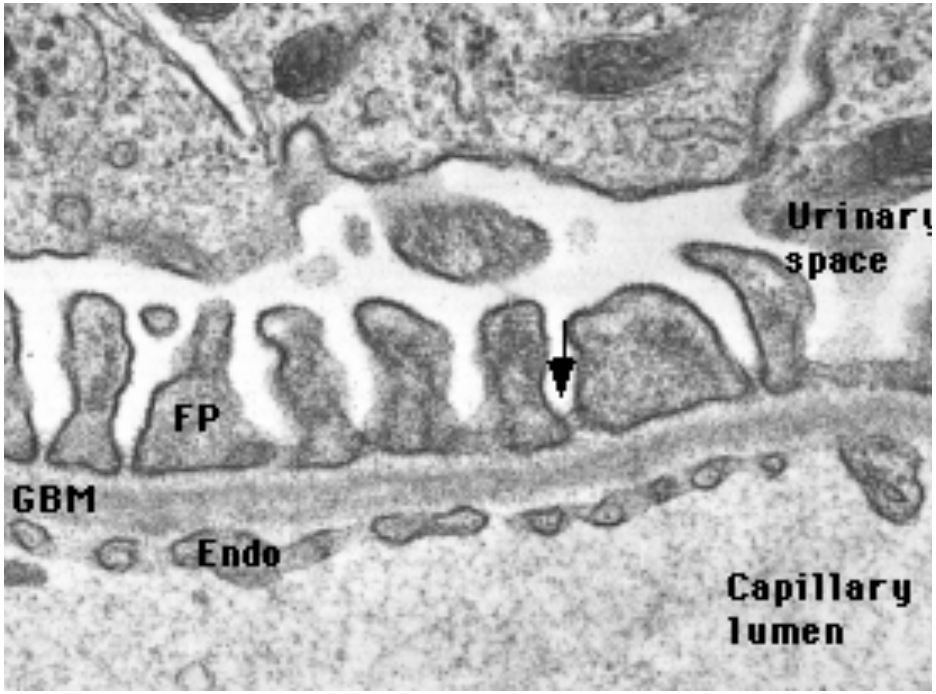
A- Endothelial cells, podocytes, GBM

B- GBM, endothelial cells, podocytes

C- Endothelial cells, GBM, podocytes

Diseases

Diseases



Diseases

- **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 immunosupprrssive agents while in secondary we treat the underlying diseases.

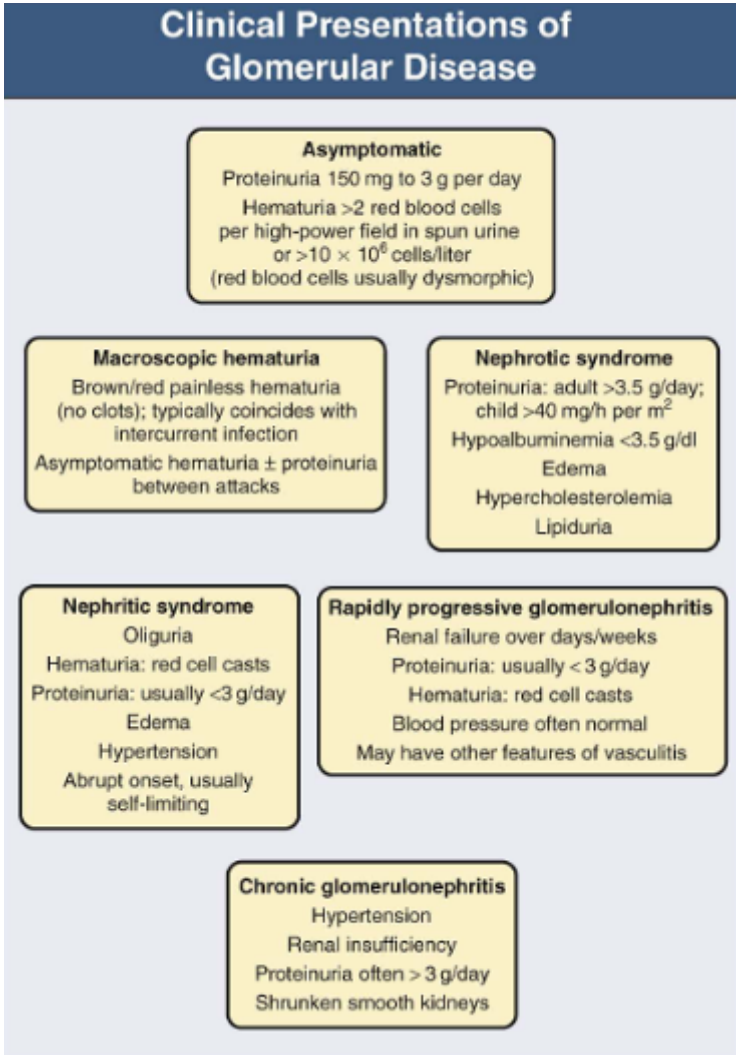
Differentiation Between Nephrotic Syndrome and Nephritic Syndrome

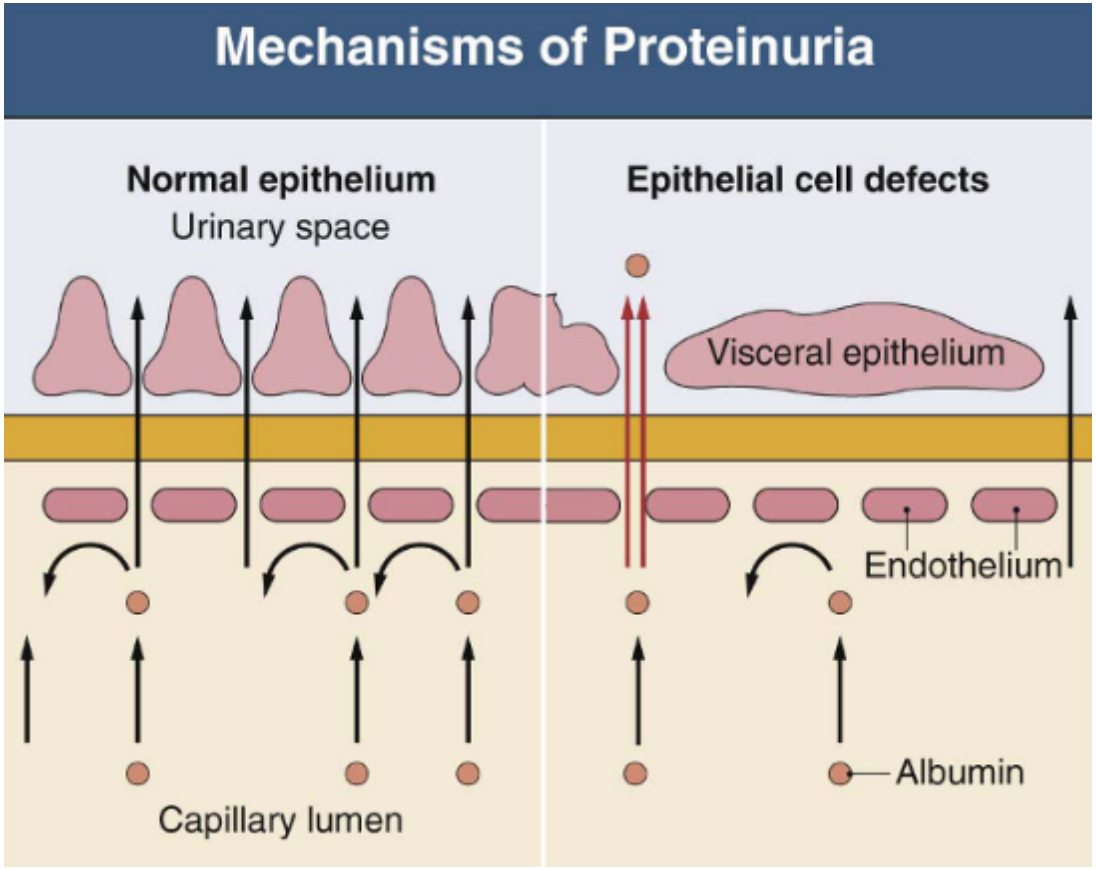
Typical Features	Nephrotic	Nephritic
Onset	Insidious	Abrupt
Edema	++++	++
Blood pressure	Normal	Raised
Jugular venous pressure	Normal/low	Raised
Proteinuria	++++	++
Hematuria	May/may not occur	+++
Red cell casts	Absent	Present
Serum albumin	Low	Normal/slightly reduced

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



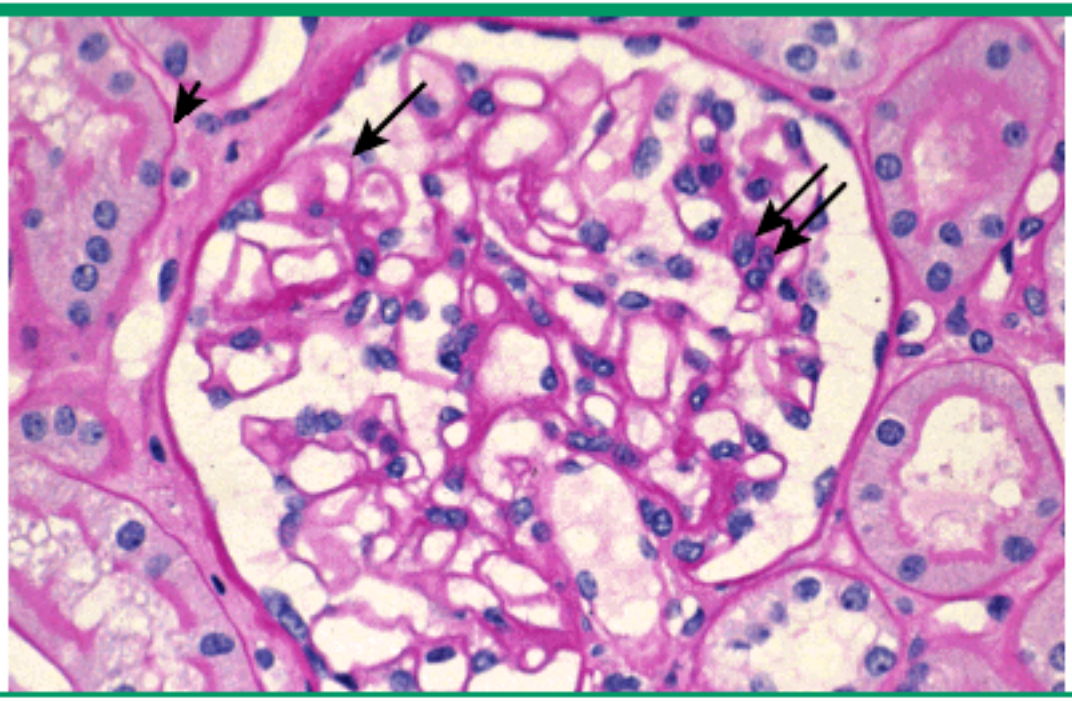


- Pathological Classification of Glomerulonephritis diseases:

- 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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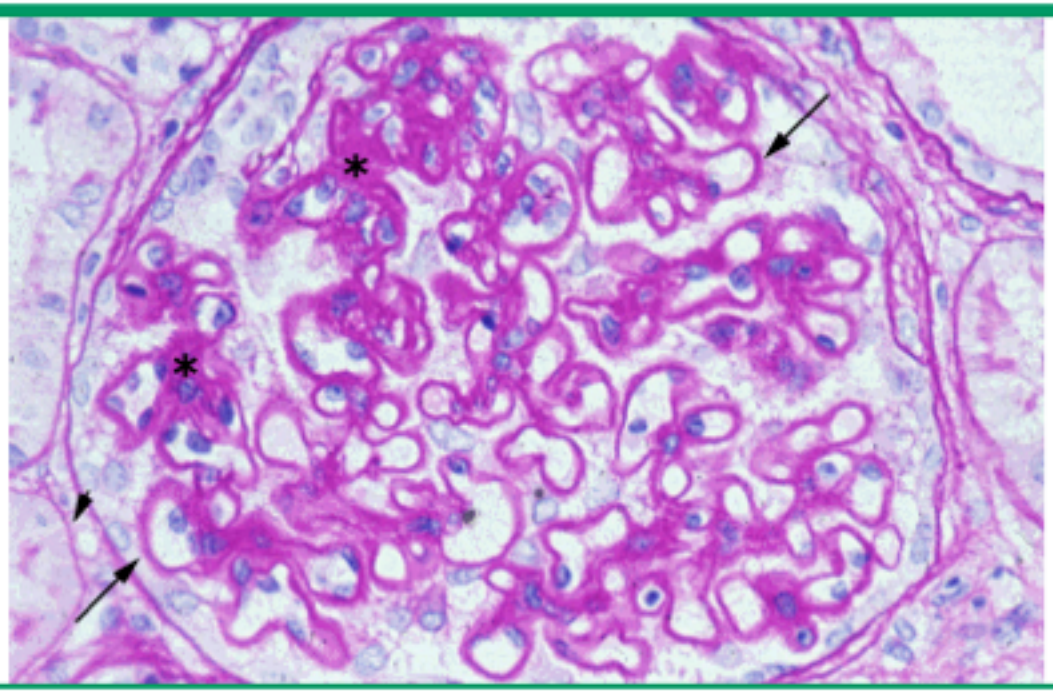
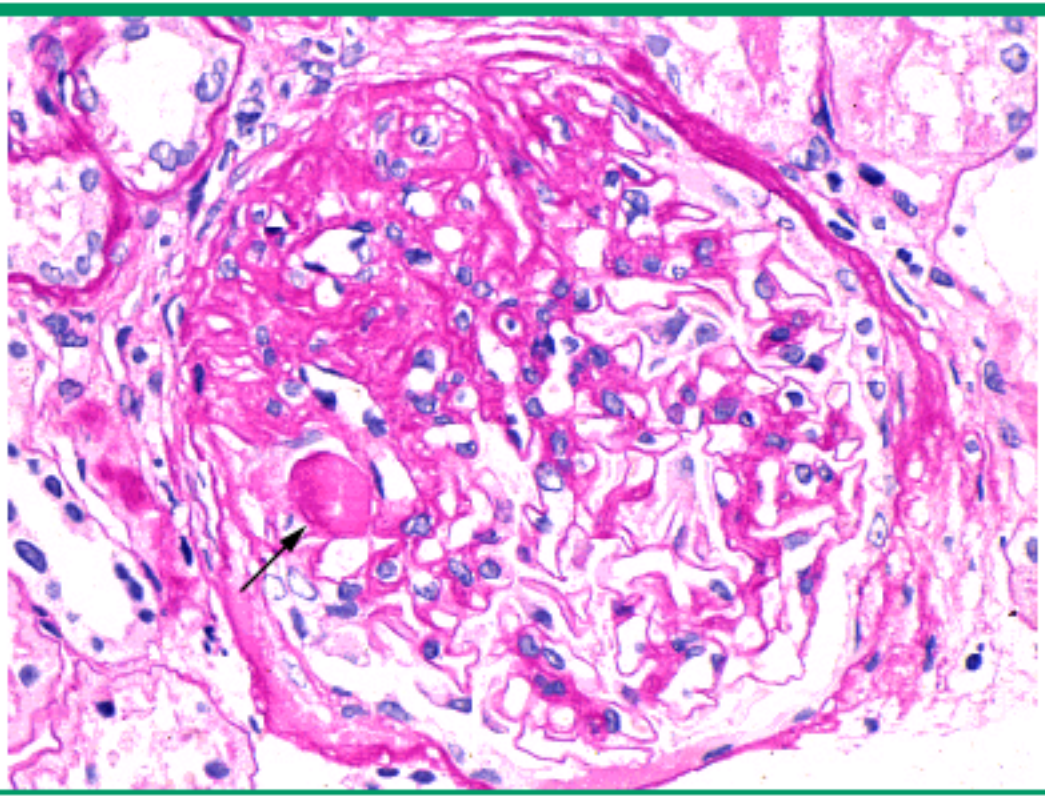
Light micrograph showing membranous nephropathy



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.

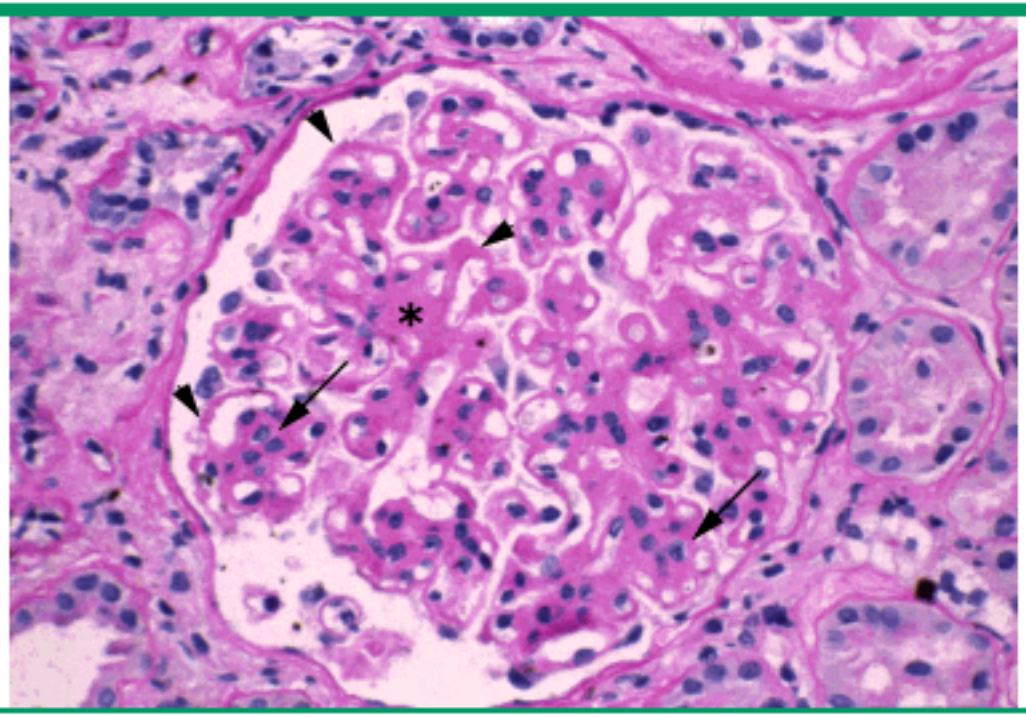
Moderate FGS



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.

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).

Courtesy of Helmut Rennke, MD.

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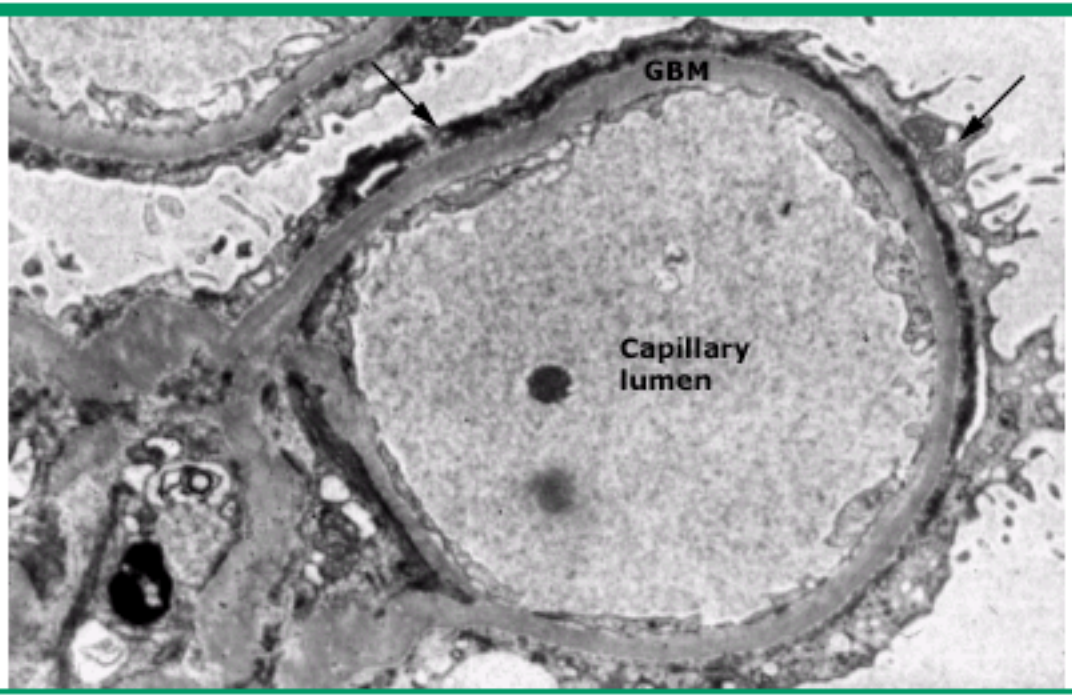
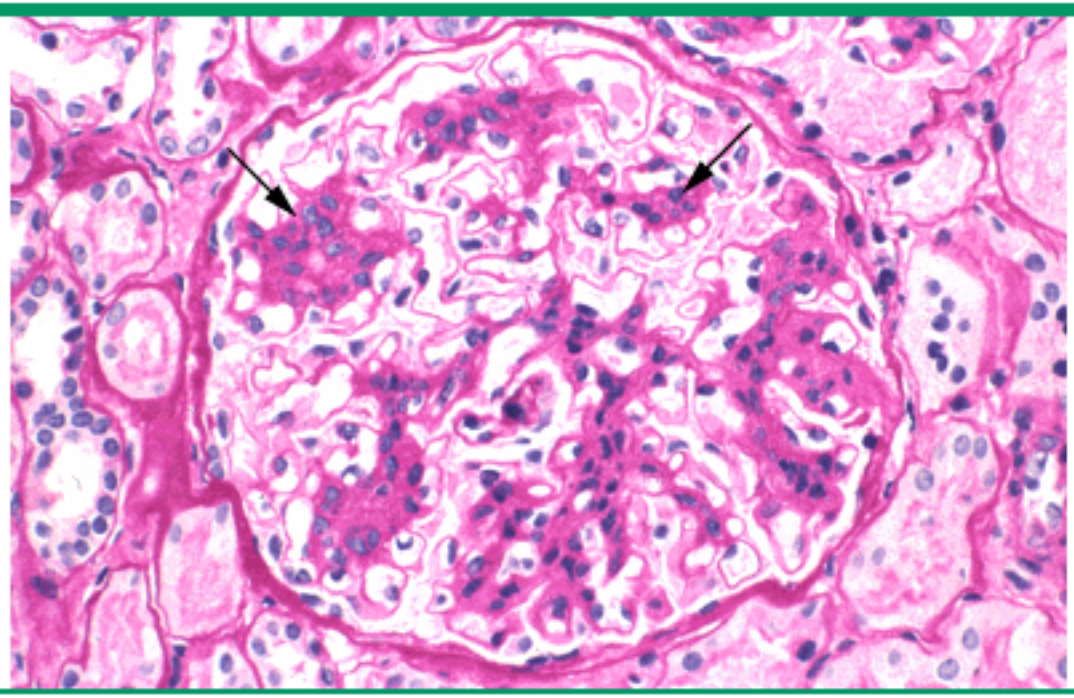
Electron microscopy in minimal change disease



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.

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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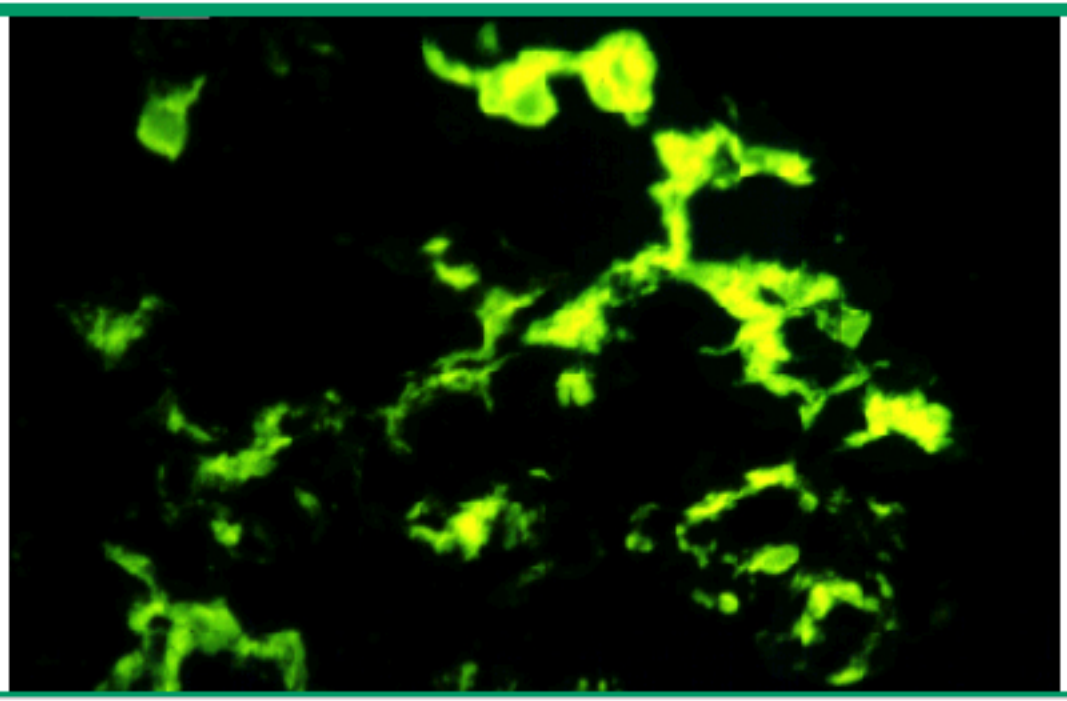
Immunofluorescence microscopy showing mesangial immunoglobulin A (IgA) deposits



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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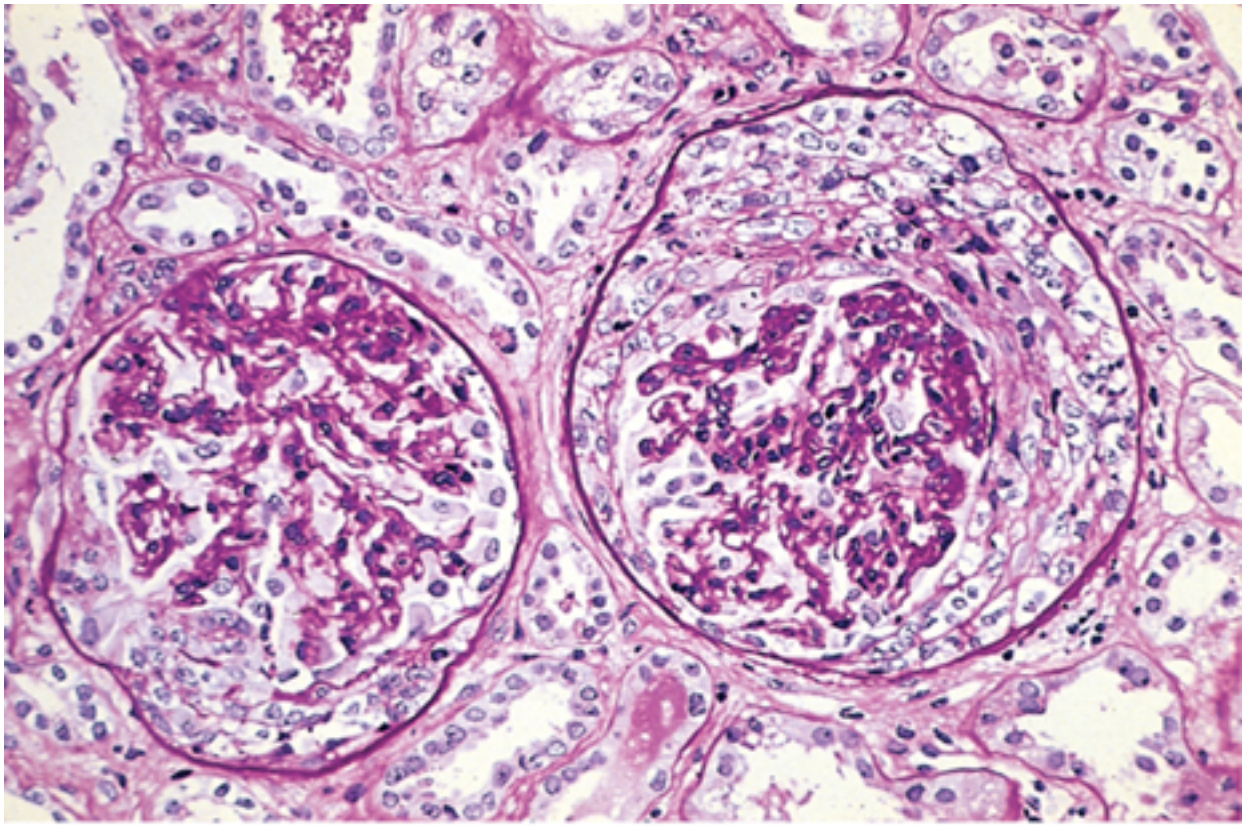
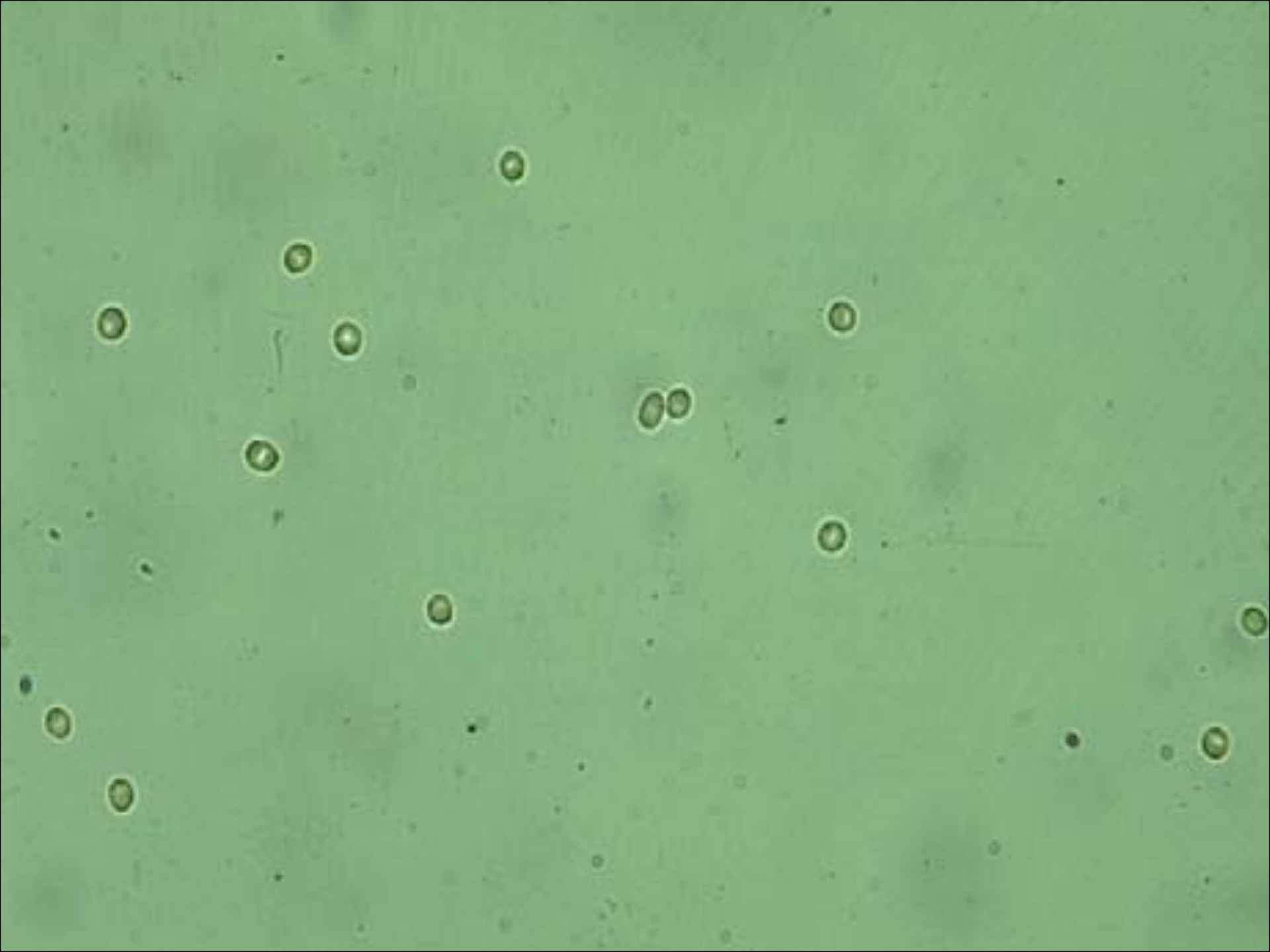


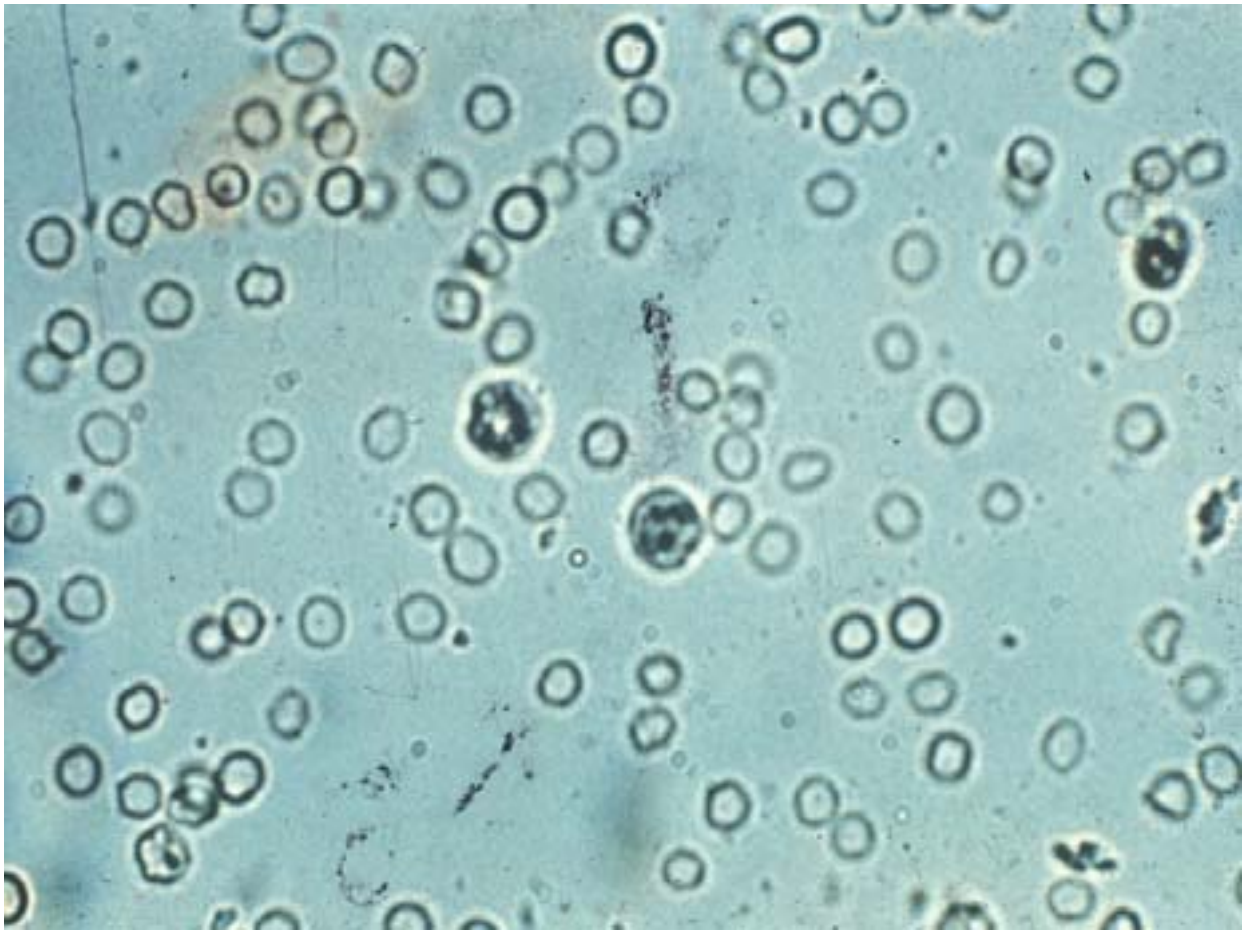
How to approach hematuria

- **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

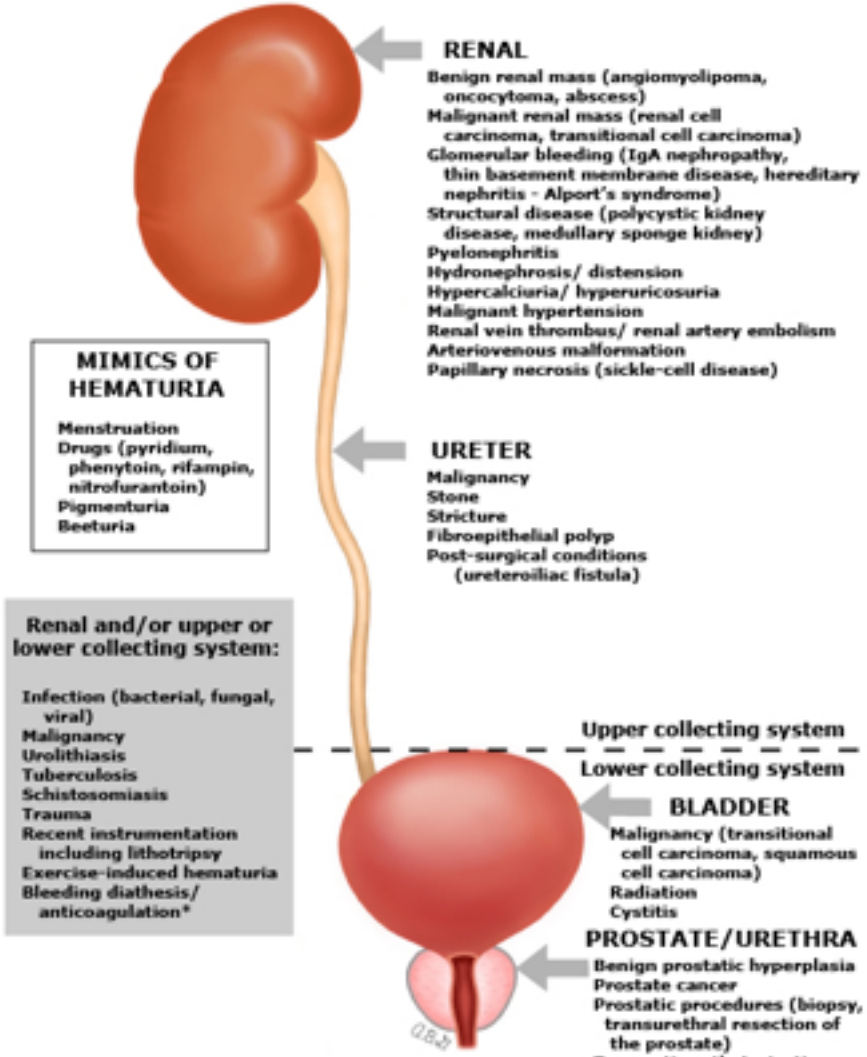
Not every dark urine means Hematuria:

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:

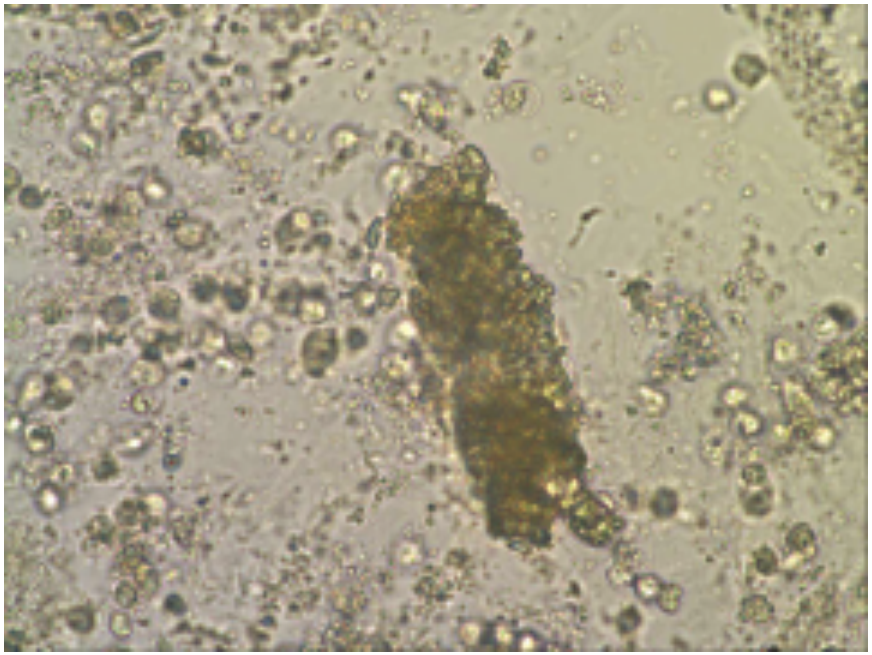
- Stones
- Tumors
- Infections
- Trauma

- 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: Glomerular vs Extraglomerular

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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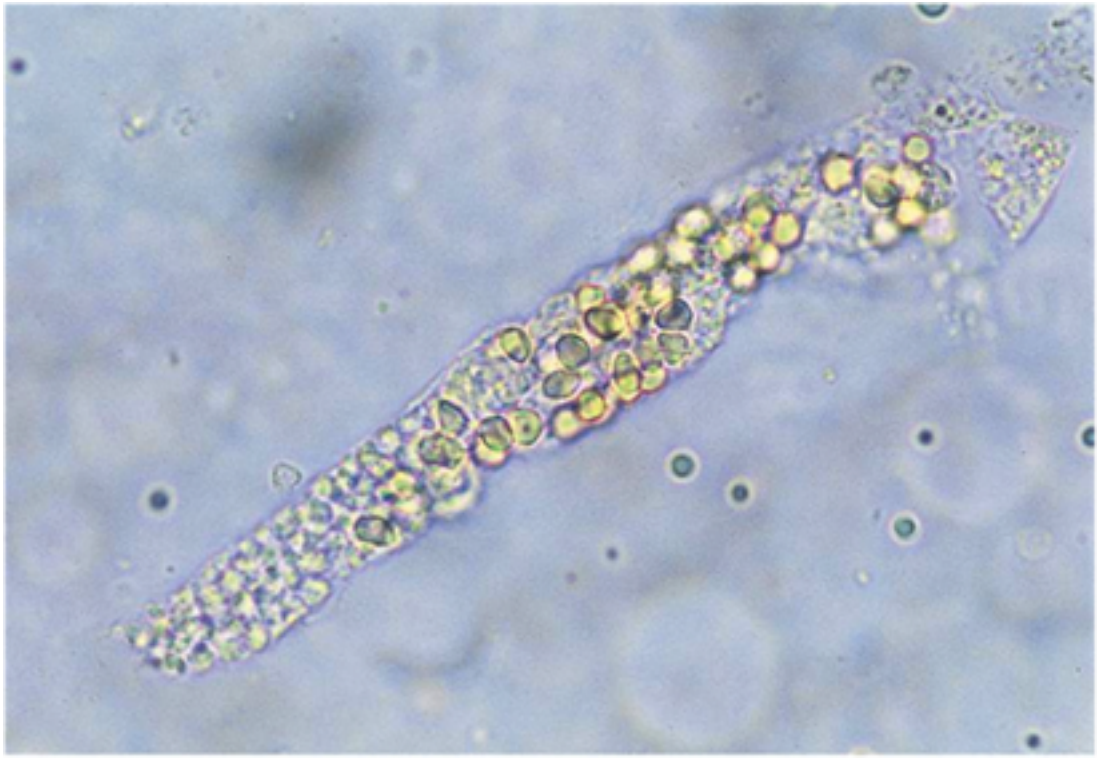
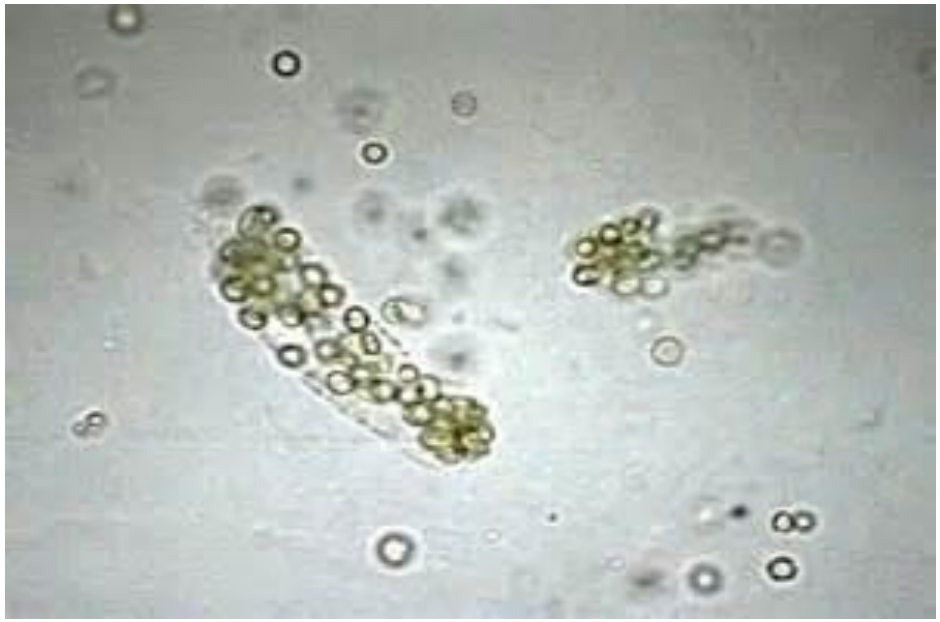
RBC Cast



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 4days after URTI symptoms) while in post infectious is usually 1 week– 2weeks.

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 syndome

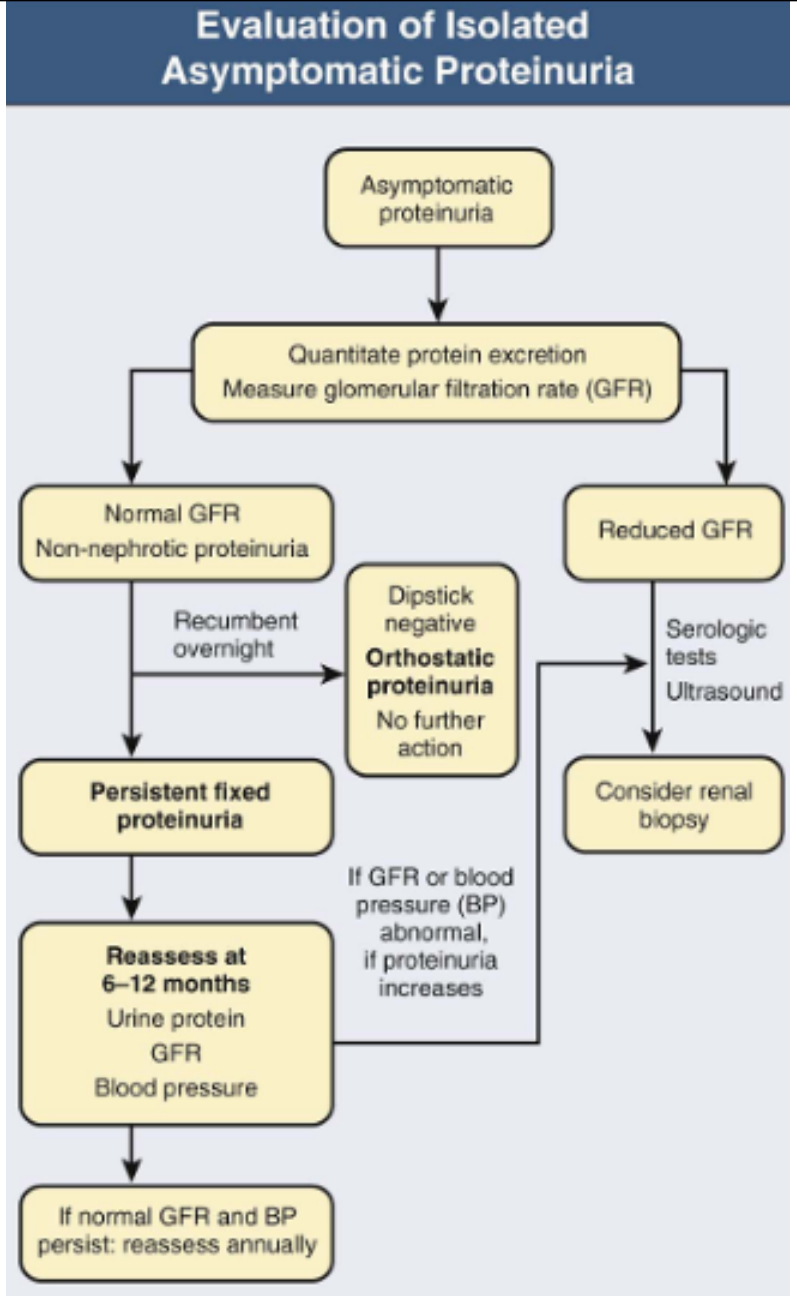
- **Indication for biopsy in microscopic hematuria:**

renal impairment or

Presence of proteinuria > 1 g/day or

HTN

Evaluation of Isolated Asymptomatic Proteinuria



Key points

- Hematuria can be benign but might indicate glomerular-based disease or urological malignancy
- Age, gender, smoking, family Hx, PHx are important factors to be considered upon approaching glomerulonephritis
- Glomerulonephritis can be primary or secondary. In Secondary causes treating the underlying disease would improve GN in most of the cases. Screening for secondary causes is worthy in adults
- Nephrotic range proteinuria indicates underlying glomerular-based disease in most of the cases

Thank You

For feedback and further questions:

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